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Governance Lessons for CRISPR/Cas9 from the Missed Opportunities of Asilomar

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ABSTRACT: The 1975 Asilomar Conference on Recombinant DNA (rDNA) research is frequently cited as a great success in the history of science and technology policy. It demonstrated that scientists could come together to develop policy recommendations that would contain emerging concerns about a new technology, while allowing the technology to develop. In the years since, the Asilomar model has been used repeatedly, on technologies from synthetic biology to geoengineering, and is now invoked repeatedly in discussions about regulating CRISPR/Cas9, the new gene-editing technology. In this article, I argue that it is both a poor and politically dangerous modes for governing emerging technologies, and for CRISPR/Cas9 in particular. While it is usually lauded for containing controversy and building consensus efficiently, I suggest that it was far too limited in terms of both its participants and its scope. As a result, it missed opportunities to anticipate and address emerging concerns related to the ethical, social, and economic concerns of biotechnology, which has embroiled much of the world in controversy since. I conclude by suggesting how we can do better in developing a governance framework for CRISPR/Cas9, by carefully deploying the insights developed by scholars of science and technology policy and by learning the lessons of history. This will require policymakers to develop a more critical understanding of problem framing and its consequences, think creatively about regulatory interventions, and incorporate public expertise.

KEY WORDS: policy, expertise, patent, socioeconomic, moral, history, science and technology studies, genetic engineering

I. INTRODUCTION

In January 2015, a group of eminent biologists and ethicists met in Napa, California, to consider the implications of CRISPR/Cas9, the new gene-editing technology that has provoked concern around the world. A few months later, this group proposed a global moratorium on the technology until responsible uses could be identified.[1]

By demonstrating that scientists could be trusted to build consensus on a controversial technology and regulate themselves, this meeting followed in the footsteps of the International Congress on Recombinant DNA molecules, held 40 years earlier and only a few miles away, at the Asilomar Conference Center in Monterey, California. Known today as the first example of scientific self-regulation that contained growing concerns about the emerging field of biotechnology, the 1975 Asilomar conference had brought together 150 experts to establish consensus on how to conduct responsible recombinant DNA (rDNA) research.[2] rDNA research involved cutting DNA at specified places and recombining it, which would produce new life forms. Scientists hoped that it would allow

them to make molecular interventions that could improve health and agriculture, among other things. But, they also worried about the hazards of this first biotechnological step, for laboratory workers, as well as for the global public and environment if the newly created genetically modified organisms escaped from the laboratory. The 1975 Asilomar conference, which was funded by the National Institutes of Health (NIH) and convened by the National Academy of Sciences, the central external advisory body for US science and technology policy, was designed to address these concerns. Conference participants reported on the state of the science, and assessed the potential benefits and risks of genetic engineering. They then worked together to develop a set of principles to guide research. These included suggestions for proper biosafety, and containment strategies based on the level of risk involved in the experiment. Soon, the NIH would adopt these recommendations to guide its approach to funding rDNA research. It convened a standing Recombinant DNA Advisory Committee (RAC), composed primarily of scientists in the field with a few non-scientists included, to review all funding requests related to rDNA research and assess its risks and the proposed containment methods. In order to receive NIH funding, scientists interested in conducting rDNA research would have to satify the RAC. The Asilomar rDNA conference, it seemed, had led to the implementation of a clear regulatory framework and largely pre-empted controversy. Of course, it only applied to NIH-funded research.

Since then, the ghost of the 1975 Asilomar rDNA conference has loomed large in the world of science and technology policymaking. In 2005, it inspired the Synthetic Biology 2.0 conference in Berkeley, California, which was designed to develop responsible research guidelines for building biological organisms *de novo* (synthetic biology).[3] In 2009, it inspired one hundred physicists and engineers—with a small handful of ethicists and social scientists thrown in for good measure—to come back to the Asilomar conference grounds, hoping that the waters of the Pacific Ocean would again produce a framework for regulating geoengineering technologies.[4] Some believe that these large-scale technologies, which involve removing carbon dioxide from the environment or limiting the impacts of solar radiation, hold promise for mitigating climate change. But even geoengineering's proponents accept that it is extremely unpredictable, and may have sweeping, universe-wide, impacts. And over the last year, the ghost has returned in the context of CRISPR/Cas9. It inspired the January 2015 Napa conference, and the December 2015 International Summit on Human Gene Editing.[5] Since then, it has been frequently invoked by those seeking resolution and a path forward for the use of this gene-editing technology, which has provoked worldwide concern because of its relative efficiency compared to now-traditional genetic engineering techniques.[5] Of particular concern is the prospect of gene-editing human embryos, which Chinese scientists have already attempted and the UK Human Fertilization and Embryology Authority has approved in limited form as of January 2016.[6,7]

But, the Asilomar approach is a poor and politically dangerous model for governing emerging technologies, and CRISPR/Cas9 in particular. While it is usually lauded for containing controversy and building consensus efficiently, I argue in this article that it

was far too limited in terms of both its participants and its scope. As a result, it missed opportunities to anticipate and address emerging concerns related to the ethical, social, and economic concerns of biotechnology, which has embroiled much of the world in controversy since. I conclude by suggesting how we can do better in developing a governance framework for CRISPR/Cas9, by carefully deploying the insights developed by scholars of science and technology policy and by learning the lessons of history.

A. The Missed Opportunities of Asilomar

When biologist Paul Berg and his colleagues convened the 1975 Asilomar conference, there were already wide-ranging concerns about the ethical, social, economic, and national security implications of biotechnology. Some scientists, especially those galvanized by the anti-war movements of the time, worried that this new technology could be used to engineer bioweapons that could transform warfare.[2,8] Other scientists and civil society groups had begun to raise both ethical and socioeconomic concerns.[9] Was it ethical to manipulate life, they asked? How might such manipulation transform the relationship between humans and the natural world? And what about the industrial concerns involved? What would be the impacts of commodifying and owning living organisms? Indeed, in 1976, when citizens in Cambridge, Massachusetts issued a report on the risks of rDNA research, they noted these issues and suggested, "The social and ethical implications of genetic research must receive the broadest possible dialogue in our society."[10] And in 1977, civil society activist Jeremy Rifkin would publish the book, *Who Should Play God? The Artificial Creation of Life and What it Means for the Future of the Human Race,* which argued that the new field of biotechnology raised moral questions about the meaning of life that were going unanswered, that the new field could cause serious damage to health and to the environment, and that the emerging governance of biotechnology did not reflect democratic principles.[11] Rifkin, who later became known as a biotechnology gadfly, was also one of the first to raise concerns about the corporate control of biotechnology, worried that a small handful of companies would be privy "to the secret of life and how to manipulate and change it".[12] By the end of the 1970s, Rifkin would assemble a civil society coalition to challenge, unsuccessfully, the patentability of life forms in the *Diamond v. Chakrabarty* case on the basis of these worries.[13]

Despite these wide-ranging concerns, and the diverse voices raising them, the 1975 Asilomar conference was narrow in its approach. It almost completely restricted participation to technical experts, and the public had no role to play. Journalists attended, but could only report on the conference proceedings afterwards and without individual attribution. In addition, on the first day of the meeting, biologist and conference co-chair David Baltimore ruled both moral and national security concerns out of the discussion. He argued that the conference provided neither the time nor the appropriate place for this discussion.[14] And while two lawyers offered their perspectives on the last night of the conference, their involvement in the discussion and in the final governance framework were limited.[15] In sum, the Asilomar conference framed the rDNA problem primarily in technical terms, and on the hazards of the new technique, with participants focused on

how, not *whether*, to move forward.[10] Since almost all of the meeting participants were eminent scientists working in the nascent genetic engineering field, this is not at all surprising. Furthermore, American political culture has a long tradition of focusing on quantitative—and specifically risk—measures to inform policy.[16,17]

It is understandable that scientists see the Asilomar rDNA conference as a great success. It enabled rDNA research to move forward, and focused regulation on issues that they were accustomed to considering. But the conference also focused US discussion about regulating biotechnology exclusively on issues of risk. The ethical and socioeconomic dimensions of the technology were treated as outside the scope of regulation. While the federal government asked bioethics committees to consider these issues, their reports served primarily to inform the public rather than to develop regulatory frameworks that could be implemented.[18,19] The moral and socioeconomic concerns themselves were treated as essentially ungovernable.

But in the years since, worries that were nascent at the time of the conference have erupted into full-scale controversy. We have seen repeated challenges, in the courts, at patent offices, and in the streets, to patents on life forms including human genes, stem cells, and genetically modified plants and animals. Citizens argue that these patents are transforming how we understand life, and relationships between humans and nature.[20] They also suggest that these patents are having harmful distributional impacts, constraining scientific research, patients' access to health care, and the autonomy of farmers.[13] Meanwhile, with each new biotechnology, from genetic testing to human embryonic stem cell therapy, comes familiar moral questions about whether we should engage in such interventions and how such interventions might transform our world.[21] And finally, social movements have mobilized to challenge the health, environmental, and socioeconomic implications of genetically modified foods, which they argue are producing an unnecessary and dangerous transformation in our food system.[22] Some worry that the rise of these controversies, and the limited regulatory infrastructure developed to respond to them, has done lasting damage to the legitimacy of science and technology policy institutions in the United States.[20]

With this legacy in mind, Asilomar no longer seems so successful. Instead, it seems like a lost opportunity to engage a broad public in biotechnology decisionmaking and to develop governance frameworks that might proactively address their concerns. While this broader approach may have constrained research in the short term, it may have reduced citizen distrust in the long term. In addition, it could have bent biotechnological development more towards social concerns and priorities.

B. Governance Lessons for CRISPR/Cas9

Clearly, those who see the Asilomar approach as a model have already learned some lessons from this history. The meetings convened to discuss CRISPR/Cas9, including the 2015 Napa conference and the December 2015 International Summit on Human Gene Editing, not to mention working groups convened by the National Academy of Sciences, have included ethicists, sociologists, and average citizens in the discussions.[23] But there are still many more lessons to be learned.

1. Develop a More Critical Understanding of Problem Framing and its Consequences

In governance discussions regarding CRISPR/Cas9, just as with regulating rDNA research, scientists doing research in the area are still seen as the primary experts, and the most important data to consider is how this technique works. This quietly and implicitly frames the discussion in technical terms. We see this technical problem framing everywhere. Newspaper articles explaining the new gene-editing technology quote scientific experts before they move to the ethical concerns, and international meetings on regulating CRISPR/Cas9 first lay the scientific groundwork before addressing the ethical, societal, and related concerns. This approach assumes that the non-scientific experts at the table are secondary to the process, and by extension, less knowledgeable and relevant. But the legacy of the 1975 Asilomar conference teaches us that this approach has two limitations. First, this technical approach privileges those who have scientific interests and excitement in moving forward with the technology. These interests likely prevent them from taking a fundamentally critical stance, and therefore force decisionmakers to focus on the question of *how* to move forward rather than to ask first, *whether* to do so. Second, it limits our ability to see and proactively address a technology's implications. Humanists and social scientists can offer specific expertise on the implications of modern biotechnology, and how to address them. But with the technical problem framing, their expertise and the issues that they raise seem to be an addition. But, if governance discussions foregrounded knowledge and expertise related to the broad implications of CRISPR/Cas9, then policymakers might be able to facilitate not just scientific interests, but the public interest more broadly.

Just imagine if we saw humanists and social scientists, many of whom have spent decades analyzing the relationships between science, technology, values, and society, as not just relevant, but primary, experts in the CRISPR/Cas9 discussions. What if they were permitted to frame the problem, and even speak first in meetings and newspaper articles? How might that reframe our approach to this technology and its social impact? Rather than focusing on the technique's efficacy, they might suggest different ways that CRISPR/Cas9 could be deployed to address the day-to-day worries of citizens. They might, for example, raise access and affordability questions, forcing scientists and regulators to think about how they might develop gene-editing so that it might maximize public benefit. They might provide a sense of the moral concerns that preoccupy citizens and offer paths forward. Or, they might invert the discussion completely. They might ask us to focus our attention on social problems like health disparities and then ask how CRISPR/Cas9 could be designated to alleviate them. Regardless, including these voices would give us a better chance of anticipating the concerns that have plagued biotechnology over the last 40 years.

2. Think Creatively About Regulatory Interventions

The Asilomar approach relied on risk assessment and management as the foundation for regulating rDNA research. And since then, biotechnology regulation has similarly

focused its attention on quantifiable risks. As a consequence, the moral and socioeconomic impacts of this emerging area of science and technology have been characterized as outside the scope of regulation or, simply, ungovernable. Policymakers seem to assume that we cannot develop evidence-based and politically legitimate science and technology policies to proactively address these issues. Of course, we know this is untrue. To provide just one example from the US context, in 1978 the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research published the Belmont Report, which summarized ethical principles and guidelines for research involving human subjects.[24] This report led to creation of the NIH's Common Rule, which transformed human subjects research in the United States and around the world.

If we look across the Atlantic Ocean, we can see more examples of regulating biotechnology on the basis of moral and socioeconomic concerns. And their regulatory tools are not limited to research funding.[13] The pan-European patent system prohibits patents on human embryonic stem cells because they involve the commercialization or exploitation of a human embryo. It requires all animal patent applications to undergo a "weighing-up" test, which involves balancing the invention's benefit to humankind against the suffering experienced by the animal. And, it has restricted licensing terms to help researchers, farmers, and patients more easily access patented technologies.

In addition, over the last 40 years, scholars have developed and tested a variety of mechanisms to anticipate the implications of emerging science and technology and attend to them within governance frameworks. These use humanistic and social scientific insights to help scientists and engineers understand how values are embedded in technological design and develop science and technology to maximize societal benefit. These anticipatory technology assessments, which include surveys, analogical case studies, and scenario-planning workshops, occur early in the technology development process and in real-time.[25,26,27] They can be particularly useful in helping innovators reflect on their assumptions about public benefit, while also anticipating and proactively addressing potentially controversial aspects of a technology in its development and design.

3. Incorporate Public Expertise

By treating rDNA as a technical problem, the 1975 Asilomar conference left the public out of the discussion. But in the years since, citizens have become quite vocal in biotechnological matters. And, scholars have shown that laypersons have important expertise to offer science and technology policymakers, whether through their disease experience, their expectations of new technologies, or simply an assessment of their priorities. To produce politically legitimate policymaking for CRISPR/Cas9, then, citizens must be engaged and treated as equals in the discussion.[28] Scholars have tested multiple deliberative democratic forums to accomplish this.[29] Bringing representative cross-sections of the public to carefully consider regulatory options, these forums are designed to ensure informed public input. Participants have the opportunity to engage repeatedly and deeply with the subject matter through written materials and

the guidance of issue experts. They also become equal partners in, rather than just consumers of, science and technology. As these forums proceed, citizens can challenge problem framing and request different evidence and expertise that they deem relevant. They usually conclude with written recommendations for decisionmakers and have successfully influenced science and technology policy on many occasions.[30,31,32] It provides them with the power to make their values and priorities clear, and to reframe the questions at stake accordingly.

Overall, rather than serving as a model for governing emerging science and technology, the 1975 Asilomar conference offers us an important cautionary tale. In order to avoid a similar fate as we develop a governance framework for CRISPR/Cas9, we must think critically about problem framing and its consequences, think creatively about regulatory interventions, and incorporate public expertise. With these tools, we will be in a better position to maximize CRISPR/Cas9's potential for public benefit and ensure political legitimacy for our science and technology governance structures in the process.

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