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The Asilomar Conference: A Case Study in Risk Mitigation

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Introduction

The Asilomar Conference on Recombinant DNA Molecules was an international meeting held in February 1975, in which a group mostly composed of scientists designed safety guidelines for conducting recombinant DNA research.[1] The conference was to address rising concerns around recombinant DNA technology, including evaluating an existing moratorium on some recombinant DNA research. Recombinant DNA technology was only a few years old at the time,[2] and progressing quickly.[3] The primary apparent risk resulting from the research was production of new pathogenic organisms, which would endanger the public and researchers. Carcinogenic gut bacteria were a prominent example.[4] The conference ended the moratorium and produced safety recommendations that were adopted by the National Institutes of Health, along with similar bodies internationally.[5]

This document answers three questions. First, *how similar is the Asilomar Conference to contemporary efforts to prepare for major artificial intelligence (AI) impacts?* In particular, did the Asilomar conference involve efforts to respond to a novel and complex risk expected many years in the future? Was support from the scientific community scarce? Were the actions that were taken as part of the Asilomar conference narrowly directed at averting the foreseen problem rather than being broadly useful regardless of whether the danger transpired? Were those actions taken with little feedback about whether they were improving the problem?

We chose to focus on these characteristics because they arguably distinguish AI safety preparations as particularly unlikely to succeed.[6] We are interested in learning whether these characteristics are really so rare in successful endeavors. Part I is a compilation of evidence addressing the question of whether the Asilomar Conference has these characteristics—in other words, how relevantly similar it is to efforts to avert impacts from AI.

For an analogous case such as Asilomar to help us judge the promise of contemporary risk reduction efforts, we need to know how successful the past case was. To this end, Part II will ask, *was the Asilomar conference successful?* We are interested in several different metrics of success, such as whether the predictions that prompted action were correct, whether they were reasonable predictions given what was known, whether the plan was good in expectation, whether it helped, and whether it would have helped if the risks had turned out to be as expected. Evaluating several of these will give us a richer understanding of the conference's success.

Third, we will ask, *what else might contemporary risk reduction efforts learn from the Asilomar conference?* For instance, how easy was it for scientists to delay research? How concrete was the problem before people became concerned about it? Was there any

earlier research before the problem arose, that contributed to the quality of the response? Part III details features of the conference and surrounding events that seem especially relevant to efforts to prepare for contemporary risks, especially those from AI.

Summary of Events

In 1972, Paul Berg and his colleagues at Stanford constructed a recombinant DNA molecule, combining DNA from the cancer causing Simian Virus 40 with DNA from the ubiquitous gut bacteria *E. coli*.[7] The natural next step in the experiment was to insert the new DNA back into *E. coli*, but another scientist, Bob Pollack, expressed concerns.[8] After discussing potential hazards with colleagues and friends, Berg decided not to continue the experiments.[9] This decision was well known.

At the 1973 Gordon Research Conference on Nucleic Acids, Herbert Boyer[10] described methods that radically improved the ease of recombinant DNA production and made it possible to combine DNA from any two organisms. According to Maxine Singer, an organizer of the conference, "the range of previously intractable questions about genetic expression that could be answered by utilizing the new method was enormous and widely perceived."[11] This produced much excitement, but also immediately led to concerns.[12] Gordon Conference attendees discussed hazards informally, then voted to write to the President of the National Academy of Sciences (NAS) asking that a group be set up to examine the risks. Singer and conference co-chair Dieter Söll, wrote this letter[13] and made it public. The NAS responded by forming a committee, chaired by Paul Berg, to examine the risks and benefits of recombinant DNA technology.

In July 1974 the Berg committee called for a voluntary moratorium on a class of recombinant DNA experiments.[14] While there was some disagreement about this action, the moratorium was universally adhered to. The moratorium was, in part, intended to give time for a conference that would assess the risks. This was the Asilomar Conference on Recombinant DNA Molecules.

The conference was held in 1975 and attracted scientists from around the world, as well as lawyers, the press, and government officials.[15] The conference was responsible for helping to determine whether the moratorium should be lifted, and if so, how the science could safely proceed. The organizing committee was responsible for filing a report to the National Academy of Sciences (NAS) on the progress of the conference, including recommendations.[16] The conference ultimately recommended that the science continue and offered guidelines under which they thought it could do so safely.[17]

The resulting guidelines were adopted by the National Institutes of Health as a condition for funding, and were adhered to by others voluntarily.[18] Over the years, the guidelines have become less restrictive as new information has emerged.[19] [20] Now (in 2015) they place few constraints on recombinant DNA research.

1. Part I: How Similar Was Asilomar to Current AI Safety Preparations?

We are interested in determining whether present efforts to address AI safety challenges are unrealistically ambitious. Thus we are most interested in whether the Asilomar conference was similar on the characteristics that make AI safety efforts look ambitious. If it is, then it can inform our optimism on AI efforts as well as suggest factors that may contribute to success.

We spoke with Alexander Berger of GiveWell about the characteristics of AI safety preparation efforts that make such efforts seem unpromising to him[21] and chose to focus on the following:

- **Novelty:** the event predicted is relatively unlike problems that have been seen before.
- **Low scientific concern:** highly credentialed and credible scientists are not very concerned.
- **Complex prediction:** the prediction is relatively complicated, e.g., more complex than the basic physical dynamics of climate change.
- **Specificity of solution:** the policy response is narrowly useful for the predicted issue (e.g., it does not contribute valuable basic research, or general capacity building that might be worthwhile in the absence of the problem).
- **Low feedback:** the response is a one-shot effort rather than an iterative process with frequent feedback about success.
- **Early action:** an event is predicted and the beginnings of action take place fifteen years or more before the event is predicted to occur.

The rest of Part I will assess the extent to which the Asilomar conference has these characteristics.

1.1. Novelty

Recombinant DNA technology prompted multiple concerns. We discuss these separately because the novelty of different problems need not coincide.

1.1.1. Concerns about Scientific Biohazards

The primary concerns that prompted action by scientists were biological risks to lab personnel, the public and the environment.[22] Issues discussed at the time included:[23]

- Carcinogenic gut bacteria (*E. coli*)[24]

- *E. coli* with cellulose degrading genes
- Plant pathogens
- Problematic proteins in *E. coli*
- Immunological hazards
- Perturbation of biochemical pathways[25]
- Drug resistant microbes[26]

These risks were in some ways similar to pre-existing biological risks, but the novelty of being man-made implied some substantial differences from past problems.

The risks were novel in the narrow sense that the specific organisms being created would be new. This makes the problems they bring likely to be somewhat novel, but probably not all that different from those produced by existing dangerous organisms. A new disease is probably still best handled with some combination of protective gloves, quarantine procedures, hospital admissions, and so on.

Beyond the specific organisms being novel, the abrupt appearance of an organism with no very close relatives in the environment is unusual, and might be expected to cause unusual disruption. This is not entirely novel however: a similar situation occurs when species are introduced from one continent to another.

Another source of novelty is in the distribution of organisms created. A new man-made process might be expected to create a different distribution of organisms from the one produced by nature. We know nature produces many benign organisms and very few extremely dangerous organisms. However a new source of organisms can't be relied upon to follow the same pattern. There would be several reasons to expect recombinant DNA techniques to produce an unnatural array of organisms. The new organisms were produced from a narrow range of pre-existing organisms (e.g., cancer viruses and *E. coli*); they were produced by unusual physical mechanisms; they were intentional rather than naturally selected; and the new methods allowed transfer of genes between organisms that could not naturally exchange them.

On the other hand, scientists already had experience with mutant organisms, which they found to be unusually feeble.[27] It also turns out that in nature, DNA often moves between different organisms,[28] making man-made recombinants less novel (though this was not known at the time of Asilomar). Furthermore, even if naturally produced organisms were rarely dangerous, science had seen enough of them to come across some fairly destructive instances. So even if the distribution of organisms produced was different, the problems do not appear to have been terribly novel.

This does not imply that humanity was adequately equipped to deal with the problems. While science had seen plenty of dangerous organisms before recombinant DNA,

similar hazards from natural organisms in the lab had hardly been dealt with in 1975.[29] The Asilomar Conference was actually the second Asilomar conference—the first one was around a year and a half earlier and was dedicated to risks from natural tumor viruses.[30] So while it appears that the practical problems to be addressed in safely manipulating recombinant organisms were probably not that novel, the solutions were not well worked out.[31]

In summary, the risks from recombinant DNA were novel in that they involved creating new organisms, creating organisms from a new distribution, and potentially creating organisms that were more different from their predecessors than usual. On the other hand, mutants and introduced species pose somewhat similar risks; DNA naturally moves between organisms in nature; and the practical problems of dealing with species of unknown danger are much like the problems of dealing with species known to be dangerous, which was not novel, though it was also not well resolved.

1.1.2. Social and Military Concerns

While the scientists involved were largely focused on biohazards, some people were also concerned about social risks, such as those arising from the genetic engineering of humans.[32] Others were concerned about potential for destructive military applications.[33] Both of these issues were explicitly excluded from the Asilomar conference.[34] Nonetheless, worries about these issues may have fuelled the broad concern that helped motivate the conference and related activities.

Human genetic engineering is historically novel in some important senses. For instance, it could have more different, sudden and extreme consequences for the composition of the human population than prior events. However the implications of genetic engineering that people were concerned about were generally not new. They included issues like loss of reproductive freedoms,[35] eugenics, changing social norms around procreation, and intelligence being associated with genetics,[36] issues that arise in many contexts.

Biological warfare based on recombinant DNA would be similar to precursor biological warfare, but could have been novel in important ways. You might expect that organisms intentionally created to be destructive would (at least after some years of research) be more dangerous than those merely selected for destructiveness from a pool which evolved to survive. There is often evolutionary reason for natural pathogens to avoid extreme deadliness, because the death of a host is disadvantageous. You might also expect humans to have fewer defenses to new organisms. In practice, however, recombinant DNA does not appear to have made biological warfare substantially more dangerous. David Baltimore, an organizer of the Asilomar Conference, says that even now natural organisms are more promising as bioweapons than artificial organisms are.[37]

Summary

The risks that prompted the Asilomar conference were novel in important ways. Nonetheless, historical precedents exist for many characteristics, such as the feared consequences and the policy responses under consideration. In this way, recombinant DNA risk is probably less novel than AI risk, which also involves unprecedented historic developments, but where the commonly anticipated consequences include unfamiliar scenarios—such as one hundred percent unemployment or governance by non-humans—and where the appropriate policies are not obviously among our repertoire.

1.2. Scientific Interest

Our question here is how many highly credentialed scientists were concerned about the risk from recombinant DNA. According to Krimsky, the list of signatories of the moratorium letter "reads like a Who's Who in molecular biology" (Krimsky 1982, 84). The Asilomar conference was organized by Paul Berg, David Baltimore, Sydney Brenner, Richard Roblin and Maxine Singer.[38] The first three of these became Nobel Prize winners: Baltimore in 1975, Berg in 1980, and Brenner in 2002.[39] So it seems the primary actors were highly respected scientists in the area at the time.

There was controversy, however. Some scientists disagreed with the concerns.[40] James Watson (another Nobel laureate; co-discoverer of the structure of DNA) signed the moratorium letter, but soon firmly changed his mind.[41] Cohen (another Nobel laureate) and Boyer have criticized the process.[42] Watson, Cohen and (Nobel laureate) Joshua Lederberg voted against the conference organizers' document at the end of the conference.[43]

Summary

In sum, many respected scientists were concerned, and some spearheaded the action, though the issue was still controversial among respected scientists. This probably makes concerns about recombinant DNA more srtongly supported by well-credentialed practitioners of the relevant field than AI risk. AI researchers are rarely the people leading action on AI risk, and public positions on the issue appear to be more mixed among experts.

1.3. Complexity of Risk

Was recombinant DNA unusually easy to deal with because the risks were especially straightforward to evaluate? The evidence is against this.

The risks that concerned scientists did not arise from any straightforward extrapolation of past events, and the debate involved complex considerations. In the absence of

clear reference classes to generalize from or standard methods to evaluate such risks, a variety of arguments were proposed, and assessment relied on intuition and speculation.

Some arguments drew on high-level reasoning about natural selection (e.g., Bernard Davis reasoned that new recombinant organisms should be selectively disadvantageous, and thus do not pose a risk to the public[44]); others involved reasoning through scenarios (e.g., "what would happen if we changed gut bacteria globally?"[45]); and others tried to understand the mechanisms that might create dangerous organisms.[46]

Assessing the risks often involved expertise from several disciplines, e.g., virology, bacteriology, and infectious disease epidemiology,[47] which the participants probably did not have.[48] Scientists involved disagreed over the level of risk and frequently called the concerns "speculative" or lamented a lack of evidence.[49]

Summary

The risks associated with recombinant DNA are not obviously simpler or more complex to evaluate than those associated with AI risk. Both conversations fall under the "speculative" heading and feature relatively novel and untested reasoning about a range of domains outside the usual areas of expertise of the interested parties.

1.4. Specificity of Solution

Were the safety precautions introduced around Asilomar useful mainly in avoiding the anticipated problem, or would they have been a good idea anyway? We want to know this because we might expect solutions that are generally useful—such as basic research—to be done more often and ultimately be more valuable than those whose value is tied closely to a specific problem, as a lot of work on AI risk is.

Some precautions we can consider include:

- The moratorium
- The conference
- The set of guidelines for laboratory safety, produced by the conference and adopted by the NIH
- The creation of the Recombinant DNA Advisory Committee (RAC)
- Biological containment methods included in the guidelines
- Physical containment methods included in the guidelines

The value of these solutions appear to be relatively closely tied to the specific problem, especially the moratorium. The moratorium delayed three types of experiments with recombinant DNA and slowed down promising research, so is unlikely to have contributed to the science. It is unclear what other ends it might have contributed to.

The conference itself was designed to discuss the promise of the technology as well as the risks, in part because the organizers thought the scientists would become bored with a discussion of the risks alone.[50] So the conference likely had some broader benefits in terms of scientific progress, though it was presumably less beneficial for those goals than spending the same resources on something more directly useful, such as a straightforward conference on the science.

The physical containment solutions are an exception: regardless of the risks associated with recombinant DNA, they had broader value. This probably could have been anticipated at the time. Paul Berg and George Church cite Asilomar's encouragement of physical safety precautions as one of its most important consequences in retrospect.[51] Prior to any concerns about the safety of recombinant DNA, lack of concern for laboratory safety had already become an issue as the rapid entry of scientists from other fields was occurring in the absence of established safety norms.[52]

Summary

The solutions to the problem of recombinant DNA were mostly not useful unless the risk was real, with the major exception of improved laboratory safety procedures. It is unclear whether the value of these improvements was anticipated. It is hard to compare recombinant DNA solutions to efforts to avert AI risks on this feature. AI risk prevention efforts are broad. In the absence of AI risk, some would appear to be fairly valuable on other grounds (e.g. basic decision theory research) and some would not (e.g. specific containment strategies).

1.5. Feedback

Problems are easier to resolve when there is feedback. That is, when you have many opportunities to learn from your past performance on the problem and you can adjust your efforts accordingly. Problems allow less feedback if they have a one-off character, or if a mistake is so costly that failing several times is too terrible to be borne.

Did dealing with risk from recombinant DNA allow for much feedback? The kinds of hazards which concerned scientists were often one-off in the sense that once a given pathogen has been released into the world, this can't be easily undone.[53] At a larger scale, there would be opportunities to learn from such errors with future pathogens, assuming your earlier error didn't become a devastating pandemic. However, each such mistake could be overwhelmingly costly, if not from the perspective of society, at least for individual labs facing the legal and social costs of releasing a dangerous pathogen.[54] The existence of the moratorium and conference suggests wide support for dealing with problems before they happen over a more experimental approach.

Even if a problem cannot be repeatedly faced, there can still be good feedback in dealing with it. This is true if there is an intermediate parameter that you know is tied to the problem, and which you can repeatedly interact with. For instance, we might be concerned about extreme climate change halting the ocean current that keeps Europe warm. If we are confident that the amount of CO_2 in the atmosphere is closely tied to the probability of this disaster, then we might have good feedback about our probabilistic effects on the ocean currents via feedback about the effects of our actions on CO_2 levels—even if the currents never slow. It is unclear to what extent this sort of intermediate feedback would have been available to scientists working on recombinant DNA at the time of Asilomar. No particularly strong examples present themselves.

Summary

Recombinant DNA risks are similar to AI risks in being potentially too terrible to deal with through learning from mistakes. This still allows for feedback on the success of intermediate actions, such as the production of relevant research results. However, neither case seems to feature particularly strong examples of intermediate feedback like this, and the extent of such feedback seems hard to compare in the two cases.

1.6. Early Action

Here we are interested in whether the Asilomar conference intended to prepare for specific risks fifteen years or more prior to when those risks were anticipated, as present AI risk efforts mostly do. At first glance, the answer appears to be no, since the conference was prompted by risks from experiments that already were on the agenda. However, since the conference dealt with a large class of risks, it may easily have dealt with some longer-term risks as well as the shorter-term risks that triggered it. Nonetheless, no evidence is forthcoming of such longer-term concerns, and there are several lines of evidence suggesting that there were none, at least in any non-trivial sense. The conference probably did not intend to deal with non-imminent risks.

One line of evidence is that conference organizers believe that longer-term risks received little if any attention. David Baltimore says the conference attendees didn't spend a lot of time considering dangers in the field that wouldn't arise for five years or more since their hands were full with what was already possible.[55] Paul Berg recalls considerations of long-term implications, but these are benefits rather than risks.[56] Further weak supporting evidence comes from records of key conference organizers expressing distaste for dealing with non-imminent risks in general.[57]

The immediate risks were both pressing and difficult to address, so it would be somewhat surprising if people had taken extra steps to deal with more remote risks. The moratorium demonstrates that the immediate concerns were considered to be fairly se-

rious. Scientists had important experiments on hold.[58] [59] New techniques had unexpectedly made a huge range of recombinant DNA experiments possible and much easier than expected, so suddenly anyone who wanted to could produce risky organisms, potentially in large quantities.[60] Not only were the immediate risks pressing, but also they were hard to resolve. There was no clear basis for assessing risks or producing policies to avoid them.[61] It was unclear whether the moratorium would be respected, and the conference organizers believed the conference would fail to reach any consensus at all, until the end.[62] According to some, the conference was quite heated.[63]

Other experts agree that there was probably little attention given to long-term risks. George Church, Professor of Genetics at Harvard University, was not at the Asilomar Conference, but has been in the field since around that time. He does not think people at Asilomar were that concerned about risks decades hence.[64] Sheldon Krimsky, author of *Genetic Alchemy: The Social History of the Recombinant DNA Controversy*, complains that Asilomar did not attend to issues beyond experiments that the participants were interested in doing. He appears to be concerned about neglect of risks from further applications of the technology, rather than future science, but his criticism suggests neglect of both:

> ". . . it appears that when specific objectives were visualized at all, they were organized around assessing hazards of experiments that scientists were particularly interested in doing . . . to restrict the field of vision to those experiments in which scientists are currently interested takes no cognizance of commercial ventures or other possible non-academic uses or misuses of the technology. This fact emphasizes the limited scope of the Asilomar Conference." (Krimsky 1982, 109)

A further reason it would be surprising if Asilomar dealt with longer-term risks is that people commonly believed that the risks would likely lessen with time as more information was gathered. They recommended and expected that guidelines would be revisited often and expected (correctly)[65] that precautions would be relaxed over time.[66]

Other writing from the time also suggests a focus on short-term risks.[67] Writings from the conference sometimes mention non-imminent risks,[68] but they are probably not anticipated to be as much as fifteen years away.[69] The recommendations of the conference included four categories of safety precautions applicable to different experiments, as well as a class of experiments to be deferred due to their risks. It appears that all of these applied to experiments that were already feasible.[70]

Concerns were expressed about potentially longer-term problems at the time of Asilomar. However, these don't appear to have been closely connected with the conference. There is also no strong reason to suspect that large investment was made in resolving these longer-term problems. Some of these concerns were about the social implications

of gene technology developing in general.[71] This was largely among people outside of science.[72] Biowarfare was another frequent concern. [73] [74] These topics were intentionally excluded them from Asilomar,[75] though one of the working groups for the conference included a statement warning of military applications and recommending their ban by international treaty.[76] It is unclear how far in the future they anticipated this threat.

One weak reason to think the conference was meant to have long-term consequences is that it did have long-term consequences. The conference gave rise to guidelines that persist in some form decades later.[77] However, there is a difference between actions intended to help with short-term risks—which will continue to address those risks for a long time—and actions intended to help with risks that won't arise for some time. The Asilomar Conference is probably a good instance of the former, but not the latter.

Summary

There is little evidence that actions were taken at Asilomar with the intention of averting problems predicted more than fifteen years hence. There are also several lines of weak evidence suggesting this was not so. While the Asilomar conference's influence has lasted several decades, and was probably intended to do so, it does not appear that any preparations were made specifically to guard against any risk that wouldn't happen for so long.

1.7. Conclusion

We were interested in whether the Asilomar Conference involved early action, novel risks, complex predictions, low levels of scientific concern, specific solutions, and low levels of feedback. We found that the conference was indeed conceived to prevent relatively novel risks from a new technology, though arguably less novel risks than those from AI. The risk was complex to reason about, and feedback was hard to get safely. The response to the risk was fairly directed, though it also hit the broader useful target of general lab safety. In these ways, the Asilomar conference is relatively analogous with current AI safety challenges. On the other hand, unlike in the AI case, many highly credentialed scientists were concerned and contributed in large part to the efforts to address safety (though some such scientists were also not concerned). Asilomar falls furthest from being analogous to present AI safety efforts in that it doesn't appear to have involved attempts to address risks more than fifteen years in the future. The risks it addressed were overwhelmingly immediate.

2. Part II: How Successful Was Asilomar?

2.1. Introduction

We are interested in several different metrics of success. Were the predictions correct? Were the actions useful? Were the predictions reasonable given the available information? Had the predictions been correct, would the actions have been useful? Investigating these and other such questions will give us a better idea of how and why Asilomar had whatever success it did. For instance, if Asilomar was not helpful overall, we would like to know whether this was due to bad predictions, inappropriate actions, or something else. If it was helpful, we are interested in whether this was due to excellent forecasting and planning or via some fortuitous side effect.

2.2. Success of Predictions

2.2.1. Were the Problems Real?

It is widely agreed that recombinant DNA research turned out to be fairly safe.[78] While dangerous organisms may be created and released accidentally, this is very unlikely.[79] Intentional hazards are a different story;[80] however, they were also not a focus of the conference. In this sense, the predictions of danger were unsuccessful.

However, note that the scientists advocating caution didn't necessarily think that the odds of recombinant DNA turning out to be dangerous were greater than 50%.[81] Since large low-probability catastrophes can also justify action, it is not inconsistent to argue that a research program is unlikely to be harmful, but that we should nonetheless prepare for the worst. Scientists should not be penalized for advocating caution per se. If they were fairly confident that safety measures would turn out to be unnecessary, then their predictions were fairly good. Nonetheless, they were less good than the predictions of people who considered the risk even smaller.

2.2.2. Were the Risks Real?

Though the problems were not real, scientists may have been correct to be concerned while they had less information. It appears to be disputed among scientists now whether or not scientists in 1975 should have known better.[82] However, it's not obvious that they are asking quite the same question (should scientists have reasoned differently using the information they had? Should they have discovered more scientific facts by then?). The opinions of modern scientists also shouldn't be relied upon too much because even if modern scientists did agree that earlier scientists were reasonable or unreasonable in their estimates, it's not clear that the rationality of modern scientists should be considered any more reliable than that of their colleagues (or past selves) a mere four decades earlier. What science has accumulated in that time is arguably almost entirely scientific

discoveries, not general reasoning abilities. Besides contemporary scientists' views, we have no strong evidence on how reasonable the past concerns were. We know of neither strong evidence that we were close to danger, nor strong arguments for safety that should have been seen in advance. Thus, the reality of the risk remains ambiguous. It seems a majority of the relevant scientists in the past thought the concern was worth acting on, so we might tentatively suppose they were right.

2.3. Success of Actions

We could consider arbitrarily many distinct actions that were associated with the conference. We will focus on a few key ones at different levels of granularity:

- The moratorium
- The conference
- The call to develop safer hosts[83]
- The creation of the Recombinant DNA Advisory Committee (RAC) at the NIH[84]
- The creation and implementation of safety guidelines

2.3.1. Success at Intermediate Goals

Although the conference organizers were not confident that they could pull it off, it appears that people universally heeded the moratorium.[85] [86] The conference successfully gathered scientists from around the world[87] and came to enough agreement to make recommendations. These presumably fulfilled intermediate goals of ending the moratorium and avoided giving up control of the regulation of the science (see Section 3.3.6). The safer hosts were developed;[88] however, it turns out they were not as safe as they seemed.[89] The RAC and its guidelines have remained in existence for many years.[90] The guidelines have been updated and weakened as new evidence came to light, as was hoped.[91] The guidelines were widely followed,[92] even by industry, who were not bound by them in any official way.[93] In sum, the major actions taken around Asilomar were largely effective at their immediate goals. This is perhaps to be expected, as these actions were chosen after the fact for being important.

2.3.2. Success at Ultimate Goals

The Asilomar conference and surrounding activities failed to avert new hazards from recombinant DNA because these turned out not to exist. This might be considered to be success or failure depending on definitions.

2.3.3. Counterfactual Success at Ultimate Goals

Had the dangers been real, it is hard to know whether the precautions would have substantially reduced the risk.[94] Broadly, stopping experiments and then thinking carefully about safety is surely helpful. However, would the specific process carried out at Asilomar have substantially prevented an otherwise imminent disaster?

Let us consider two scenarios separately. In the first, everything looks as it did to the scientists. However, recombinant DNA research turns out to be toward the more dangerous end of what was considered plausible. Here the question is whether the exact precautions the scientists took would have averted such dangers. In the second scenario we consider, not only are there great dangers, but the risks appear to be much worse to the scientists when they consider them. Here the question is whether the scientists' general procedure could have responded appropriately to observing that the dangers were great.

Let us begin with the first scenario and question. Had recombinant DNA research turned out to be quite dangerous, how much would the precautions the scientists took—a set of guidelines for lab safety—have helped? At least somewhat, it seems. The containment strategies and rules developed at the time have apparently been useful for lab safety independent of recombinant DNA, so they would likely also reduce risks from recombinant DNA organisms. It is unclear by how much, however. Also note that the biological containment developed at the time—*E. coli* that was purportedly unable to survive in the wild—was less crippled than it was believed to be, so the risk reduction would have been somewhat less than expected.[95]

If these precautions correspond to moderate reductions in the probability of dangerous organisms escaping, it matters what kind of problem we think we are dealing with. Suppose organisms escape from the lab about once a month, and elaborate safety procedures can reduce the probability of an outbreak by half. Then, if the organisms merely give people a brief stomach ache, the problem has been halved. However, if the organism immediately decimates human civilization, such precautions would only buy a month for the world, scarcely reducing the problem at all.

Whether the safety precautions made at Asilomar would have reduced the probability of release of dangerous organisms enough to substantially avert extreme risks is unclear. It might become clear if we investigated the frequency of harmless organisms escaping in the wake of Asilomar, but that is outside the scope of this project. We might also trust the scientists who decided to continue that their procedures were enough to handle this case. In sum, the procedures developed by Asilomar probably would have helped somewhat in cases of extreme danger, but it is unclear whether this help would have made a substantial difference to the risk.

Now let us consider what would have happened if the problem had looked much worse to the scientists. Could they have arranged more extreme safety measures? Could they have extended the moratorium rather than ending it, had the science looked too dangerous to continue?

The guidelines produced at Asilomar contained several levels of safety precautions for experiments carrying different levels of risk, including a category of experiments that should not be done at all. This means that for many experiments, had they appeared more dangerous yet still worthwhile, they could plausibly have been moved up into a higher risk category. It also means there were some experiments already for which the scientists could not create adequate safety measures. These facts suggest that the scientists could have dealt with many of the experiments being more dangerous (at least in some ways) by moving those experiments to higher risk classes, but that they would not have easily been able to create precautions for higher risk categories than those they already had.

What if the experiments had—on closer consideration—appeared to be too dangerous to do at all? Could the group of scientists have paused the field indefinitely?

The guidelines did successfully proscribe a small number of particularly dangerous experiments. This and the successful moratorium suggest that research could have been impeded further for the sake of safety. However, a complete halt to research would be a vast sacrifice, so these lesser successes are probably not very informative.

Some suggestion about how the scientists would have responded to a more dire assessment of the situation comes from examining the nature of their decision processes. For instance, if it appeared that the decisions reflected political compromises to a large extent, we might expect precautions to be less well suited to problems than they would be if they were directed solely to that end. Such observations are noisy indicators, but are nonetheless worth considering.

Section 3.2.4 discusses some purported weak points in the Asilomar decision making process. Two of these features that seem likely to stand in the way of efforts to close down a large swathe of dangerous research are the strong involvement of values other than public welfare—such as the desires to avoid regulation and continue with experiments[96] [97] and the apparently common moral sense that science ought not to be constrained.[98] Had the experiments appeared likely to be dangerous after some consideration, but had there been no strong evidence of this, it does not seem obvious whether forces for the continuation of science (such as the two just mentioned) would have been overcome by a common subjective sense of moderate public risk.

2.3.4. Other Consequences

The value of Asilomar *ex post* depends in part on its side effects. This section outlines a few important ones.

General Lab Safety

One important consequence of the Asilomar conference was that it improved general attention to safety in labs.[99] [100] This had been at a low point because fast progress had attracted scientists from other fields who did not have backgrounds in handling microorganisms. Their procedures for doing so were shocking to more experienced scientists. Asilomar forced safety education upon these researchers.

Redirecting Attention from Natural Bioweapons

Baltimore says concern about bioweapons using recombinant DNA probably had the effect of lessening concern for natural bioweapons, though natural bioweapons are likely still more effective.[101]

Public Relations

According to Berg, the openness of the Asilomar process and apparent virtue of scientists willing to draw attention to dangers in their own research, hold a moratorium, and accept strict guidelines, got the scientists a lot of public trust that they would not have had if the issue had been brought up against them.[102] Nonetheless, there has been plenty of criticism of the process and the scientists,[103] and participants had mixed feelings about the value of the foray into public engagement.[104]

Avoiding Regulation

The guidelines that came out of Asilomar were not regulations, but merely NIH recommendations that were required for funding.[105] Commercial organizations also followed the guidelines voluntarily. There was substantial concern at the time that without the scientists acting to regulate themselves, the government would regulate them. While the guidelines would have been hard to ignore, they had at least two potential merits over regulations from the perspective of the scientists.[106] They were designed by the scientists themselves and so were deemed more appropriate and well informed. They were also flexible, relaxing quickly as risks subsided. There were never any other federal regulations brought in to control the issue, though the Cambridge Local Council had its own ban on research and then formed an experimental review board comprised mostly of non-scientists to oversee.[107]

Influence as a Model for Setting Science Policy

The Asilomar Conference has become a well-known model for science policy making.[108] For instance, an Asilomar-like process was attempted in stem-cell research, but was apparently unsuccessful because the controversial issues there are not scientific ones.[109]

2.4. Conclusion

Asilomar was unsuccessful in the sense that it probably did not avert the dangers it set out to avert: these dangers appear to have been close to non-existent. Whether scientists should have known better with the information they had is disagreed upon. The actions involved successfully brought about the intended short-term consequences. It is unclear how well the actions would have averted the dangers had they existed. It seems likely that the improved laboratory safety would have helped and that disabled hosts would have helped—though less than believed at the time. Probably the scientists could have provided greater precautions had the dangers appeared somewhat greater to them. Whether the conference would have chosen to halt a substantial fraction of science in the counterfactual case where the science appeared seriously risky is unclear.

The conference created value in terms of general lab safety practices. It was also valuable from the scientists' perspectives in averting regulation and maintaining good terms with the public. Whether those effects are positive for society as a whole depends on whether it is best for the scientists or the government to regulate such scientific activities. The conference probably produced some disvalue by diverting concern away from natural bioweapons, but the scale of this is unclear.

3. Part III: What Can We Learn from Asilomar?

3.1. Introduction

We are looking at the Asilomar Conference in the hope of learning something about similar efforts in the future, such as those directed at AI safety. What might we hope to learn, and how? One obvious thing to learn is whether such efforts tend to be successful. We looked at that in the last section.

We might also learn about features of the world that we think are persistent and important in both cases, but that we don't know the values of. For instance, how imminent does a risk have to be before scientists are likely to act on it? Or, how well does social pressure enforce costly rules? We can add only one data point from this case to those questions, but one data point may be valuable when we have few. We are most interested in features such as these if they are likely to be persistent because what we learn might apply to future cases.

We might also learn about the features of the recombinant DNA controversy that seemed especially important in shaping the outcome, but which we weren't necessarily aware might be relevant in future cases. For instance, it seems that the threat of government regulation was important, as was the cooperation of funding bodies in enforcing the safety guidelines. Knowing what mattered in the past may help future efforts. For instance, if we found that the support of high-profile scientists appeared to be important in the Asilomar case, this would suggest prioritizing collaborating with such scientists in future efforts.

Answering these kinds of questions requires making subjective judgments about complex situations based on scattered information. The judgments in this section are a combination of mine, and where possible those of more expert observers. This is the best I have to offer, but I cannot guarantee accuracy or relevance.

3.2. Relevant Features of the Situation

3.2.1. General Efficacy of Informal Social Mechanisms

How good are informal social mechanisms for maintaining safety in science? Asilomar offers a few data points on this question:

- Alarms were raised by scientists who had not been officially tasked with paying attention to such things.
- The moratorium was organized, and the conference was suggested by scientists with the help of journals and the National Academy of Sciences: more formal, but non-government parties.[110]
- The moratorium was universally observed, in spite of disagreements about its concerns and methods.[111]
- When Robert Pollack complained to Berg about the safety of Berg's proposed experiment prior to Asilomar, Berg (in spite of some annoyance and disbelief) spoke to colleagues and eventually resolved to put the experiment on hold.[112]
- Two of the people tasked with running working groups at the conference responded by writing to a network of acquaintances, seeking information about possible risks.[113]
- While corporations were never required to adhere to the guidelines, they apparently always did. This appears to be due to social pressure.[114]

In sum, informal social mechanisms played an overwhelming part in producing a pause in research and triggering further action. They also played a large part in allowing scientists to gather information about the risks and in enforcing compliance with the safety guidelines selected.

3.2.2. Concreteness of Risks When Taken Seriously

It is sometimes thought that people will fail to act on perceived risks if the risk they face is not very concrete. Concreteness is low if for instance the risk is understood only in abstract terms, if it isn't clear how it would physically manifest, if it feels speculative, if it is unlike things that are seen regularly, and if its probability is hard to estimate and may be very low.

Risks at the time of Asilomar often seem to have been considered both very improbable[115] [116] and hard to estimate.[117] [118] Risks were often referred to as speculative, hypothetical, or the like.[119]

On the other hand, the risks were concrete in the sense of being often very specific scenarios suspected to arise in the very near future if a person took some known physical actions that were available with current equipment. They were also concrete in the sense that at least one potentially dangerous recombinant organism had already been created.[120]

Depending on what aspects of concreteness one supposes to matter for enlivening concern, this may or may not be a counterexample.

3.2.3. Importance of Forethought

In many cases of response to risks, visible action to avert a threat doesn't seem to occur until the threat is imminent. However, this doesn't imply that early actions are not common or helpful—it could be that a particular large visible response is partly triggered and aided by less visible research and preparations that occurred earlier. For instance, a visible protest might be possible only because a smaller group organized it, because an even smaller group gathered the evidence needed to make a case for it, because one person convinced some friends that it was worth looking in to. It would be valuable to know in general whether larger scale action tends to stem from early smaller-scale efforts like this, or whether it tends to be more spontaneous. We are specifically interested in the value of any work that is closely directed at a problem ahead of time, rather than merely helpful some way (there is plenty of that for any problem, e.g., basic science).

In the case of Asilomar, moderate research reveals no evidence of recombinant DNA technology being foreseen many years ahead of time. The discovery of efficient methods was also quite a surprise; Baltimore did not know of anyone predicting such an event ahead of time, and he would have been likely to know about it if someone was.[121] It is unclear whether earlier thought helped with the technical or social challenges of Asilomar. It does seem that earlier attention to related ethical topics (such as genetic engineering ethics, and the role of scientists) helped to motivate concern.[122] However, this was not narrowly directed at the problem of recombinant DNA.

3.2.4. Quality of Decision-Making Process

The apparent quality of decision-making processes around Asilomar is important to investigate not only for the purpose of predicting future decision-making, but also in assessing the likely success of Asilomar had the threat been real (see Section 2.3.3). Instead of trying to list the myriad good qualities of the process, this section lists a few features that from the outside seem as though they might impede good decision-making. These are the features we will look at:

- Bias about risk of experiments
- Decisions controlled by small groups
- Philosophical views on science and risk
- Motives other than public well-being

Bias about the Risk of Experiments

Scientists appear to have systematically underestimated the apparent danger of their own experiments. Berg, Watson and Singer have all commented on the phenomenon of people believing their own experiments are safe while agreeing that others' may not be.[123] This could be explained by everyone having greater information about their own experiments and all experiments in fact being safe. However, if problems were only due to information discrepancies, we might imagine discussion among well-informed experts to resolve them quickly. It could still be that views about one's own experiments are the reasonable ones, and scientists have a bias toward excessive fear about others' experiments. However, Pollack—the scientist who first complained to Berg about his experiment—says he probably would have rationalized away his concerns if his own work might have been affected, and that he sees this behavior in others.[124] He describes a "shade" that comes over one's eyes when the problems affect one's own work. Berg also puts the phenomenon down to self-serving behavior.[125] On a possibly related note, top scientists became much more concerned when recombinant DNA became available to less skilled scientists.[126] This may be another instance of the same phenomenon, or it may be that less expert science is legitimately less safe, or both. In sum, scientists at Asilomar likely exhibited a bias toward nonchalance about their own experiments.

Decisions Controlled by Small Groups

Relatively small groups controlled decisions about recombinant DNA safety at two different levels; both were criticized. In general, decisions' being controlled by small groups is concerning because it suggests less incentive to make decisions that are broadly

beneficial and that take into account all relevant interests. It can also be evidence that someone was trying to avoid such incentives, having interests that were perhaps more narrowly defined.

One such narrowly defined group criticized for controlling decisions was the conference organizing committee. The conference organizers were tasked with producing recommendations based on inputs from the conference, not to produce recommendations that the conference-goers supported in particular.[127] In fact, the organizers intended to avoid a vote altogether, toward the end of the conference,[128] preferring instead to present the report as their own statement[129] [130] because they thought the conference would not reach consensus. When participants insisted on a vote, however, the conference overwhelmingly supported the recommendations.[131] Nonetheless, the statement was edited further after the vote, and some people were unhappy with the resulting dissimilarity.[132]

A worse complaint along these lines is raised by Henry Bourne, author of Paths to Innovation: Discovering Recombinant DNA, Oncogenes and Prions in one Medical School Over One Decade, on the basis of claims from Cohen and Boyer. He suggests that the atmosphere was so unpleasant at Asilomar that scientists were afraid to speak their minds or vote according to their true beliefs, and that even the apparent consensus was just due to this fear.[133] The organizing committee again was seen as controlling the output, but here they are further criticized for implicitly intimidating the larger group into supporting them.

On a larger scale, the whole conference—still a relatively small group of scientists—was criticized for making decisions that affect society, perhaps catastrophically, while declining much input from anyone else.[134] Participants chosen for their expertise on the topic are also incidentally those who benefit most from the research continuing, making it harder to distinguish a selection of relevant participants from a self-serving selection. There are accusations that the conference was kept mostly to those with a strong interest in the science continuing intentionally, evidenced by the exclusion of apparently relevant experts from outside the field (e.g., experts in health sciences or environmental sciences).[135]

While participants were largely chosen for involvement in the field, they were apparently at least to some extent selected to be concerned about the consequences.[136] Also, Asilomar did include a minority of people from outside science. These were speakers on law and ethics and many members of the media, who both participated in and reported on the conference.[137]

While the involvement of ill-motives and social pressure at either of the aforementioned levels is hard to assess, it seems clear that the organizing committee had authority to write the recommendations, with or without the support of the conference participants; and that the conference produced decisions without a large amount of input from

experts in other fields, or the public. Whether these features of the process were for the better or worse is debatable.

Philosophical Views on Science and Risk

Some conference participants felt that science should never be constrained, as a moral principle. It seems they were a minority, but a significant one.[138] This is a concerning feature of the decision-making process because such a norm of absolute scientific freedom would clearly cause great destruction by the lights of anyone with broader human values as soon as destructive scientific experiments became possible.

Related ideas include that science should proceed until someone demonstrates strongly that it should not, and that science should proceed except when this will cause very extreme destruction. These kinds of strong presumptions in favor of science seem to have been supported by some parties.[139] A view of "risk" as something that arises when demonstrated strongly, rather than potentially arising from ignorance, might explain some of these attitudes.[140]

Influence of Motives Other Than Public Wellbeing

Participants in the controversy had major things at stake other than public wellbeing, and these motives were not necessarily well aligned with public wellbeing. Many scientists were quite concerned with avoiding regulation from forces outside of the scientific community.[141] This was probably an impetus to self-regulate, but could have also encouraged giving the appearance of control over the situation beyond what was warranted by the facts. For example, one of the working groups disagreed with the conference recommendations, but the organizers would not have the minority view published at length alongside the main recommendations. Krimsky suggests this was to avoid giving a costly impression of disagreement, which might have prompted others to take control.[142]

Scientists also presumably cared a lot about the success of their careers and the progress of their science. The suggested experiments to defer in the moratorium were limited in part to increase the chance that others would accept them at all.[143] As well as such motives potentially distorting decisions away from being socially optimal, their existence might make it harder for people to trust one another[144] and for outsiders to trust the group of scientists.

There appear to have been further motives at play such as concern that scientists would be seen as covering up dangers[145] and opposing fear that talking to the public was risky.[146]

3.3. Factors that Seemed to Matter

In a case such as Asilomar, there are many social variables we could imagine influencing the outcome. It is interesting to see which ones appeared to matter in this case. This gives us some evidence about which factors might be important in other such cases. It also allows us to see how many of them we would have predicted to be important and to calibrate our expectations.

Below is a list of factors that have been cited as important by observers and participants in the Asilomar conference. Each one will be elaborated on later in this section.

- Cooperation of funding bodies (Section 3.3.1)
- Media presence (Section 3.3.2)
- Scientific nature of the issue (Section 3.3.3)
- The conference discussed science as well as risks (Section 3.3.4)
- Risk of legal liability (Section 3.3.5)
- Risk of future legislative control (Section 3.3.6)
- Commercial involvement (Section 3.3.7)
- Earlier conference (Section 3.3.8)
- Fiction (Section 3.3.9)
- Size of field (Section 3.3.10)
- Public intellectual trends (Section 3.3.11)

3.3.1. Cooperation of Funding Bodies

The Guidelines that came out of the Asilomar conference were mandatory for recipients of NIH funding, as well as funding from some other non-governmental bodies.[147] This was because the NIH was behind the RAC process and also provided the majority of funding. This arrangement with the funding bodies forced almost all biological researchers to follow the guidelines, so it was plausibly quite important. However, note that the moratorium was not enforced and also enjoyed universal compliance.[148]

3.3.2. Media Presence

Paul Berg thinks having a large minority of participants be from the media was an important contributor to the success of Asilomar.[149] It protected against it seeming like "a secretive meeting of scientists, coming out with some conclusion that everybody had to live with."

3.3.3. Scientific Nature of the Issue

Both Baltimore and Berg say the conference's success depended greatly on their restricting it to scientific issues,[150] [151] though Krimsky criticizes it for this.[152] According to Baltimore and Berg, this kind of conference is not well suited to areas in which the problems are not scientific, such as stem cell research.[153] [154] It could perhaps work for a borderline scientific question such as whether certain potentially dangerous research should be published.[155]

3.3.4. The Conference Discussed Science as well as Risks

Berg thinks a big contributor to the meeting's success was that it was organized to discuss the science as well as associated risks.[156] This kept people engaged, and made the attendees come prepared to talk about science.

3.3.5. Risk of Legal Liability

When law professor Roger Dworkin heard about the Asilomar conference, he wrote to Paul Berg and asked for a chance to speak at it.[157] He presented on the last night with other speakers from law and ethics. His topic was legal liability: what might happen to scientists and scientific institutions if anyone was harmed by recombinant DNA research.[158] The session overall and Dworkin's talk in particular was widely considered to have a strong effect on its listeners.[159] It scared them, and encouraged them to produce some recommendations the next day.

3.3.6. Risk of Future Legislative Control

It is often suggested (by both attendees and critics) that a large motive of the Asilomar Conference's attendees was to avoid regulation of their new technology by outsiders.[160] By being open about the problems and placing boundaries on their own work, they bought public trust and defused fears that might have prompted external parties to control them.[161]

3.3.7. Commercial Involvement

As early as the Asilomar conference, a few commercial organizations were involved in the discussions.[162] Paul Berg believes what later caused people to lose interest in banning recombinant DNA research (after US congress showed an interest in doing so) was the prospect of commercialization.[163] He says if there are concerns about research, it is important for publicly funded scientists to find common cause with the public before commercial interests become involved.[164] Martin Rees suspects a voluntary consensus

such as at Asilomar would be harder to achieve today, in part due to competition being more intense, in part as a result of commercial pressures.[165]

Many people thought the commercial sector would be a problem because the guidelines were not imposed on them, so they were at liberty to ignore them.[166] This was not the case: the commercial sector had strong incentives to follow the guidelines, and more money to invest in safety than academia had. Consequently, they heeded the guidelines more rigorously than most academic organizations.

3.3.8. Earlier Conference

The so-called Asilomar Conference was really the second Asilomar Conference. The first was a year and a half earlier and dealt with risks from working with tumor viruses.[167] This earlier conference probably aroused concerns that helped the second conference garner support.[168]

3.3.9. Fiction

The 1971 Michael Crichton film *The Andromeda Strain* is frequently claimed to have livened public fears regarding recombinant DNA.[169]

3.3.10. Size of Field

Martin Rees suspects the small size of the field in Asilomar days made voluntary consensus more achievable.[170]

3.3.11. Public Intellectual Trends

Krimsky argues that the political and cultural atmosphere in the time before Asilomar probably influenced people's behavior around the recombinant DNA controversy.[171] In particular, science and engineering had been the focus of political activism. The issues of contention related to the responsibility of scientists to the public good, especially after morally ambiguous scientific efforts to contribute to the Vietnam War. The role of scientists in creating atom bombs had also not been forgotten.[172] There were many activist groups composed of scientists. College campuses such as MIT were full of such drama. Janet Mertz, a graduate student from Paul Berg's lab whose discussion with Pollack prompted his reaction to Berg's (and Mertz's) experiment, expressed concerns about their work, apparently prompted by her recent time as a "middle-of-the-road-radical" at MIT.[173] David Baltimore also connects his actions on biohazards to the broader political climate.[174]

The public's view of science had been worsened by factors such as Rachel Carson's *Silent Spring* and the active environmental movement.[175] In 1973, there was already a

considerable bioethics literature, including on the topic of genetic engineering. Most scientists in the area would have come into contact with it.[176]

Conference organizers Singer and Roblin were in close contact with bioethicists. The bioethicist Leon Kass was a friend of Singer's, and she invited him and Paul Berg for dinner together in 1970.[177] Kass followed up after the meeting with an outline of their conversation and recommendations. One of these was to draw attention to ethical problems by writing to a journal. It is unclear whether this affected Singer's part in doing that at the Gordon conference three years later. Singer's own husband was a lawyer interested in bioethics and one of the law speakers at the Asilomar conference.[178] Roblin was interested in the impacts of genetic engineering on society and had published an essay in *Science* outlining a responsible course of action for human gene therapy.[179] He was also a member of the Council for Biology in Human Affairs.

3.4. Summary

Asilomar and the surrounding events can inform us on several questions relevant to dealing with other novel technological risks. They demonstrate that informal social mechanisms can work well to do some things, in at least one circumstance. They show that improbable, hard to assess, never observed risks can be taken fairly seriously by the academic community, at least in a case where they were also immediate and concrete in other senses. They provide an instance of a large reaction to risk with little apparent precursor in the form of earlier small-scale research efforts. We saw that the Asilomar process had several apparent flaws that might be expected to undermine its ability to react safely: the people involved were likely to be biased in favor of continuing research, a relatively small group had the power and inclination to ignore other interested parties in producing recommendations, motives unrelated to social welfare were important drivers of decisions, and philosophical views on science were sometimes troubling.

We also learned about factors that seemed to matter to the success of Asilomar, according to participants and observers. The support of funding bodies for the guidelines helped them to be taken seriously. The media presence at the conference helped maintain good relations with the public. The scientific nature of the issue made it possible to talk about it usefully and come to agreement. The non-risk component of the conference was probably important to keeping people interested. The threat of legal liability created fear and consequent willingness to produce guidelines restricting the science. The threat of future legislative control also provoked concern and motivated self-regulation. Commercial involvement was low initially, which may have helped with producing constraints on the field. Later when it was higher, it probably helped prevent further regulation. Commercial incentives to comply with the guidelines were important for bringing about the high compliance. The earlier Asilomar conference probably helped enliven

concerns motivating interest in the next one. The fictional Andromeda Strain also scared the public. The small size of the field made it easier to organize anything. Lastly, the social environment of activism, along with the recent scientific involvement in morally ambiguous matters, heightened consciousness of scientists' responsibilities to society, and probably encouraged action in those who acted.

4. Conclusion

In many regards, Asilomar seems closely analogous to present efforts to prepare for AI safety challenges: the threats were relatively novel, the predictions were not straightforward, the possibility for feedback was limited, and the response was quite directed at resolving the problem. However, many top scientists were concerned, and Asilomar did not involve any action years ahead of any perceived risk. The conference was successful in some ways, and unsuccessful in others. It did not ultimately prevent the risk, largely because recombinant DNA did not turn out to present much risk. To the extent that Asilomar was successful, we can see a variety of factors that influenced this success. Regardless of its success, Asilomar also sheds light on several important questions about how risk reduction efforts might tend to unfold.

Notes

1 "February 24-26 of this year [1995] was the 20th anniversary of the Asilomar Conference that considered the public health implications of what was then a new genetic technology—recombinant DNA. . . . That conference, held at the Asilomar Conference Center on California's Monterey peninsula in the USA, included scientists from throughout the world, lawyers, members of the press and government officials. One aim of the meeting was to consider whether to lift the voluntary moratorium and, if so, under what conditions the research could proceed safely. Although there were few data on which to base a scientifically defensible judgment the conference concluded, not without outspoken opposition from some of its more notable participants, that recombinant DNA research should proceed but under strict guidelines. Such guidelines were subsequently promulgated by the National Institutes of Health and by comparable bodies in other countries." (Berg and Singer 1995)

"The regulatory framework put in place at the Asilomar conference was mandatory for recipients of NIH funding, and voluntary for industry." (Baltimore and Grace 2015, 2)

2 The first man-made recombinant DNA was created in 1971. (Chemical Heritage Foundation 2010)

3 "When Berg and his colleagues did their earlier experiments, most people felt that it was so technologically demanding and required such a large number of different kinds of enzymes, along with the skill of using those enzymes, that very few people were going to use such methods to make recombinants.

"It was only a year later, in Berg's lab, that a student discovered the enzyme that made the process easy. Now creating such recombinants could literally be a high school science experiment. All of the reagents were available commercially, and no special skills or materials were needed." (Berg and Grace 2015, 4)

4 "The primary motivation for the prompt actions taken by scientists and governments in the period 1973-1976 was to protect laboratory personnel, the general public, and the environment from any hazards that might be directly generated by the experiments. In particular, there were speculations that normally innocuous microbes could be changed into human pathogens by introducing genes that rendered them resistant to then available antibiotics, or enabled them to produce dangerous toxins, or transformed them into cancer causing agents." (Berg and Singer 1995)

5 See endnote 1.

6 See Berger, Christiano, and Grace (2015).

7 "In 1972, using a technique somewhat different from those presently being discussed, Paul Berg and his colleagues at Stanford constructed a DNA molecule made up in part of DNA from the oncogenic virus, Simian Virus 40, and in part of DNA from *E. coli*. Berg recognized the possible hazards of reinserting the newly constructed molecule into *E. coli* and decided not to proceed with such insertion (although it was the next logical step in the experiments). Berg discussed this problem with a variety of his colleagues and friends, including members of the Hastings Institute, and his final decision was influenced by these conversations. The decision was widely known, and was germinal to the next incident in the story, which took place at the June 1973 Gordon Research Conference on Nucleic Acids." (Singer 1975)

8 "And she [Berg's student Janet Mertz] described our intent and success in creating the first recombinant and how we intended to use it. That seemed to have invoke a huge concern amongst the teacher in that course, named Bob Pollack. And Pollack told her he thought that was the most dangerous and outrageous experiment that anybody could possibly do. And shortly thereafter I got a telephone call from Bob, telling me the same thing, that he thought this was, asking me had I realized how dangerous an experiment this would be, that the idea of trying to put genes that were known to cause cancer in animals into a bacterium that inhabited the normal human intestinal tract." (Berg n.d.)

9 See endnote 7.

10 ". . . We begin with the controversy about safety of recombinant DNA—a controversy Boyer ignited, quite unwittingly, with his unscheduled talk about recombining antibiotic resistance genes at the Nucleic Acids Gordon Conference in June, 1973." (Bourne 2011, 96)

11 "At the meeting, experiments indicating a new way to join DNA from any organism with DNA from any other organism, and most particularly, with bacterial plasmids, were described. The new method was less tedious and simpler than the one used by Berg. The range of previously intractable questions about genetic expression that could be answered by utilizing the new method was enormous and widely perceived." (Singer 1975)

12 "The intellectual excitement engendered by the new experiments was tempered when some members of that Gordon Conference immediately pointed out the potential hazards. That evening, when the formal sessions were completed, serious discussion of the problem of the hazards went on in an informal manner. The next morning, the last of the meeting, the group voted overwhelmingly to write to the President of the National Academy of Sciences asking the Academy to set up a study group to consider the issues raised by the experiments. In a less overwhelming vote, but by a substantial majority, the group decided to make the letter public by publishing it in *Science Magazine*." (Singer 1975)

13 Following a vote at the conference's business meeting, its two chairs, Maxine Singer and Dieter Söll, wrote a public letter to the US National Academy of Sciences . . . to express concern that scientist had too little solid information to predict the actual dangers, and to suggest developing explicit guidelines for future experiments. The Singer-Söll letter prompted the NAS to form a committee, chaired by Paul Berg, to "examine the scientific prospects and potential risks of what came to be known as recombinant DNA."

14 "But improvements in the technology, most notably the ability to clone DNA segments from virtually any organism on our planet, triggered a new level of concern which culminated in mid-1974 with a call for a voluntary moratorium on certain recombinant DNA experiments. In spite of widespread consternation among many scientists about the proscriptions, the validity of the concerns, and the manner in which they were announced, the moratorium was universally observed. One goal of the moratorium was to provide time for a conference that would evaluate the state of the new technology and the risks, if any, associated with it." (Berg 2004)

15 "The second Asilomar Conference on biohazards (hereafter, Asilomar) held in February 1975 was called into being following publication of the Berg letter." (Krimsky 1982, 99)

"That conference, held at the Asilomar Conference Center on California's Monterey peninsula in the USA, included scientists from throughout the world, lawyers, members of the press and government officials. One aim of the meeting was to consider whether to lift the voluntary moratorium and, if so,

under what conditions the research could proceed safely. Although there were few data on which to base a scientifically defensible judgment the conference concluded, not without outspoken opposition from some of its more notable participants, that recombinant DNA research should proceed but under strict guidelines. Such guidelines were subsequently promulgated by the National Institutes of Health and by comparable bodies in other countries." (Berg 2004)

16 "The committee was responsible for filing a formal report to the NAS on the progress achieved by the conference, including any recommendations. The NAS would review the report, make any changes it saw fit, and then release it for publication" (Krimsky 1982, 144)

17 See endnote 1.

18 "The regulatory framework put in place at the Asilomar conference was mandatory for recipients of NIH funding, and voluntary for industry. Everyone in the industry obeyed every RAC recommendation. The framework prevented people from running ahead, and influenced decades of recombinant DNA research." (Baltimore and Grace 2015, 2)

19 ""The conference put in place the Recombinant DNA Advisory Committee (RAC) process, which controlled the development of recombinant DNA methodologies over a couple of decades. This was intended to last for as long as it was needed. Today RAC works on genetic engineering questions rather than biological safety, as the biological research community has become less concerned about the dangers of Recombinant DNA research." (Baltimore and Grace 2015, 2)

"Both the guidelines and the Recombinant DNA Advisory Committee remain as critical components of the genetic engineering research oversight system . . . many of the processes first proposed at the Asilomar Conference remain in place, though some have changed in the intervening years as understanding of risks has improved." (Bonham et al. 2010)

20 "One of these benefits was the willingness of government officials to adopt guidelines that were initially strict—they included proscriptions of certain lines of research and required rigorous physical and biological containment—but allowed for timely relaxation as knowledge about the modified organisms accumulated. Consequently, after 20 years of research and risk assessment, most recombinant DNA experiments are, today, unregulated. Such experiments are now even part of the curriculum in good high schools." (Berg and Singer 1995)

"The guidelines were deliberately designed to be reviewed periodically and to determine if unexpected outcomes had arisen. Over a period of several years—during which a huge number of recombinants were created—nothing of any serious consequences happened. So, the guidelines have withered away except regarding some very, very extreme possibilities. The guidelines covering general recombinant DNA procedures are gone. The guidelines now largely address introducing recombinant DNA into humans. The field of gene therapy is the principal field that the recombinant DNA advisory committee at the NIH actually oversees now." (Berg and Grace 2015, 10)

"The recommendations are still in effect. Every recombinant DNA experiment has to go through RAC (Recombinant Advisory Committee) approval. The getting of approval, and defining what biological safety you're at, and using disabled hosts, that's still in effect." (Church and Grace 2015, 4)

"With input from NIH RAC, NIH has modified the NIH Guidelines nearly 30 times since their inception in order to keep pace with advances in science and biosafety." (Bonham et al. 2010)

21 See Berger, Christiano, and Grace (2015).

22 See endnote 4.

23 "The correspondence written between September 1974 and February 1975 has been divided according to the following major scenarios of risk: (1) creation of plant pathogens; (2) *E. coli* with cellulose-degrading genes; (3) troublesome proteins in E.coli; (4) natural recombinations versus artificially created DNA molecules; (5) immunological hazards; (6) tumor viruses; (7) perturbation of biochemical pathways; and (8) drug resistance genes in *E. coli*." (Krimsky 1982, 115)

24 "Geneticists, bacterial geneticists and biochemists liked to work with the bacteria Escherichia coli, or *E. coli*. Because *E. coli* inhabits the human intestinal tract, there was a concern that putting new DNA sequences into *E. coli* might produce something dangerous. There was speculation about serious consequences: People could allow their imaginations to wander and say, 'Well, what happens if you would put in a Botulinum toxin gene into *E. coli*? Could you produce large quantities of Botulinum toxin? Could you put genes that confer resistance to normally used antibiotics that might go into *E. coli*, but then escape *E. coli* and inhabit the bacteria that produce serious disease?' . . . There was a concern that inadvertently cloning such a cancer gene and putting it into *E. coli* might lead to an epidemic of cancer. This was the type of concern often raised." (Berg and Grace 2015, 6)

25 "Ecological niches were also on the mind of Allan Campbell, a Stanford University biologist, and one of the scientists Donald Brown had written for some views on the hazards of transferring nitrogenase genes into exotic species. Campbell's response focused on the potential hazards of disturbing biochemical pathways. Suppose we introduce the nitrogenase (nitrogen-fixing genes) into organisms that are lacking them. Campbell maintained that there would be an extremely minute chance of producing a catastrophic result. . . . Next to the problem of a possible disturbance to the biochemical cycles, Campbell wrote, the worry that rDNA research might cause a few thousand extra cancer deaths seemed less significant." (Krimsky 1982, 122–123)

26 "Three classes of experiments were identified by the Berg committee as warranting special attention. The first two were recommended for postponement. For the third, deferral gave way to a more modest "handle with care." Type I experiments were those for which two types of genes were linked to bacterial plasmids. Plasmids are the small, circular extrachromosomal DNA that can be implanted in a bacterium and replicate in the bacterial host. The first class of genes is that which codes for antibiotic resistance factors; the second class codes for toxins." (Krimsky 1982, 84)

27 "Before Asilomar, people were probably aware that it was fairly easy to make biological systems feeble. The whole history of microbial genetics was, you make a mutant and the thing is feeble." (Church and Grace 2015, 4)

28 "We now know that all cells and microbes in nature are taking up foreign DNA all the time." (Berg and Grace 2015, 7)

29 See Section 1.4.

30 "The 1975 Asilomar conference was actually the second such Asilomar conference that had been held, after another about a year and a half earlier. That one dealt with the issue of whether there were risks in working with tumor viruses. This was sponsored by the NIH and organized in part by Berg. Here the risk was just with working with the viruses themselves, rather than with creating new organisms." (Berg and Grace 2015, 1)

31 See Section 1.4.

32 "Roblin, a member of the Council for Biology in Human Affairs, was interested in the impacts of biology on society, especially genetic engineering. He already had published an essay in *Science* outlining a responsible course of action for human genet therapy. . . . When Roblin was asked . . . to suggest people to serve on the panel, the names he came up with were Leon Kass and Jonathan Beckwith. . . . Beckwith and Kass were primarily concerned about the social uses of science, while Berg's thinking had focused exclusively on biohazards." (Krimsky 1982, 81–82)

See also Section 3.3.11.

33 "Prior to the discovery of recombinant DNA techniques, David had had concerns about the potential for military exploitation of biological research. The USA had had an active program to develop lethal biological weapons, and existing organisms—bacteria and viruses such as smallpox—were the subject of military investigation. The new possibilities apparent with the advent of recombinant DNA technology, beginning in the late '60s, exacerbated concern for David and many others in the biological research community.

"David was involved with a professional society called the American Society for Microbiology, which attracted many researchers working on biological warfare. Some of those in the organisation who were not directly involved in military research became concerned that they could have been inadvertently helping the development of potent biological weapons." (Baltimore and Grace 2015, 3)

34 "Two tangential long-term issues concerned people at the time: germ warfare, and 'ethics with a capital E'. The Asilomar conference explicitly avoided both of these topics. The participants felt they had no control over germ warfare, and it seemed better to focus the conference on the immediate issue, rather than simultaneously engaging the whole field of ethical dilemmas raised by future medical use of such technologies." (Berg and Grace 2015, 6)

". . . Those exclusions were given public utterance at the opening session of the conference when David Baltimore pointedly noted that two issues were to be kept outside the scope of the meeting. The first was the utilization of rDNA techniques for genetic engineering. These issues, he held, are replete with values and political motivations. They will obfuscate the technical discussions related to biohazards. The second was the application of gene-splicing techniques to military weapons." (Krimsky 1982, 106)

35 ". . . The ethical questions about genetic manipulation will be dependent in part upon the purpose served. Obviously, once a technique is introduced for one purpose, it can then be used for any purpose. Therapeutic use is one thing, eugenic, scientific, frivolous, or even military are quite another. Thus there are two questions to be considered: a. What would be the range of ethically legitimate purposes? b. How could one limit use to those purposes? I have my own views on the first for which I would argue ('therapeutic use only'), but more importantly, I would insist that we need to foster public deliberation about this question, since I don't think this is a matter to be left to private tastes or to scientists alone. I defer the question of control until later. 4. Possible undesirable consequences of ethical use for ethical purposes. In the previous paragraph, I considered the problem of so-called 'good' vs. 'bad' ends. We have also to consider 'bad' consequences of a technique used only for 'good' purposes. This is a far more difficult problem, and unfortunately, I think, a more pervasive one in the whole biomedical area. The inevitable social costs of desired progress are probably higher than the costs of progress willfully perverted by bad men. We must consider and weigh the following kinds of questions in deciding about the first use of a new technique: a. What are the biological conse-

quences in future generations of widespread use of gene therapy on afflicted individuals? Anything but treatment of gonads, gametes, and zygotes will work to increase the frequency of the given gene in the population. (1) Are we wise enough to be tampering with the balance of the gene pool? That we do so inadvertently already is no argument for our wisdom to do so deliberately. (2) What are our obligations to future generations? Do we want to commit them to the necessity of more and more genetic screening and genetic therapy to detect and correct the increasing numbers of defects which our efforts will have bequeathed to them? b. Do we ourselves wish to embark upon a massive program of screening and intervention? With federal support? Under compulsion of law? Are we not moving toward more and more laboratory control over procreation? What are the human costs of this development, especially for marriage and the family?" Leon Kass (quoted in Krimsky 1982, 35).

36 "The GSG [Genetics and Society Group] study group initially had chosen to address two types of issues: (1) social or psychological theories grounded on genetic evidence, that is, the genetic determinants of IQ; (2) scientific research programs designed to generate evidence that social or political behavior was genetically determined." (Krimsky 1982, 136)

37 "Nonetheless, if one wanted to develop a biological weapon, David thinks natural organisms would be a more promising place to look. Pathogens from nature have been tested thoroughly, while synthetic bioweapons need to be tested and the type of testing that is needed might pose difficulties." (Baltimore and Grace 2015, 4)

38 See Berg et al. (1975a).

39 See Nobel Media (2015).

40 "Some scientists, and public officials as well, were certain that recombinant DNA research was flirting with disaster and that lifting the moratorium was a blunder. Others, reflecting their intuition and expertise, argued that such cells, viruses and recombinant DNAs posed no risk at all." (Berg 2004)

41 ". . . the lawyers pointed out the legal problems. And challenged Jim Watson with the idea—because he had now turned, and he was totally opposed to any kind of regulation, whereas he had been a signer of the original letter—they said, people could close down cold springs harbor if there's any danger or anything that happens, and then people's own personal risks were beginning to play on." (iBio Magazine 2011)

42 " '[T]he Asilomar conference was a nightmare,' Boyer said, 'There were a lot of a lot of accusations and shouting from the floor. [It was] an absolutely disgusting, . . . exhausting week. I was so upset . . . I couldn't sleep. . . . [T]he whole thing was counterproductive.' Cohen's response to the conference revealed a similar disgust. 'What I did not expect was the almost religious fervor. . . . [It was] not so much a meeting called . . . to address an issue . . . , but rather . . . an emotionally uplifting event. The mood among some of the organizers was self-congratulatory. [A]n issue . . . raised because of scientific concerns [was] taken out of the hands of scientists and . . . turned into a sort of witch hunt. [P]eople who had contrary positions were afraid to say so. It was the first time I had encountered a situation where scientists were fearful of speaking their mind about scientific issues. [A] steam roller had taken over.' . . .

"Although the organizers tried to argue that the conference reached a consensus, the "acrimonious discussion" Cohen observed in the final session argued to the contrary. As the meeting ended, the organizers asked for a vote approving a document they would write after the meeting. "I . . . voted against giving [them] . . . authority to prepare post hoc a statement that would be presented as the

'consensus' of the group at Asilomar." . . . Voting against senior figures like Paul Berg and David Baltimore was a brave gesture, joined by few other attendees. Indeed, Cohen saw the uplifted hands of only two other scientists voting with him—James Watson and Joshua Lederberg [?], each of whom had been awarded a Nobel Prize." (Bourne 2011)

43 See endnote 42.

44 "One of the strongest consistent proponents of the view that rDNA techniques would not introduce anything that nature has not already created is Bernard Davis, Adele Lehman Professor of Bacterial Physiology of the Harvard Medical School. Davis presented this line of reasoning in a letter to Paul Berg in September 1974. His reconstructed argument takes the following form: DNA recombinants are arising all the time in nature—including in the human gut. Whether the new recombinants reproduce and proliferate into the environment depends upon their selective advantage with respect to other organisms with which they are competing (Darwinian selection). The new recombinants developed in the laboratory do not have a selective advantage in nature, otherwise they would already be widespread. Therefore, the only people at risk from the laboratory creation of DNA recombinants are the workers, who may risk getting an infection." (Krimsky 1982, 125)

45 "Four days after his response to Chakrabarty . . . Curtiss had a change of mind. He sketched out two possible hazards in implanting cellulose-degrading genes into *E. coli*. They were based upon the dietary importance of unreduced cellulose as roughage in healthy bowel activity. The following are two reconstructed arguments based upon Curtiss' remarks. . . . *E. coli* with cellulose-degrading genes in the human gut can result in a reduction in life span. . . . If the resident bacteria in the human gut degraded the cellulose in the diet, thereby eliminating the usefulness of roughage, there could be a higher incidence of bowel-related diseases, including cancer. . . . When Chakrabarty responded . . . he explained the potential benefits . . . if this type of experiment was successful, the implications for a new Green Revolution were substantial. In countries where there have been substantial food shortages, Chakrabarty saw great promise in a technology that enabled people to utilize high-cellulose-content foods for their untapped calories." (Krimsky 1982, 118–119)

46 "[Robbins] said that when one tries to create a new recombinant a possible outcome could be the production of a defective virus, which is analogous to what is done by radiation. . . . In creating recombinants, can scientists produce a product that is more dangerous than any of its component parts. . . . Renato Dulbecco, an eminent scientist at the Imperial Cancer Research Fund Laboratories in London, England, put forth several arguments . . . that had led [him] to the view that working with rDNA viruses required no greater precaution than working with ordinary transforming viruses. . . . The evidential support included these observations: the plasmid or phage DNA containing a transforming gene would have a probability of infection similar to that of SV40 in the absence of adjuvants; the laboratory strain of *E. coli* entering the intestinal tract would have no selective advantage and would subsequently disappear, and a plasmid carrying bacteria would disappear even faster; if a cell is infected by DNA in the gut, it will not be the source of reinfection." (Krimsky 1982, 121)

47 "Each issue touched upon several disciplines. For example, scientists would begin with a bacterium; but then the DNA of an animal virus would be inserted into it; and finally, it would enter the human intestinal tract. Since the individuals discussing the potential risks generally did not have expertise in all relevant fields (bacteriology, virology, and infectious disease epidemiology), it was incumbent upon the decision makers to view the problems across scientific disciplines" (Krimsky 1982, 125)

48 "I think we all went in with a state of mind not knowing much about microbiology, infectious diseases and so on. There was a lot of speculation. . . . " (Boyer n.d.)

49 "Although there were few data on which to base a scientifically defensible judgment the conference concluded, not without outspoken opposition from some of its more notable participants, that recombinant DNA research should proceed but under strict guidelines." (Berg 2004)

"It is generally understood that the Asilomar II scientists guessed at the risks. A few planned and executed risk assessment experiments sponsored by NIH did not resolve some of the core questions of creating new hazards." (Krimsky 1982, 244–263)

"There were no laboratory surveillance programmes to determine whether the agents they worked with infected scientists and lab workers. Asilomar II gave the appearance of offering a technical response to problems of risk, but most commentators recognize that uncertainties in science are too great to avoid the intrusion of values and self-interest." (Krimsky 2005)

"The risk assessments made at the time of the Asilomar conference were very broad. Some parties thought that there was next to no risk, while others believed it was very dangerous to continue to conduct recombinant DNA research, unchecked. The risk turned out to be at the lower range of people's uncertainty.

"The Asilomar conference discussions concluded that the risk of recombinant DNA research was unclear." (Baltimore and Grace 2015, 1)

"There was no evidence of any such harm [from speculated *E. coli* which produces botulinium toxin, or is resistant to antibiotics], but when the speculations began to become more and more fanciful, and some of them were, we knew that there were such things as cancer genes." (Berg and Grace 2015, 6)

50 "The meeting was designed to keep everybody engaged. There was a danger of scientists becoming bored by discussion only of risks. So they talked about the science itself, and at the same time talking about the possible risks associated with that particular kind of approach."

> "I think, if we'd gone and tried to have a meeting just to deal with risks, many people would not have come and they might not have stayed and they would have been completely bored. Which is the general nature of the scientific community. On the other hand, they were confronted with, 'Here's a technology that has enormous potential. If I want to do it, I have to think about whether there is any risk associated with that experiment.' It was possible to have a discussion interwoven between the benefits and the potential risks." (Berg and Grace 2015, 7)

51 "One thing that came out of Asilomar was increased emphasis on physical containment. . . . This movement paid off for dealing with natural pathogens as well as recombinant DNA versions of those. Natural pathogens already presented more risk than any recombinant form. Asilomar helped to raise the urgency and the consciousness level for these kinds of biological safety issues. Chemicals and radioactive materials were already studied using glove boxes; it was obvious that they should also be used for Ebola and Lassa Fever and other nasty things. . . .

"Church doesnât know when the first chemical, physical and biological use of glove boxes was, but that might be a fairly easy thing to find, historically. All three of them occurred before Asilomar, and they were important milestones leading up it. Further pressure for physical containment in these ways was one important thing that came out of Asilomar." (Church and Grace 2015, 2–3)

"One accomplishment of the guidelines was educational. It forced people to learn how to carry out the procedures and the manipulations in a safer way. It changed the way people worked."

> I can remember there were people very experienced with pathogenic microorganism who were horrified to see the way biochemists generally dealt with these kinds of experiments who were appalled at seeing students in the lab pouring gallons of culture fluid with organism right down the lab drain. That was a very important component of the guidelines and I can't say that those saved our lives or that prevented a huge [disaster, but . . .] . . . (Berg and Grace 2015, 10)

52 "Recombinant DNA technology came on the scene very suddenly. It was very attractive, and attracted many people who were inexperienced in dealing with microorganisms or had never handled pathogens. They were used to mouth pipetting, and pouring things down the sink. 'There was a kind of general behavior that biochemists used which was very far from what the norm would be for anybody dealing with an organism that had some potential pathogenic properties.' " (Berg and Grace 2015, 9–10)

"[A] large number of people were suddenly working with so-called oncogenic viruses and other viruses of that ilk and there was a potential biohazard. And a large number of these people were trained in biochemistry or molecular biology and had very little microbiological training, and therefore were not familiar with the procedures you'd generally use to keep the investigator himself from getting infected, no less the general population. And so in study sections [peer review committees that looked at grant proposals for the NIH] in places like that, these particular grants were flagged, and there was a biohazards committee at the NIH set up. We were concerned that people be made aware of what they were handling." Norton Zinder (quoted in Krimsky 1982, 25)

53 "Altering life forms or changing climate have the same possibility of irreversibility. Changes in both the climate and microbes can be perpetuated indefinitely. 'You can't make a local change.' This was a reason to be especially concerned about recombinant DNA". (Berg and Grace 2015, 11)

54 "[Speakers on law and ethics at Asilomar] informed the conference about the consequences if in fact the public was exposed to any risks. They were 'very, very effective'. They warned that you could not walk away saying nothing could be done, because you would be making yourself legally and financially vulnerable should anything happen. 'A number of the scientists, when confronted with some of those consequences, blanched.'

"That was the last evening of the meeting and Berg feels these presentations changed the discussion and the outcome of the meeting quite dramatically. 'People who had said, "Oh, it's not a big deal. We'll just go on."—These ethicists and lawyers put the fear of God [in them], and put everybody who were there at risk. Generally, there was a very strong feeling toward the end of the scientific and discussion meeting, that we could not avoid making a recommendation. We couldn't just say, "We don't know and let's do what we want." ' " (Berg and Grace 2015, 8)

55 See Baltimore and Grace (2015).

56 "The conference addressed a few obvious longer term beneficial possibilities, what they referred to as the 'low hanging fruit': what could be done today that couldn't have been done yesterday, and what will be possible tomorrow as the technology expands. People probably didn't bring up experiments that hadn't been conceived of previously.

"Gene therapy and agriculture were longer term implications that were discussed, but in the context of benefits rather than risks. For instance there were hopes of improved yields and nutrition,

and dreams of making many plants nitrogen fixing, to avoid the need for fertilizer. They correctly anticipated insulin production through genetically altered bacteria or yeast, and growth hormones." (Berg and Grace 2015, 6)

57 ". . . This choice of agenda [exclusion of GM implications] was due neither to oversight nor unawareness; it was deliberate, partly because of lack of time at Asilomar and partly because it was premature to consider applications that were *so speculative and certainly not imminent.* In 1975, the principal and more urgent concern for those gathered at Asilomar was the possible effects of recombinant DNA on public health and safety . . . " (Berg and Singer 1995; emphasis added)

"An often-voiced criticism of the Asilomar Conference discussions was the failure to consider the ethical and legal implications of genetic engineering of plants, animals and humans. . . It should not be forgotten that *these possibilities* [biowarfare, misuse, ethical implications of genetic screening and therapies, environmental consequences from GM plants] *were still far in the future* and the more immediate issue confronting the Asilomar organizers and participants was the one the scientists had raised: the potential risks to human health and the environment posed by the expanding recombinant DNA technology. *We could not avoid the question of whether there were serious health hazards associated with going forward with the experiments that were being planned.* In short, the agenda for the three-day meeting had to focus on an assessment of the risks and how to eliminate or reduce the risks that seemed plausible. *We accepted that the other issues would be dealt with as they became imminent and estimable."* (Berg 2004; emphasis added)

". . . predicting the time for accomplishment of particular scientific matters is a foolish exercise doomed to failure and therefore a waste of time . . . while I believe that discussion of such matters is important, *the development of policy is certainly premature.*

"I also decline to list the items in order of priority. Because of our inability to predict, *we are stuck with simply letting things happen. Scientists generally investigate those problems that are tractable at any given time.* Therefore I believe in allocation of resources to broad areas (such as genetics itself) with scientists deciding which experiments to do first . . . " (Singer 1978; emphasis added)

58 See 7.

59 "I was depressed about Asilomar because I couldn't see when we were going to be able to start our experiments, was it going to be a six-month delay, several years. As it was, it turned out a couple of year delay and, but we were finally allowed to do what we did, what, what we wanted and it was wonderful. But for a couple of years I just thought about regulations, not about science." (Watson n.d.)

60 "When Berg and his colleagues did their earlier experiments, most people felt that it was so technologically demanding and required such a large number of different kinds of enzymes, along with the skill of using those enzymes, that very few people were going to use such methods to make recombinants.

"It was only a year later, in Berg's lab, that a student discovered the enzyme that made the process easy. Now creating such recombinants could literally be a high school science experiment. All of the reagents were available commercially, and no special skills or materials were needed. This raised concerns, both because now many more people could create recombinants, and because they could combine almost anything. . . . The advent of this new technique was very surprising. It also meant that if anyone wanted to, they could produce dangerous things in large quantities. One could grow a hundred thousand gallons of culture, with each cell in the culture containing a copy of that piece

of DNA that you inserted into the bacterium. This advance both improved the potential for great benefits from the research but it also raised the issues of safety." (Berg and Grace 2015, 4–5)

"At the meeting, experiments indicating a new way to join DNA from any organism with DNA from any other organism, and most particularly, with bacterial plasmids, were described. The new method was less tedious and simpler than the one used by Berg. The range of previously intractable questions about genetic expression that could be answered by utilizing the new method was enormous and widely perceived. Parenthetically, the discovery basic to the new capabilities was of a group of enzymes making specific cleavages in DNA molecules at given sequences of nucleotide bases. These enzymes have many other important uses in genetics and molecular biology beside their use for recombination of unrelated DNAs. The description of the enzymes also elucidated certain long standing observations in bacterial genetics. There was no way to predict that these enzymes would permit in vitro recombination . . . the relevant properties of the enzymes were unexpected and unique." (Singer 1975)

"David says that he was completely surprised by the recombinant DNA methods, which represented an enormous jump from where scientists had been to where they could now go. He hadn't spent any time beforehand considering the idea that anything like it could be possible. While he won't speak for others, he says that it is likely that that he would have had more warning if the advances had been predicted." (Baltimore and Grace 2015, 1)

61 It is generally understood that the Asilomar II scientists guessed at the risks. A few planned and executed risk assessment experiments sponsored by NIH did not resolve some of the core questions of creating new hazards. (Krimsky 1982, 244–263)

See also endnote 49 and Section 1.3.

62 "An important concern of Baltimore was whether this small but distinguished group of scientists could effect a moratorium. There were no precedents to go by, and therefore some doubted that other members of the scientific community would embrace the standards of social responsibility set by this panel." (Krimsky 1982, 82)

"[W]e did not expect [our draft] to have a very good reception. . . . [W]e had this big discussion as to whether we would have a vote, and we decided we wouldn't allow a vote . . . because we thought we would be voted down." (Frickel and Moore 2005)

"Berg did not see a clear pattern of consensus emerging in the first three days of the meeting. Consequently, the Organizing Committee chose to interpret the final report as their statement and not a statement of the entire Asilomar body. . . . Berg [said]: 'I tried to put forth the view that this was our paper, and we were obliged to make a report to the Academy of some recommendations, and that these were our understandings of what we think are plausible recommendations and the way of proceeding; it comes from having listened to the debate and the discussions.'

". . . Finally, Sydney Brenner requested a vote, and Berg conceded to having a show of hands, beginning with the first paragraph of the statement. After an overwhelming acclamation was given to the principles behind the statement, it was clear that Berg and others had underestimated the degree of support the assembly was prepared to offer. . . . one observer noted, 'at every point the Organizing Committee won overwhelmingly with never more than five or six hands raised in opposition'." (Krimsky 1982, 143–145)

63 See endnote 42.

64 "Church does not think people at Asilomar were that concerned about risks decades hence. It could be argued that they were visionary in the sense that they were worrying about something improbable. Church thinks the thing they should have been thinking about—even though it wasn't an issue even forty years later—was intentional abuse, or intentional release. He doesn't recall this receiving much attention at Asilomar, though it came up shortly after. Surely someone was thinking about it, but lots of people who think ahead get forgotten." (Church and Grace 2015, 5)

65 "One of these benefits was the willingness of government officials to adopt guidelines that were initially strict—they included proscriptions of certain lines of research and required rigorous physical and biological containment—but allowed for timely relaxation as knowledge about the modified organisms accumulated. Consequently, after 20 years of research and risk assessment, most recombinant DNA experiments are, today, unregulated. Such experiments are now even part of the curriculum in good high schools." (Berg and Singer 1995)

66 "Since the estimation of potential hazards is conjectural and speculative, the levels of containment required for potentially hazardous organisms should be set high initially, and modified only when there is substantial relevant information to advise such modifications. And finally that the guidelines are to be reviewed at least annually in order to account for new information." (Singer 1977)

". . . Moreover, the standards of protection should be greater at the beginning and modified as improvements in the methodology occur and assessments of the risks change. . . . In the longer term, serious problems may arise in the large scale application of this methodology in industry, medicine and agriculture. But it was also recognized that future research and experience may show that many of the potential biohazards are less serious and/or less probable than we now suspect. . . . 'Thus, the ways in which potential biohazards and different levels of containment are matched may vary from time to time, particularly as the containment technology is improved. The means for assessing and balancing risks with appropriate levels of containment will need to be reexamined from time to time. . . '

". . . Research in this area will develop very quickly and the methods will be applied to many different biological problems. At any given time it is impossible to foresee the entire range of all potential experiments and make judgements on them. Therefore, it is essential to undertake a continuing reassessment of the problems in the light of new scientific knowledge. . . . There are many questions in this area, the answers to which are essential for our assessment of the biohazards of experiments with recombinant DNA molecules. It will be necessary to ensure that this work will be planned and carried out; and it will be particularly important to have this information before large scale applications of the use of recombinant DNA molecules is attempted . . ." (Berg et al. 1975b)

"We are all trying to stop any interest in legislation, as that does not seem appropriate and would be inflexible. One can certainly anticipate that the rules will change as knowledge is accumulated." (Singer 1976)

67 Some examples of writing from the time suggesting a focus on short term risks:

"At the recent conference on Recombinant DNA Molecules in Asilomar, California, this question [of potential for biological warfare] was not discussed because we were more concerned about the potential public health consequences of current research using this methodology." (Baltimore 1975)

". . . then following that a second conference [Asilomar II] to discuss the kinds of experiments that people are doing, whether they pose any hazard, how you would find out if they posed a hazard, what we would do while we were waiting?" (Krimsky 1982, 62)

". . . in a letter from Paul Berg to E.S. Anderson, the following objectives were outlined: to identify the kinds of experiments scientists would like to do with hybrid molecules; to stipulate the kind of information such experiments could provide; to identify the possible risks involved for the investigator and others; to develop means by which biohazards could be tested and minimized in order that the work could proceed . . . " (Krimsky 1982, 109)

68 Some examples of writing from the conference mentioning longer term concerns:

"Many of the future developments in the cloning, amplification, and utilization of eukaryotic DNA sequences will, however, require other vectors and host cells. The long-term objectives of genetherapy, for example, can only be achieved by transfer of new sequences to animal cells, for which the obvious vectors are animal viruses. Similar systems are attractive for furthering the basic molecular biology of eukaryotic cells, both animal and plant, but they immediately present an additional range of potential biohazards." (Brenner et al. 1975)

Hazards associated with large scale applications:

"Although it may be that eukaryotic genes are not normally transcribed and/or translated with fidelity in bacteria we presume that such conditions can be obtained by genetic manipulation of the bacterial genome, or of the vector-eukaryote hybrid DNA. Numerous applications of this kind of eukaryotic gene activity have been suggested—for example, the bacterial production of insulin in pharmaceutical factories. These applications will generally involve the growth of very large numbers of the relevant bacteria, and the eukaryotic gene products they contain may well be hazardous to the general population. The problems of containment associated with these applications are likely to be increased substantially over those considered previously. We therefore set them apart from the hazard ratings given above. We recommend that such applications be undertaken only after it can be demonstrated that the bacteria are 'safe'; that is, they will not be hazardous even if they escape the confines of their intended use. The concept of safe bacteria is discussed in the report by the plasmid group." (Brenner et al. 1975)

"In the longer term, serious problems may arise in the large scale application of this methodology in industry, medicine and agriculture. But it was also recognized that future research and experience may show that many of the potential biohazards are less serious and/or less probable than we now suspect." (Berg et al. 1975b)

"We believe that perhaps the greatest potential for biohazards involving alteration of microorganisms relates to possible military applications. We believe strongly that the construction of genetically altered microorganisms for any military purpose should be expressly prohibited by international treaty, and we urge that such prohibition be agreed upon as expeditiously as possible." (Krimsky 1982, 130–131)

"There are many questions in this area, the answers to which are essential for our assessment of the bio-hazards of experiments with recombinant DNA molecules. It will be necessary to ensure that this work will be planned and carried out; and it will be particularly important to have this information before large scale applications of the use of recombinant DNA molecules is attempted." (Berg et al. 1975b)

69 One type of potentially farsighted concern raised was regarding large scale, perhaps commercial applications. These in fact occurred within five years: "Recombinant human insulin first entered clinical trials in humans in 1980" (MJ 1989)

Also, David Baltimore suggests that predictions of progress at the time were if anything optimistic:

"[David Baltimore] says it seemed at the time that there was no conceptual limit to how far modern biology could go, and this still seems true. Progress has perhaps been less quick than some original estimates, but David has never found predicting times of discovery to be very useful." (Baltimore and Grace 2015, 2)

Further evidence that commercial applications were not expected to be far away comes from commercial interests such as Eli Lilly attending the Asilomar conference: "A few corporate people participated in the Asilomar conference. For instance Eli Lilly was represented, because they were the major producers of insulin, so the prospects of being able to make insulin through recombinant DNA was important for them." (Berg and Grace 2015, 9)

Another type of risk raised in the plasmid working group paper was regarding biowarfare, but the conference explicitly did not intend to resolve anything in that area. See endnote 75.

The other risks mentioned to be 'long-term' regard transfer of new gene sequences to animal cells. The first animal containing foreign DNA was created in in 1973 (see Jaenisch and Mintz [1974]), before the paper was written, so this seems unlikely to have been a distant concern.

70 "A perusal of the conference summary statement suggests that all classes of safety precautions covered at least some already feasible experiments. For instance, while they suggested avoiding some experiments altogether using available safety measures, even this most extreme category included already feasible experiments:

"There are feasible experiments which present such serious dangers that their performance should not be undertaken at this time with the currently available vector-host systems and the presently available containment capability." (Berg et al. 1975b)

71 "The radicals, on the other hand, looked at the impact of science on society principally in terms of how science served to strengthen existing economic and social relations and saw the responsibility of the scientists to be active opposition to those conditions. The aspect of gene-splicing technology on which they focused initially was the potential it held for genetic engineering, and this was not something that could be dealt with by a simple technological fix." (Krimsky 1982, 21–22)

"What are our obligations to future generations? Do we want to commit them to the necessity of more and more genetic screening and genetic therapy to detect and correct the increasing numbers of defects which our efforts will have bequeathed to them?" Leon Kass (quoted in Krimsky 1982, 35)

72 "The discussions over the impact of the new techniques for the genetic manipulation of man were carried out mainly by people outside of the profession—writers, environmentalists, ethicists and the like, with a sprinkling of scientists, whose voices in the distance were ignored." (Krimsky 1982, 80)

73 See endnote 33.

74 "After Asilomar, Baltimore wrote a letter to Fred Iklé at the United States Arms Control and Disarmament Agency pointing out that recombinant DNA may worsen risks from biowarfare, and asking if the Biological Weapons Convention would be interpreted as prohibiting such dangerous work." (Baltimore 1975)

75 "Two tangential long-term issues concerned people at the time: germ warfare, and 'ethics with a capital E'. The Asilomar conference explicitly avoided both of these topics. The participants felt they

had no control over germ warfare, and it seemed better to focus the conference on the immediate issue, rather than simultaneously engaging the whole field of ethical dilemmas raised by future medical use of such technologies.

"Scientists foresaw that people could make extremely nasty organisms by incorporating new genes. This was in the Cold War, and it was often suspected that the Russians were conducting such research, and that the Americans might also be doing so. However scientists felt there was little they could usefully say about this problem, and it was hard to evaluate. They felt they were not the people who should be worrying about it." (Berg and Grace 2015, 6)

"In planning the Asilomar conference, David says that he and his colleagues were mostly worried about dangers such as those that would arise from laboratory experimentation. They did not mean to address any ethical or moral issues. He says that those at the conference were all quite aware of those problems, but as scientists, felt unqualified to answer questions about them on behalf of the rest of civilisation." (Baltimore and Grace 2015, 3)

76 "We believe that perhaps the greatest potential for biohazards involving alteration of microorganisms relates to possible military applications. We believe strongly that construction of genetically altered microorganisms for any military purpose should be expressly prohibited by international treaty, and we urge that such prohibition be agreed upon as expeditiously as possible." Plasmid Working Group (quoted in Krimsky 1982, 130)

77 See endnote 19.

78 "It turned out that recombinant DNA technology was not very risky." (Baltimore and Grace 2015, 1)

"Others [scientists], reflecting their intuition and expertise, argued that such cells, viruses and recombinant DNAs posed no risk at all. The overwhelming assessment today is that the latter view was correct. Literally hundreds of millions of experiments, many inconceivable in 1975, have been carried out in the last 30 years without incident. No documented hazard to public health has been attributable to the applications of recombinant DNA technology." (Berg 2004)

"We can't cite any incidents resulting from the recombinant DNA methodology that have produced an untoward outcome. Everybody looks back now and thinks there was probably very little or zero risk, except for people who wanted to clone really nasty things. Such things were imagined, and those were put in a special category, requiring very specialized equipment and facilities. That sort of experiment was not in the mainstream. Nobody has yet found a novel recombinant that arose naturally that has proven to be dangerous." (Berg and Grace 2015, 7)

79 "In the 1970s, the concern was that recombinant DNA research would produce dangers accidentally. Paul Berg was creating SV40 hybrids, but the worry was that this intentional construct, which was not intended maliciously, could end up causing intestinal cancer, or something like that. Recombinant DNA is safe in that regard.

"There is a kind of blurring of recombinant DNA into synthetic biology, where for instance they created an IL-4 mouse pox virus combination that they thought would be less pathogenic. It turned out to be more pathogenic. This confused them at the time, but makes perfect sense with hindsight: when you are dealing with very powerful combinations of genes and vectors and so forth, you can create something that works in the opposite direction, or is more powerful than you expected. You get things like that in synthetic biology.

"It's possible to accidentally make quite dangerous things, it's just very unlikely. You would have

to both make it and release it successfully. You would have to make it so it would survive in the wild. You would have to do a whole bunch of things accidentally to really cause a problem. Even if Paul Berg's SV40, *E. coli* hybrid had been pathogenic, it probably wouldn't have survived.

"The bigger risks are making something intentional. It doesn't take much thought to make something malicious that would survive in the wild. Although even that's not trivial, because almost everything you do to a wild organism makes it less fit in the Darwinian sense." (Church and Grace 2015, 2)

80 "Following the fall of the Soviet Union, it was revealed that recombinant DNA techniques had been used to engineer bioweapons. Research reported to be ongoing at the time included production of chimera viruses and bacteria and viruses possessing enhanced virulence, transmission, infectivity, as well as resistance to existing antibiotics, vaccines, or therapeutics." (Federation of American Scientists 2014)

81 "I would say if you sampled our true feelings the members of the committee believed the experiments probably had little or no risk, but if you asked anybody to put a probability on it, nobody could say zero risk." (Berg and Grace 2015, 5)

82 "A quarter century after the Asilomar conference, Paul Berg acknowledged that 'we overestimated the risks, but we had no data as a basis for deciding, and it was sensible to choose the prudent approach.' " (National Library of Medicine 2007)

"Many of Berg's colleagues now say we should have known better. We now know that all cells and microbes in nature are taking up foreign DNA all the time. The general consensus, after a year or two of oversight, was probably that the guidelines were unnecessary." (Berg and Grace 2015, 7)

"The Asilomar moratorium soon came to seem unduly cautious, but that doesn't mean that it was unwise at the time, since the level of risk was then genuinely uncertain. James Watson, codiscoverer of DNA's double helix, regards this attempt at self-regulation as, in retrospect, a mistake. (Watson is generally 'bullish' about the applications of biotechnology, believing that we should be uninhibited about using new knowledge of genetics to 'improve' humanity. He has asked rhetorically 'If biologists won't play God, who will?')." (Rees 2003, 76)

83 "There was a call to the scientific community for the development of safer hosts and vectors as well as experimental investigations on the risks of recombinant organisms [in the recommendations of the Asilomar conference]." (Krimsky 1982, 148)

84 "28 February. . . . First meeting of the Recombinant DNA Molecule Program Advisory Committee (RAC)." (Krimsky 1982, 350)

85 See endnote 14.

86 See endnote 62.

87 "There were over fifty foreign participants at Asilomar." (Krimsky 1982, 111)

88 "Another interesting idea coming out of Asilomar was biological containment. An example of that was Roy Curtiss III's methods by which the vector, the host, would be disabled in certain genes, so it required the investigator to provide it with food of a certain type. The idea is that if it ever escaped from the laboratory to make it into the sewers, then the compound to which it was addicted would not be there, and it would die. . . .

"Before Asilomar, people were probably aware that it was fairly easy to make biological systems feeble. The whole history of microbial genetics was, you make a mutant and the thing is feeble. What happened is probably a bit at the meeting, but certainly after the meeting, people like Roy Curtiss III said, 'We need better biological containment. This is how we make wimpier hosts.' For microbiologists, this was an easy call to arms. It would have been very obvious that they could do it. So they did it, or they claim they did it." (Church and Grace 2015, 3–4)

89 "Unfortunately, the easiest way to do that is to just remove a gene involved in a biosynthetic pathway. Which means that the same biosynthetic pathway is still present in *E. coli* in your guts and in the sewers, where this gene hasn't been deleted. So if these *E. coli* break open, their guts can feed the disabled bacteria. Church and others recently went back and redid some of those experiments to check whether that was possible, and it was. They showed that if you take wild *E. coli*, break them open in the presence of these disabled strains, the disabled strains would survive.

"It turns out that since wild and lab *E. coli* ecologically tend to fall into the same places, so it's not safe to assume that wild *E. coli* are not spilling their guts. Church and his colleagues investigated this in part because they had developed a new method of truly disabling *E. coli* (and probably any species), suspecting previously that their method didn't truly disable them." (Church and Grace 2015, 3–4)

90 See endnote 19.

91 See endnote 20.

92 "The Asilomar recommendations began as strong recommendations that became, essentially, the only way to operate. They were also not very hard. The recommendations were probably somewhat helpful for bringing about the progress in physical and biological containment discussed above. They had an impact almost immediately, and caused people to build slightly fancier facilities. These were probably overkill for the kinds of things Paul Berg was worried about." (Church and Grace 2015, 4)

93 "Satisfying their terms is a condition of NIH funding, and they are also widely accepted and followed voluntarily by scientists and organizations, both public and private, across the research enterprise. In addition, other government agencies, including DOE, the Department of Veterans Affairs, and USDA, currently have policies in place that state that all recombinant DNA research conducted or funded by those agencies must comply with the NIH Guidelines. Through an active process of public engagement and deliberation, they have become a 'gold standard' that is cross-referenced by numerous resources, including Biosafety in Microbiological and Biomedical Laboratories (BMBL)." (Bonham et al. 2010)

". . . From a legal standpoint, however, the Guidelines were quite weak, not even achieving the status of a regulation. It was generally felt that the only legal basis for enforcement arose from contract law. Institutions which received funds from the NIH could lose such funds for violation of the guidelines. To provide a stronger contractual basis for the revocation of funds, the NIH initially required a 'Memorandum of Understanding and Agreement' to be signed by an institution indicating, that it would abide by the guidelines.

"With contract law providing the means of enforcing compliance, there was a rather large loophole in enforcing the guidelines. Individuals or organizations not dependent on the NIH for funding were not required to comply with the Guidelines. From a comprehensive standpoint, the legal basis for the Guidelines left many questions unanswered." (Barkstrom 1985)

94 The rest of the section corroborates this, and David Baltimore agrees: "David doesn't know whether preparations would have averted problems had the technology been as risky as it was sometimes feared

to be. He suggests that the only way to answer that question seriously might be to develop specific scenarios and ask whether each scenario would have been averted by putting certain safeguards in place, rather than trying to think about it in generality." (Baltimore and Grace 2015, 1)

95 See endnote 88 and endnote 89.

96 "Nevertheless, public unease, heightened by perceptions of conflicts of interest on the part of scientists entrusted with regulating their own research, fuelled media and political debates. The environmental activist Jeremy Rifkin called for a national referendum on recombinant DNA research. Science for the People, an activist organization, filed a lawsuit against NIH when the agency issued the guidelines without an Environmental Impact Statement, as required by federal regulations (although Singer helped draft one the following year)." (National Library of Medicine 2007)

"Scientists were often criticized for assuming leadership in formulating policies, which led some to feel public debate was a great threat, but seemingly also to efforts at public information" (Berg 2004)

97 "A more general criticism which can be applied to Asilomar and subsequent proceedings is that what began as a sincere interest in safety was slowly turned into a legalistic and somewhat transparent shield, useful in the on-going fight against government regulation. Asilomar, it would be argued, was proof positive that the scientific community could regulate itself. From what transpired at the conference, it becomes apparent that the motivation for self-regulation was not always the fear that human tragedy might result from experimentation. Instead, a prime mover for self-regulation was the fear of and contempt for government involvement." (Barkstrom 1985)

"What did the actions taken by the scientific community achieve? First and foremost, we gained the public's trust, for it was the very scientists who were most involved in the work and had every incentive to be left free to pursue their dream that called attention to the risks inherent in the experiments they were doing. Aside from unprecedented nature of that action, the scientists' call for a temporary halt to the experiments that most concerned them and the assumption of responsibility for assessing and dealing with those risks was widely acclaimed as laudable ethical behavior." (Berg 2004)

"Brenner repeatedly warned of the consequences of doing nothing, predicting that such apparently self-serving behaviour would be publicly condemned and that government interference or even legislation would follow." (Berg 2004)

"The threat of regulation constraining the research inappropriately was some motivation for the scientists to ensure they produced recommendations themselves. After that last evening's discussion everybody eventually agreed that if nothing was done, constraints would be imposed on them by the government. It seemed better for them to try to design what they thought was an appropriate oversight. 'The conferees agreed nearly unanimously that it was not possible or feasible to conclude that there was no risk; everybody opted for the necessity of imposing modest guidelines that would mitigate the foreseen risks or possible risks, but allow the research to go on.' " (Berg and Grace 2015, 8)

"[The Berg letter and the forthcoming Asilomar meeting was] an open invitation for the establishment of a burgeoning bureaucracy concerned with monitoring and regulating genetic experimentation." Irving P. Crawford (quoted in Krimsky 1982, 114)

"For, without factual cause and induced by panic of error, a costly bureaucracy would thereby be created whose sole known effect would be to inhibit the considerable benefits to both health and agriculture that will result from this research. Some of these benefits we can now specify without

recourse to speculation. For example, we now know and can define the steps required to produce a medically useful protein, such as insulin, in large amounts in E.coli K12. I choose insulin for this example because there is a verified and increasing shortage of this protein that cannot be met by existing modes of production." (Hogness 1977)

". . . We are all trying to stop any interest in legislation, as that does not seem appropriate and would be inflexible." (Singer 1976)

". . . the one thing that occurred to me during this meeting was that out of this I think there was an attempt to self-regulate science to avoid any government regulation and, and in a way that seemed to be self-serving to me. That's just my opinion, you know." (Boyer n.d.)

"The general feeling I was getting from them was they were looking, you know, it's like the Titanic, they were, they were looking at the possibility that their careers which had suddenly blossomed with the new technologies, was going to be smothered." (McElheny n.d.)

"I was depressed about Asilomar because I couldn't see when we were going to be able to start our experiments, was it going to be a six-month delay, several years. As it was, it turned out a couple of year delay and, but we were finally allowed to do what we did, what, what we wanted and it was wonderful. But for a couple of years I just thought about regulations, not about science." (Watson n.d.)

98 "There were differences among committee members—particularly on two issues. . . . Roblin recalls that some individuals were opposed to a moratorium purely on philosophical grounds. For them the idea of free scientific inquiry was an absolute, and constraints, whether voluntary or mandatory, were a transgression of this inalienable right." (Krimsky 1982, 83)

"A major tension developed during the meeting between those who refused on principle to proscribe any experiments and those she considered it appropriate for some rDNA experiments to be deferred. The latter group had been in the majority and the Asilomar statement reflected its position." (Krimsky 1982, 153)

99 See endnote 51.

100 See endnote 52.

101 "Concern about natural bioweapons has died down in recent years. Attention probably turned from there to artificial organisms arising from recombinant DNA research. Nonetheless, if one wanted to develop a biological weapon, David thinks natural organisms would be a more promising place to look. Pathogens from nature have been tested thoroughly, while synthetic bioweapons need to be tested and the type of testing that is needed might pose difficulties." (Baltimore and Grace 2015, 4)

102 See endnote 97.

103 "Nevertheless, public unease, heightened by perceptions of conflicts of interest on the part of scientists entrusted with regulating their own research, fuelled media and political debates. The environmental activist Jeremy Rifkin called for a national referendum on recombinant DNA research. Science for the People, an activist organization, filed a lawsuit against NIH when the agency issued the guidelines without an Environmental Impact Statement, as required by federal regulations (although Singer helped draft one the following year)." (National Library of Medicine 2007)

"Scientists were often criticized for assuming leadership in formulating policies, which led some to feel public debate was a great threat, but seemingly also to efforts at public information." (Berg 2004)

104 Paul Chapin (Director, Linguistics Program): "I am concerned about the scenario that unfolded after Asilomar. Many scientists were so embittered by the results that they swore they would not willingly take such an open, responsible position again."
William Blanpied (International Policy Specialist, STIA Directorate, NSF): "Some of the prime movers—Maxine Singer, for example—said she would not touch another public policy issue for 100years. David Baltimore and James Watson have also been very negative about the aftermath of Asilomar."
(Toumlin 1985)

"But another Asilomar participant, David Baltimore, remains proud of the episode: in his view it was right 'to engage society in thinking about the problems, because we know that society could block us from realising the tremendous benefits of this work unless we square with them and lead them in thinking through the problems.' " (Rees 2003, 76)

105 See endnote 19.

106 See endnote 97.

107 See endnote 163 for evidence that federal legislation was never passed.

"[Singer] participated in hearings by the city of Cambridge, Massachusetts, about recombinant DNA research at MIT and Harvard in the summer of 1976, at which she defended the efficacy of the NIH guidelines. The council nonetheless imposed a three-months ban on such research, later extended to six, and created the Cambridge Experimental Review Board, a majority of its members non-scientists. Singer joined other prominent researchers in giving expert testimony in Congress opposing federal recombinant DNA bills." (National Library of Medicine 2007)

108 "The Asilomar conference has become a very celebrated event, because of how it emerged, and the issues it addressed. 'Some people believe that the Asilomar Conference suggests a way to solve a problem in science is to get together a lot of the people who know something about the field and be able to provide a way forward. The Asilomar conference was the most formal way of addressing it that ever occurred, that I know of.' " (Berg and Grace 2015, 10)

"Singer has gone further, suggesting that this approach should be applied to the approval process for all new biological technologies, such as genetically modified crops." (National Library of Medicine 2007)

"The success of the conference can be judged on its initial objectives, but its unintended impact was far reaching. Asilomar emerged as a model for setting science policy, and it is this outcome which has stimulated as much debate as the recommendations themselves." (Krimsky 1982, 148)

109 "Berg has doubts whether that model will work in many other situations. Asilomar worked because there was an over-riding necessity to come to a solution to the issues that were raised. They were not hampered by ethical, religious or political concerns. Similar attempts during the debates about GM foods and the embryonic stem cell issues failed because the scientific issues took a back seat to the concerns mentioned above." (Berg and Grace 2015, 10)

"David says that a fundamental reason for the success of the Asilomar conference was that it was limited to questions of a scientific nature; questions that had been discussed and upon which those involved were confident of some expertise. Even on areas where a strong moral case could be made, such as bioweapons, the conference avoided that kind of discussion.

"People have called for a similar conference for questions surrounding such topics as stem cell research, but David says that it would be impossible to take that approach because, looking at stem cell research, the questions that are being asked are based on religious grounds and societal beliefs, not anything within the scientific domain.

"One example that David gives of a topic that might benefit from something like the Asilomar conference is the question of what kinds of research on viruses, the influenza virus in particular, should be published. He says that some research may be too dangerous to publish, because to do so would enable biological warfare capabilities. Though the subject is somewhat outside the realm of science, David says that it's close enough that scientists can and do discuss the question, which is at the moment, in the hands of journal editors." (Baltimore and Grace 2015, 3)

110 ". . . a copy of the [Gordon Conference] letter was sent to *Science*, where it was published on 21 September 1973." (Krimsky 1982, 76)

"1974 26 July . . . Letter published in *Science* (183:303) by Paul Berg and ten other scientists on the potential biohazards of rDNA molecules." (Krimsky 1982, 348)

"It was decided then that the Berg panel should have the full backing and prestige of the NAS behind its recommendation. The panel was given official NAS status and named Committee on Recombinant DNA molecules, Assembly of Life Sciences." (Krimsky 1982, 84)

"The final statement of the Committee on Recombinant DNA Molecules of the National Academy of Sciences had four parts. . . . Third, the Berg panel requested that the director of NIH establish an advisory committee to accomplish three things: (a) oversee an experimental program of risk assessment; (b) develop procedures to prevent the spread of recombinant molecules; and (c) develop guidelines. . . . The final recommendation called for an international meeting, for the purpose of exchanging scientific information related to the problems raised in the statement." (Krimsky 1982, 87–88)

"On the same day that Paul Berg held a press conference on the moratorium letter (18 July 1974), NIH director Robert S. Stone released a statement that said he would take prompt action in the recommendations of the Berg committee. Very soon after the press conference, Berg, Baltimore, and Leon Jacobs of NIH began a series of discussions on the financial arrangements for running an international conference. . . . When the NIH wrote the contract for the Asilomar Conference, it designated the National Academy of Sciences (NAS) as the recipient. This meant that the NAS was responsible for transmitting a final report to the NIH. It signified that the Organizing Committee was directly responsible to the NAS." (Krimsky 1982, 103–105)

111 "In spite of widespread consternation among many scientists about the proscriptions, the validity of the concerns, and the manner in which they were announced, the moratorium was universally observed." (Berg and Singer 1995)

112 "Berg remembers that Pollack raised the concern that introducing SV40 DNA into bacterium could result in escape of such bacteria and colonization of human beings. '[I] think I reacted negatively to his suggestion. I raised counterarguments, he would make other arguments, and the debate moved back and forth; I remember specifically Pollack saying that he thought the experiment shouldn't be

done. I recall that I was quite annoyed.' . . . But Pollack pressed him on the matter, and Berg decided to consult with several colleagues; their reaction was generally negative. Even some of those he did not speak to personally, such as Cold Spring Harbor's Jim Watson of double-helix fame, were reported to have been critical. On one of Berg's trips to the east coast [sic], he discussed it with Baltimore.

" '[Paul] . . . was [being] attacked from many sides . . . and we talked bout it at some length. . . . I remember one night [at Cold Spring Harbor] we went out for pizza and we spent the whole night talking. . . . [T]he discussion [by others] had at first shocked Paul, but later he realized the basic validity of the worries. . . . I believe that I advised him not to do the proposed experiment. . . . We felt that the probability of hazard was small, but could not argue that it was zero. That was the beginning of a line of reasoning that has led us to where we are now'

". . . Berg . . . was sufficiently persuaded by the arguments over hazard, and by his own assessment of the possible payoff of the experiment, to postpone the planned studies." (Krimsky 1982, 31–32)

113 "When the chairmen of the Asilomar working groups were chosen, two of these individuals, Aaron Shatkin and Donald Brown, sent out a net of correspondence to their colleagues in the scientific community. These letters requested information about the possible risks associated with the types of experiments for which the panels in question were responsible." (Krimsky 1982, 113)

114 "Many people were critical of the guidelines because the guidelines were only imposed on those who had funding from the federal government, and so did not impact the commercial sector. There was a lot of concern whether the industry was going to bypass the constraints, as mild as they were. Berg never worried about industry. As it turned out, industry conformed more so than almost any academic center.

"Berg believes, and thinks many of his colleagues agreed, that the commercial sector would be at great risk if they obviously and openly flaunted the guidelines because their plants and research labs are in amongst communities. Furthermore, it would be to their considerable detriment if their local communities learned that any of their recombinant DNA experiments could be dangerous. Berg speculates that they would have been picketed and closed down if it became known that they had avoided the guidelines. It was much more economically feasible for them to build the most secure facilities that anybody can think of." (Berg and Grace 2015, 9)

115 See endnote 81.

116 "Therefore, I made the decision not to do the experiment, even though I was quite upset about the whole matter and was thinking to myself, 'Well, here is a really good thesis project that I've gotten started on and these guys are telling me I can't do my project.' On the other hand, coming from a radical-type background, I figured, 'Well, even if it's only a one-in-10^{30} chance that there's actually something dangerous that could result, I just don't want to be responsible for that type of danger.' I started thinking in terms of the atomic bomb and similar things. I didn't want to be the person who went ahead and created a monster that killed a million people. Therefore, pretty much by the end of the week, I had decided that I wasn't going to have anything further to do with this project, or for that matter, with anything concerned with recombinant DNA." Janet Mertz (quoted in Krimsky 1982, 31)

117 "The second argument was based upon the notion that our concerns over risks should reflect our current knowledge and not our ignorance. There were some reasonable expectations about how a tumor virus might behave if placed into a bacterium, but that was not so with unknown DNA segments. Consequently greater caution was warranted for the scenarios for which there was knowledge as compared with those that were more conjectural. " Roblin (quoted in Krimsky 1982, 87)

118 See endnote 1.

119 "[Charles A] Thomas, a member of the Recombinant DNA Molecule Program Advisory Committee, which proposed the guidelines to NIH, said that 'none of the experiments have been shown to have high risks and the dangers are purely hypothetical.' " (Takeshita 1976)

"The main concerns people had at the time were concrete ones about cancer causing genes being inserted into intestinal bacteria. But there were also many more speculative concerns around extreme scenarios. . . ."

> "People could allow their imaginations to wander and say, 'Well, what happens if you would put in a Botulinum toxin gene into *E. coli*? Could you produce large quantities of Botulinum toxin? Could you put genes that confer resistance to normally used antibiotics that might go into *E. coli*, but then escape *E. coli* and inhabit the bacteria that produce serious disease?"

"There were a series of this speculations as to whether these kinds of things might be harmful. 'There was no evidence of any such harm, but when the speculations began to become more and more fanciful, and some of them were, we knew that there were such things as cancer genes.' " (Berg and Grace 2015, 5–6)

"The scientific orthodoxy in the rDNA debate looked for evidence that a particular scenario was plausible. It was not sufficient for these decision makers to pose a hypothetical situation illustrating a hazard that did not contradict any evidence. In a sense, these scientists were saying that it is incumbent on those who believe there are risks to show the plausibility of a hypothetical scenario. This is in contrast to the view that scientists bear the responsibility of proving that what they are doing is safe." (Krimsky 1982, 87)

". . . since the estimation of potential hazards is conjectural and speculative, the levels of containment required for potentially hazardous organisms should be set high initially, and modified only when there is substantial relevant information to advise such modifications. And finally that the guidelines are to be reviewed at least annually in order to account for new information" (Singer 1977)

"I think we all went in with a state of mind not knowing much about microbiology, infectious diseases and so on. There was a lot of speculation . . . " (Boyer n.d.)

See also Section 1.3.

120 ". . . at the same time that this debate [about Berg's experiment] was going on, there actually existed a candidate for such an organism [that could carry a tumor virus into the human population], and its 'keeper' was wondering what to do about it. The organism in question was a virus that was a hybrid between the monkey tumor virus SV40 and an agent of acute respiratory disease in young adults and children called adenovirus." (Krimsky 1982, 39)

121 See endnote 60.

122 See Section 3.3.11.

123 "I was struck by how often scientists willingly acknowledged the risks in others' experiments but not in their own." (Berg 2008)

"People, I think, were being very self-serving . . . as I'd discovered two years earlier, everybody [would] like to draw a circle around their work and stamp it as pre and unadulterated, and it's what you're doing which is nasty and needs to be proscribed." Paul Berg (quoted in Krimsky 1982, 143)

"The operative rule among participants was that while one's own experimental system was safe, there was no reason to assume one's neighbor's was." Watson (quoted in Brante, Fuller, and Lynch 1993)

"In her July 1975 interview with MIT's Oral History Program, [Maxine Singer] expressed the opinion that younger scientists were more likely to raise broader socially oriented questions, with the exception of those individuals who were primarily involved in the research under discussion." (Krimsky 1982, 75)

124 "[I] could safely, without threatening my own career, say I was worried about the consequence of raising the infectious concentration of a tumor virus gene by a factor of a hundred million. . . . That worried me, and I could afford to be worried about it. . . . I'm trying to make [it] clear, that I see in my own work, and I see in other people's work, that a shade comes over your eyes when the problems affect your own work. I'm just lucky that by being at Cold Spring Harbor I was exposed to all of this kind of technology without having to use it. I think if I were using it, I probably would have found my own rationalization for not worrying about it. But to be constantly right at the edge of where these things are going on, and to know exactly what was going on in a technical sense, and not to need it, gave me a chance to worry about it. I think that, more than any higher ethical development, is what got me in this business of making noises." (Krimsky 1982, 30)

125 See endnote 123.

126 "One of the factors that prompted concern by top-level scientist related to the ease with which gene transplant could be accomplished. When the technique became available to scientists who did not possess exceptional skill, it began to trouble those who had, up until this time, a virtual monopoly on these procedures." (Krimsky 1982, 95)

127 "Without some form of voting, how could the assembly reach a conclusion? The answer lies in the special relation the organizing committee had with the NAS. The committee's mandate did not include using the assembly as a legislative body. Its job was to produce some recommendations based upon input from the participants." (Krimsky 1982, 143)

128 "[W]e did not expect [our draft] to have a very good reception. . . . [W]e had this big discussion as to whether we would have a vote, and we decided we wouldn't allow a vote . . . because we thought we would be voted down." (Frickel and Moore 2005, 393)

129 "We want to get their views on it [the provisional statement] and where their views are acceptable and useful to us, we'll incorporate them." Paul Berg (quoted in Krimsky 1982, 144)

130 See endnote 62.

131 "Nevertheless, as one observer noted, 'at every point the organizing committee won overwhelmingly with never more than five or six hands raised in opposition'." (Krimsky 1982, 145)

132 "In the end we voted positively in order to meet the deadline and get out, for a document the composition of which we don't precisely know yet." Ephraim Anderson (quoted in Frickel and Moore 2005, 394)

"It seemed to me that they had incorrectly summarized the results of the conference and that the final report was different in several significant respects from the actual draft which everyone asked and voted on the last day." Robert Sinsheimer (quoted in Frickel and Moore 2005, 394)

"When the Committee drafted proposed guidelines, controversy stirred appreciably. Meeting at Woods Hole, Massachusetts in July of 1975, the Committee essentially overrode a draft prepared by a subcommittee and, it was charged, considerably weakened some recommended safety measures. Led by Harvard Medical School's Richard Goldstein, forty-eight biologists petitioned the NIH, complaining that the Committee's draft lowered 'substantially' the safety standards deemed necessary by the scientific community. . . . Extremely sensitive to the criticism, the Committee reviewed drafts of three proposed guidelines, and from these developed a final proposed set of guidelines. Finally, after public meetings and hearings, the formalized Guidelines were issued on June 23, 1976." (Barkstrom 1985)

133 See 42.

134 "Frequently heard in the 1970s were criticisms of scientists for assuming leadership in formulating policies that were matters of public concern." (Berg 2004)

"There were strong appeals on the part of certain nonscientists, who had been consulted for their views of the social and ethical issues, for broad public input into such discussions. But these voices were heard in vain." (Krimsky 1982, 95)

135 "In the matter of selection of participants, the meeting was subsequently criticized for drawing its scientific expertise from too few fields. Most participants were from disciplines that would draw benefits from the new research program. There was little representation from the health sciences and no participants representing environmental interests. An alternative way to convene a conference of this nature might have included: contacting the professional associations that had the expertise in a relevant area (infectious disease, medical microbiology, immunology) for nominations of participants; an open request for papers on the potential risks of using certain hosts in the cloning experiments; contacting environmental organizations for their expertise in problems of monitoring agents that are disseminated in the environment, soliciting participation from agencies and organizations concerned about occupational health. . . . However opening up the process in this way posed the risk of losing control of the issues. This concern was preeminent among the Asilomar organizers." (Krimsky 1982, 151–152)

136 ". . . Richard Novick, chairman of the Plasmid Working Group, explained his interest in having scientists who were (i) involved in the basic foundations of the field and (ii) were also concerned about the consequences of rDNA molecules." (Krimsky 1982, 110)

137 "Another aspect of the conference that Berg credits with helping its success was inclusion of the media. More than ten percent of participants (around 15 people) were from the media. This was a deliberate choice on the part of the organizers. . . .

"A third important factor was inviting a number of other non-scientists. These included ethicists and lawyers. They informed the conference about the consequences if in fact the public was exposed to any risks. They were 'very, very effective' ". (Berg and Grace 2015, 8)

138 See endnote 98.

139 "On the possible diseases created by recombinant DNA, Watson wrote in March 1979: 'I would not spend a penny trying to see if they exist' (Watson 1979:113). Watson's position is that we must go ahead until we experience serious disadvantages. We must take the risk of even a catastrophe that might be hidden in recombinant DNA technology. According to him that is how learning works: until a tiger devours you, you don't know that the jungle is dangerous." Watson (quoted in Brante, Fuller, and Lynch 1993, 260)

"I am personally fearful that one day an experiment in this area is going to produce unexpected and unfortunate results. . . . On the other hand, I would hate to see a world in which there was an enforced prohibition against such experiments. Basically this leads me to a pessimistic outlook for the future . . . " Galston (quoted in Krimsky 1982, 116–117)

"The scientific orthodoxy in the rDNA debate looked for evidence that a particular scenario was plausible. It was not sufficient for these decision makers to pose a hypothetical situation illustrating a hazard that did not contradict any evidence. In a sense, these scientists were saying that it is incumbent on those who believe there are risks to show the plausibility of a hypothetical scenario. This is in contrast to the view that scientists bear the responsibility of proving that what they are doing is safe." (Krimsky 1982, 87)

"Older scientists [at the Gordon Conference discussions], although somewhat mixed in their reactions, according to Singer, were concerned about the possibility of restricting scientific research." (Krimsky 1982, 75)

140 E.g., "We must keep reminding ourselves and others that no one has demonstrated, on the basis of fact, that any hazard is indeed posed by this research." (Hogness 1977)

"Later in 1973, in a draft of the Discussion section of their paper on frog ribosomal DNA . . . Cohen and Boyer . . . added this cautionary sentence: 'However the implications and potential biohazards of experiments exploring this research should be carefully considered, since the biological role of molecular chimeras containing both prokaryotic and eukaryotic genes is unknown.'

"Calling this 'ridiculous, . . . a vague ominous warning,' a reviewer of the manuscript pointed out that the authors had no information to offer about potential dangers, and urged removing the sentence. The authors did so . . . "(Bourne 2011, 96)

"The second argument was based upon the notion that our concerns over risks should reflect our current knowledge and not our ignorance. There were some reasonable expectations about how a tumor virus might behave if placed into a bacterium, but that was not so with unknown DNA segments. Consequently greater caution was warranted for the scenarios for which there was knowledge as compared with those that were more conjectural." Roblin (quoted in Krimsky 1982, 87)

141 See endnote 96.

142 "Some of the most intense opposition to the consensus statement came from members of the plasmid panel. Stanly Falkow recalled the events in an interview with a member of the Oral History Program at MIT. He felt that, for the most part, the plasmid panel was ignored by members of the Organizing Committee when the provisional statement was drafted. . . . 'even though we had gone to great extremes, it seemed that the most stringent prohibitions were being put on the people who worked with microorganisms. So we . . . felt that we had done a lot of work, and they had overlooked a lot of what we had done, and we were very angry about that.' . . . After Asilomar, Falkow revised the plasmid section in the provisional statement. It was passed around the members of the Plasmid Working Group, and finally sent to Berg for insertion in the final version of the report. Novick had

pressed to have the plasmid report published in its entirety because he felt the summary of it that appeared in the provisional statement did not do justice to its scientific findings. The Organizing Committee rejected that proposal. They were concerned that publishing it might give the impression it was a minority report. This has special significance in view of Baltimore's early remark: If the scientists cannot reach consensus, the issue will be taken out of their hands." (Krimsky 1982, 147)

143 "Baltimore puts that decision into perspective. 'But we felt, strategically, that the recommendations about the type one and the type two experiments were obvious enough that people would accept them without a . . . lot of deep thinking. Whereas the arguments about these other types,which have now become known as type three experiments, . . . were more convoluted, that the types of information talked about were vaguer, that we would have much more difficulty getting the statement accepted if we went strong on those than if we went weak on those.' " (Krimsky 1982, 86)

144 "In a very early episode, Andrew Lewis had a potentially dangerous hybrid organism which he hesitated to share with other labs, as was the usual custom. According to Krimsky, 'after Lewis's presentation [at a workshop they were attending], a remarkable scene took place. Watson, whom Lewis did not at first recognize, confronted him during the coffee break with the claim that Lewis had no right to talk about the hybrids if he was not also willing to send them to Cold Spring Harbor. Watson then accused Lewis of conspiring with Lewis's former boss, Huebner, to keep the agents at NIH. . . . Watson then threatened to force release of the virus by one of three mechanisms: (1) He would personally write to the director of the NIH to say there was a conspiracy to keep valuable agents from the scientific community. (2) He would write a letter to *Science* telling them, Lewis later reported "what kind of guy I was, and that I was sitting on these agents and had no right to be doing this when other people were interested in working with them." (3) He would write to congress saying that "public money was being spent to develop reagents not being made available to other people." ' " (Krimsky 1982, 44)

145 "Everybody was worried about a cover-up, you see the Watergate's echoes were so strong. Very few Europeans understood that, but they were so strong, the idea of self-service and cover-up were what is, you know, what are the scientists trying to conceal, sort of thing. So I think that that was, I remember the very first day, all the Press were there, and there was a motion that there was an official tape-recording, and there was a motion that people might wish to speak of free accord. And so they agreed they would switch off the tape, the official tape, if everything, so the question is, would the Press have to switch off their tapes as well. And there was a vote on this and I was the only one who voted for the Press switching off the tape." (Brenner n.d.)

146 "Scientists were often criticized for assuming leadership in formulating policies, which led some to feel public debate was a great threat, but seemingly also to efforts at public information." (Berg 2004)

147 "The regulatory framework put in place at the Asilomar conference was mandatory for recipients of NIH funding, and voluntary for industry. Everyone in the industry obeyed every RAC recommendation. The framework prevented people from running ahead, and influenced decades of recombinant DNA research.

"The thing that safeguarded against deviance from the path set out by the RAC was that the funding agencies took it seriously; even some non-governmental sources insisted on their benefactors following RAC advice. This meant that the whole population of biological researchers almost had to adhere to that advice.

"The funding agencies got on board because the federal government and in particular, the National Institute of Health (NIH) was behind the RAC process. At the time, upward of 90% of the money that went into research was provided by the NIH, so it had significant leverage. The American Can-

cer Society and Howard Hughes Medical Institute were private funders who agreed to follow the directive of the NIH on adhering to the regulations. Even private companies then felt a tremendous pressure to adhere, both under threat of bad publicity and in acknowledgement of the expertise of those who were issuing the advice." (Baltimore and Grace 2015, 2)

148 See endnote 108.

149 "Another aspect of the conference that Berg credits with helping its success was inclusion of the media. More than ten percent of participants (around 15 people) were from the media. This was a deliberate choice on the part of the organizers. They understood that this was a big issue. It had been raised and hyped in the media already. So it was important that this not be "a secretive meeting of scientists, coming out with some conclusion that everybody had to live with". The media attendees were full participants; they could ask questions and make comments, and were indistinguishable from the scientists in terms of being part of the formal discussions and the bull sessions in the evenings. The only constraint on the media participants was that they not try to publish anything during the conference. They were free to publish anything right after it. Everybody subscribed to that. The members of the media produced some excellent articles and some books." (Berg and Grace 2015, 8)

150 See endnote 108.

151 ". . . we made some decisions that were smart in retrospect. for instance one of the things we did not do, and did not include in any way was the ethics, we didn't talk about genetic testing, we didn't talk about . . . we talked about real experiments, and what the impact of those experiments would be in the field, so agriculture, nitrogen fixation you know people had all kinds of ideas of what we called the low hanging fruit." (iBio Magazine 2011)

152 "As a policy-making model for the rDNA debate, Asilomar was severely limited in the following ways: . . . boundaries of discourse. . . . The Organizing Committee had placed specific boundaries on the types of issues it would review. Problems associated with willful misuse of the new technology, the role of rDNA in genetic engineering of humans, and the commercial applications and misapplications were bracketed from the discussions. Thus, the international scientific assembly could, at best, provide one set of the inputs into the policy. While the biohazards were an important input, they did not fully represent the problem." (Krimsky 1982, 151–52)

153 See endnote 108.

154 "An example of this kind of conference failing can be seen in embryonic stem cell research. There the debate could not bypass a religious and ethical one. It is not about whether the science is dangerous (it is not). There were several conferences to discuss these issues but it was impossible to get consensus on anything. People spoke past each other; conversations about when life begins, or what it is, prevented any meaningful exchanges." (Berg and Grace 2015, 11)

155 "One example that David gives of a topic that might benefit from something like the Asilomar conference is the question of what kinds of research on viruses, the influenza virus in particular, should be published. He says that some research may be too dangerous to publish, because to do so would enable biological warfare capabilities. Though the subject is somewhat outside the realm of science, David says that it's close enough that scientists can and do discuss the question, which is at the moment, in the hands of journal editors." (Baltimore and Grace 2015, 3)

156 "We organized it very well so that the meeting was not all talking about risk, it was talking about science. And that was probably a saving grace, why the meeting succeeded because people came prepared to talk about scientific experiments and they were balanced by discussion. There's a lot of interesting science that came out of the Asilomar meeting. One was the safe bug—the engineered microbe which could not escape from the lab. . . . The crippled hosts. . . . so that was Sydney Brenner's idea. . . . He brought that to the meeting and I think that was what turned people around a lot because suddenly we could now answer that question that we could devise the experiments in some way that would markedly lessen the likelihood of escape. So this organism wouldn't be able to live outside the lab. So there were a number . . . right in that meeting, you could see science taking over, people thinking oh we can do this . . . " (iBio Magazine 2011)

"The meeting was designed to keep everybody engaged. There was a danger of scientists becoming bored by discussion only of risks. So they talked about the science itself, and at the same time talking about the possible risks associated with that particular kind of approach."

> "I think, if we'd gone and tried to have a meeting just to deal with risks, many people would not have come and they might not have stayed and they would have been completely bored. Which is the general nature of the scientific community. On the other hand, they were confronted with, 'Here's a technology that has enormous potential. If I want to do it, I have to think about whether there is any risk associated with that experiment.' It was possible to have a discussion interwoven between the benefits and the potential risks." (Berg and Grace 2015, 7)

157 "Roger Dworkin reached Asilomar much on his own initiative. When he got wind of the conference, he contacted Paul Berg directly, requesting an invitation to speak." (Krimsky 1982, 141)

158 "Dworkin's talk took a very practical turn in comparison to the other lawyers. Foremost on his agenda was an examination of liability." (Krimsky 1982, 141)

159 "The turning point of the meeting frankly was the last night, when the lawyers had their session, and the ethicists . . . the lawyers pointed out the legal problems. and challenged Jim Watson with the idea—because he had now turned, and he was totally opposed to any kind of regulation, whereas he had been a signer of the original letter—they said, people could close down cold springs harbor if there's any danger or anything that happens, and then people's own personal risks were beginning to play on. And eventually I think everybody said 'we cannot walk out of here tomorrow morning saying we don't have any advice'." (iBio Magazine 2011)

How did the talks given by the legal experts affect the scientists at Asilomar? The evidence (from oral interviews of Asilomar participants, questions raised during the discussion period, and from the written account of those who attended) suggest that the social issue of greatest concern to the scientists was their personal liability emphasized in Roger Dworkin's talk. Dworkin's account of the reaction to his talk is found in his post-Asilomar recollections. "What a legal audience would have regarded as commonplace, elementary, and obvious, struck the distinguished scientists as novel, shocking and frightening. Calling the researcher's attention to their potential liability induced a fear in them akin to a layperson's fear of virulent bugs crawling out of a laboratory."

Another participant at Asilomar, Robert Sinsheimer, also felt that the scientists responded to the lawyers strictly from their concern about suits and not because of any moral response to issues raised. Sinsheimer was disturbed about this lack of ethical fiber among the scientists: "If somebody gets cancer because you've done . . . [an experiment,] the point isn't that you're going to pay them a

million dollars to recompense them for it. And yet that kind of attitude was expressed."

As a consequence of Dworkin's presentation, scientists began to understand that their laboratories could fall under the jurisdiction of the Secretary of Labor. The Secretary has the responsibility of implementing the Occupational Safety and Health Act (OSHA). John Lear gives an account of the interrogative period after Dworkin's paper:

> "The question-and-answer session that followed Dworkin's talk left no doubt that he made the deepest impression of the evening. The vision he had conjured up of inspectors from the U.S. Department of Labor swooping down on research laboratories without warning and slapping fines or jail sentences on slovenly experimenters was too much to contemplate with serenity, so alien was it to the permissive regulations of the NIH, which are promulgated at least as much by the researchers themselves as by the officials who are ultimately responsible.
>
> "Richard Roblin recalled that many scientists in the room listened attentively when the OSHA laws were discussed. Roblin observed that there was little awareness among scientists that the secretary of labor and not the secretary of HEW was responsible for the safety of the workplace. As a consequence of this session, some scientists were willing to proceed more cautiously with their work and accept a modicum of regulation. Moreover, they preferred that any oversight came from their benefactor, NIH, and not from 'alien' sectors of government." (Krimsky 1982, 141–142)

"A third important factor was inviting a number of other non-scientists. These included ethicists and lawyers. They informed the conference about the consequences if in fact the public was exposed to any risks. They were 'very, very effective'. They warned that you could not walk away saying nothing could be done, because you would be making yourself legally and financially vulnerable should anything happen. 'A number of the scientists, when confronted with some of those consequences, blanched.'

"That was the last evening of the meeting and Berg feels these presentations changed the discussion and the outcome of the meeting quite dramatically. 'People who had said, "Oh, it's not a big deal. We'll just go on"—These ethicists and lawyers put the fear of God [in them], and put everybody who were there at risk. Generally, there was a very strong feeling toward the end of the scientific and discussion meeting, that we could not avoid making a recommendation. We couldn't just say, "We don't know and let's do what we want." ' " (Berg and Grace 2015, 8)

160 See endnote 97.

161 "Restrictive national legislation was avoided, and in the long run, scientists benefitted from their forthrightness and prudent actions in the face of uncertainty." (Berg and Singer 1995)

162 "A few corporate people participated in the Asilomar conference. For instance Eli Lilly was represented, because they were the major producers of insulin, so the prospects of being able to make insulin through recombinant DNA was important for them." (Berg and Grace 2015, 9)

163 Larry Goldstein: "So when did the Congress get into the act? When did the politicians decide that this was something they should worry about?"

Paul Berg: "Okay, so, the Asilomar meeting was held in February of 1975. The rest of that year there were small groups that were meeting to devise the guidelines. The guidelines came out in the summer of '76. And that ruled the day. And then sniping occurred. And the sniping occurred from different people who said, "well, these guidelines are not rigorous enough," or, "we don't trust the scientists or abide by them." Congress began to respond to these little barbs and they set on a course that they were actually going to prohibit recombinant

DNA research in the country. And I remember spending a lot of time in Congress and I can remember vividly one Senator from Arkansas who is normally a liberal and was a pretty good guy getting up and saying on the floor of the Senate, "I never got through high school chemistry, and I don't profess to understand any of this science, but I believe this is the most dangerous work ever undertaken in this country, and I would recommend prohibiting it." There were a lot of people who shared that view, and I am cynical enough to now realize that what changed the whole picture and obliterated the concerns was the founding of Genentech and the first phase stock issue."

Larry Goldstein: "Ahh, money."

Paul Berg: "Money. Suddenly it became clear that this was going to be a commercial entity and important, and to put any prohibitions on it was like shooting yourself in the foot. And the whole thing disappeared."

Larry Goldstein: "So the promise of making insulin for kids was not the winning message, you think?"

Paul Berg: "It was a message, but when you actually saw something happen that was the, I believe, that was thing that actually was the switch. And the atmosphere changed completely as soon as it became a couple of companies starting up to take advantage of this technology to do this that and the other thing."

Larry Goldstein: "So ultimately the resolution of this was, if I understand, if I remember correctly, no law was ever passed in the Congress."

Paul Berg: "No law was passed."

Larry Goldstein: "And it was all done by scientists driving the development of good regulation through the funding bodies, which then spread."

Paul Berg: "Exactly."

(iBio Magazine 2011)

164 ". . . there is a lesson in Asilomar for all of science: the best way to respond to concerns created by emerging knowledge or early-stage technologies is for scientists from publicly funded institutions to find common cause with the wider public about the best way to regulate—as early as possible. Once scientists from corporations begin to dominate the research enterprise, it will simply be too late." (Berg 2008)

165 "There are now even more reasons for exercising restraint, but a voluntary consensus would be far harder to achieve today: the community is far larger, and competition (enhanced by commercial pressures) is more intense." (Rees 2003)

166 "Many people were critical of the guidelines because the guidelines were only imposed on those who had funding from the federal government, and so did not impact the commercial sector. There was a lot of concern whether the industry was going to bypass the constraints, as mild as they were. Berg never worried about industry. As it turned out, industry conformed more so than almost any academic center.

"Berg believes, and thinks many of his colleagues agreed, that the commercial sector would be at great risk if they obviously and openly flaunted the guidelines because their plants and research labs are in amongst communities. Furthermore, it would be to their considerable detriment if their local communities learned that any of their recombinant DNA experiments could be dangerous. Berg speculates that they would have been picketed and closed down if it became known that they had avoided the guidelines. It was much more economically feasible for them to build the most secure facilities that anybody can think of. Academia, on the other hand, had less money for such infrastructure. They could afford some simple modifications of existing labs. It is also perhaps relevant

that the industry scientists were a long way behind the academic scientists. When the technology emerged, there was nobody in the commercial labs or in their ranks who know how to use it. For the first five or ten years even, most corporate research labs didn't have anybody there working along these lines or anyone who understood the technology. Berg's department sponsored an industrial affiliates program to educate industry scientists about the technology, the potential, and some of the things that could be done with it." (Berg and Grace 2015, 9)

"Even private companies then felt a tremendous pressure to adhere, both under threat of bad publicity and in acknowledgement of the expertise of those who were issuing the advice." (Baltimore and Grace 2015, 2)

167 See endnote 30.

168 "One circumstance that increased enthusiasm for the Asilomar Conference was that people's concerns had already been aroused by the earlier Asilomar meeting on tumor viruses. Now, suddenly, tumor virus genes could be manipulated easily, which upped the ante of that concern." (Berg and Grace 2015, 5)

169 "Exacerbating public fears, Michael Crichton's novel *The Andromeda Strain* had been published in 1969 and spent thirty weeks on the New York Times bestseller list. His horror story tracked a deadly virus that kills the residents of an Arizona town by turning them into heaps of powdered bone. It included a slew of authentic touches, including long scientific explanations, computer printouts, historical facts, and references to actual scientific papers. It was made into a motion picture within eighteen months of publication. *The Andromeda Strain* did for biology what *Jaws* did for beaches. Americans are afraid of diseases and fascinated with their invisible power. On the day after the Asilomar conference, the Boston Globe ran a front page headline, 'Scientists to Resume Risky Work on Genes: Danger of Andromeda Strain Posed.' " (Crotty 2001, 112)

"Public fears were fed by science fiction scenarios such as Michael Crichton's *The Andromeda Strain*." (Berg 2008)

"Public fear was fanned by the popularity of *The Andromeda Strain* and the myriad 'what ifs' floated by both serious and demagogic commentators." (Berg and Singer 1995)

170 See endnote 165.

171 ". . . the very vigor of the response at the Gordon Conference and the rapidity with which it set in motion a chain of events that were to have local, national, and international repercussions suggests that the ground had already been prepared.

"For several years prior to the advent of the specific technology designated as recombinant DNA (abbreviated rDNA) techniques, there had been concerns about related research problems within the scientific community. These concerns, which were precursors to many or most of the elements in the later debate, reflected more general problems related to science's ethical, social, and political ramifications. Thus , while the previously inchoate state of these anxieties came to a focus in the gene-splicing technology reported at the Gordon Conference, they certainly existed prior to that meeting. . . .

". . . [the 1960s and early 1970s] marked a watershed in the political consciousness of many who were later to be embroiled in the rDNA controversy. That consciousness was formed under the twin impacts of the abrupt tearing of the American social fabric as civil disorder and violent protest hit city after city and the consequences of American military adventure abroad. . . .

". . . [MIT] was in many ways typical. The institute seemed to be torn apart as students and fac-

ulty violently opposed to the war confronted their classmates and colleagues who, if not exactly in favor of the war, at least saw nothing wrong with working on research projects whole sole aim was to further US capabilities to wage it. . . . On one hand, [technology] offered the means for reducing US casualties. But . . . it meant prolonging the engagement and increasing the effectiveness of weapons intended for the destruction of the environment and human life. Some believed technology could make war more humane. . . .

". . . In this heady atmosphere there functioned an array of scientist-oriented political-interest groups whose modes of operation were also to be recreated by others in the rDNA debate. . . . The oldest, largest, and strongest of these groups was the politically moderate Federation of American Scientists. . . . Several groups were similar to the FAS in their conception of the 'special responsibility' of scientists to inform and, if need be, instruct the public on matters of technoscientific importance. . . .

". . . [these moderate-scientist political-interest groups] were primarily composed of professionally established scientists from recognized elite institutions like Harvard and MIT. . . . Their critiques of government policy generally excluded critiques of the economic and political system itself. This is not true of the radical groups that were also active in this period. Two of these groups deserve special mention: The Medical Committee for Human Rights (MCHR) and Scientists and Engineers for Social and Political Action (SESPA) . . .

". . . MCHR had by 1972 twenty-four local chapters . . . [and it] brought to the medical faculty the same questions that were put to their scientist and engineering colleagues by radical activists on the liberal-arts campus: 'Who will profit from your work? Who might be harmed by it? Whose interest does it serve? What alternatives are there?' . . . SESPA, now more generally known . . . as Science for the People, was formed by physicists in 1969. . . . Confronting the scientific establishment at professional meetings like the American Association for the Advancement of Science (AAAS) became a favorite tactic . . . their focus on the tendencies in science to justify the status quo and the legitimate social and economic meritocracies made genetics and genetic engineering one of the natural issues to attract Science for the People members; and the later rDNA debate proved to be no exception to this general pattern." (Krimsky 1982, 13–20)

172 ". . . some participants in the rDNA debate have drawn explicit parallels between the gene-splicing technology and the early years of the application of atomic energy. The secrecy shrouding the development of a nuclear arsenal was a great source of guilt and embarrassment to some members of the scientific establishment. Henceforth, that period became an effective reference point for looking at policy issues involving the use of rDNA technology." (Krimsky 1982, 17)

"We were troubled . . . by the fact that except for the scientist and the Army there was no foreknowledge of the tremendous implications of the atom bomb." Aaron Novick (quoted in Krimsky 1982, 17)

"The parallels between recombinant DNA and nuclear energy were drawn early by both scientists and the public. Before the Asilomar conference, in correspondence on the hazards of recombinant DNA, Daniel Singer sent Baltimore a copy of the 1939 letter from Albert Einstein and Leo Szilard to Franklin Roosevelt on the danger of the atomic bomb. In 1972 , Baltimore had given a lecture at a faculty lunch meeting about the dangers of biology 'commonly analogous to the atom bomb.' When the recombinant DNA controversy began to heat up, Baltimore was also involved in a public discussion at MIT with Philip Morrison, the physicist who armed the *Enola Gay's* atomic bombs on Tinian Island and had since been vocal in efforts to eradicate nuclear arms. The discussion, titled 'When Does Molecular Biology Become More of a Hazard than a Promise?' explored the parallels between the development of atomic weapons and recombinant DNA. Morrison found only a few historical parallels, but he strongly believed that the power created by the new technology needed careful assessment. A number of the physicists involved in the Manhattan Project were at MIT.

'Those people were around here—Vicki Weisskopf and Philip Morrison and Jerry Weisner—and were friends,' Baltimore noted. 'So we were very conscious of that as a precedent. I think it's fair to say that they had set a very good example of scientific responsibility—of looking coldly at what they had done and saying, "There are implications for this in society—on our own terms, and not simply the politicians'." ' Baltimore chuckled as he continued, 'They had been notably unsuccessful in doing that, but they were the conscience of a country. It takes a long time for things to come around, but I think that they, in the end, had a very salutary influence in the country. And yes, we were certainly aware of that parallel. Even though it was a very different situation than nuclear war. No weapons of mass destruction. We hoped, anyway,' and Baltimore smiled faintly." (Crotty 2001, 112–113)

173 "In any event, Mertz thought of herself as an MIT-type 'middle-of-the-road radical' and was similarly disposed to view genetic engineering with disfavor. When Berg suggested the lambda phage-SV40 experiment to her, she wondered to herself whether she were not now about to take another step toward that undesirable possibility: 'I remember after talking with [Berg] . . . I went off and spent a long time thinking about this whole thing because . . . I wanted to work for [him] at that . . . time . . . but there was the whole question that bothered me, in terms of thinking back to MIT, of whether I wanted to be involved in developing genetic engineering techniques.' " (Krimsky 1982, 29)

174 "I guess I had kind of undergone a certain transformation over the period from probably '68 to '70, which a lot of people did, from being involved or trying to be involved in larger political issues—as a speaker I'd . . . been involved in the Left Wing in San Diego [while at the Salk Institute], and here [MIT], to a certain extent, I'd been involved in the March 4th organization [a one-day work stoppage to protest university involvement in the war], that kind of thing—to the feeling that if I was going to do anything, it ought to be within the field I know best, because I'd been . . . ineffective outside of it. Like everybody else was, or almost everybody else. And so I was sensitized to issues that involved the biological community, and felt that if I was going to put in political time, it should be there rather than anywhere else. And this specific issue of biohazards became a concern to me because I was a newcomer to a field which presented the greatest potential hazard at the time, which was tumor viruses. And I saw people being incredibly sloppy about things, but also I found a kind of know-nothingism among a lot of people working with phages and bacteria and biochemistry who didn't have anything to do with animal virology who were just on me all the time." David Baltimore (quoted in Krimsky 1982, 26)

175 "*Science's* reputation had been tainted by a number of technological horrors in the previous two decades. Rachel Carson's *Silent Spring*, published in 1962, exposed the dangers created by the chemical industries, most prominently represented by DDT and PCBs, and later Agent Orange and asbestos. Her stories about the deadly effects of chemicals helped start a massive environmental movement in the United States, one that focussed on the devastating results of the ignorance and complicity of scientists and the self-serving shortsightedness of the chemical industry. Millions of Americans participated in Earth Day in 1970, celebrating the earth and condemning pollution. By the time of the Asilomar conference, environmental groups such as the Natural Resources Defense Council and the World Wildlife Fund were mobilizing to lobby against recombinant DNA." (Crotty 2001, 112)

176 "By the time of the 1973 Gordon Conference, there was a considerable body of literature on bioethics in general and genetic engineering in particular. Most scientists active in the area had been exposed to at least some speculation about the moral dilemmas inherent in the development of the field." (Krimsky 1982, 22)

177 "Knowing of these possibilities and of Kass's interest in them, the Singers had invited Berg to have dinner with them at their home in Washington in the fall of 1970; Leon Kass was also invited. . . .

They talked at great length about the 'ethical basis of science.' A few days later, Kass sent Berg a letter, with a copy to the Singers, recapping the discussion and raising some questions he felt merited further discussion 'sooner rather than later'. . . in recalling their conversation later, Berg remarked, '[I] was unpersuaded. I was pretty much convinced that many of the fears people were expressing were red herrings. . . . ' Maxine Singer, to whom a copy of the letter was also sent, may have taken it more to heart. The action she took at the Gordon Conference in the summer of of 1973 in publicizing the potentially adverse consequences of a new scientific development was precisely one of the recommendations that Kass had made in his letter." (Krimsky 1982, 33–36)

178 "Most of the concerns were about the biohazard aspects of the experiment. But there were those besides Janet Mertz who looked to the larger issues, and two of these were Daniel Singer, a real-estate lawyer and former general counsel of FAS, who is the husband of biochemist Maxine Singer. . . . Kass and Daniel Singer were also friends and associates of the Hastings Institute of Society, Ethics and the Life Sciences, a bioethics think tank located outside New York City." (Krimsky 1982, 32)

"The three lawyers who participated in this session were Daniel Singer (affiliated with a Washington, DC, law firm and with the Hastings Institute), Roger Dworkin (a law professor at Indiana University), and Alex Capron (a law professor at the University of Pennsylvania)." (Krimsky 1982, 138)

179 See endnote 32.

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