The Protective Oversight of Highly Consequential Biological Research

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The fundamental problem of biosafety arises from two circumstances: First, it is generally evident that the momentum of discovery in molecular biology in particular is simultaneously enabling therapeutic and destructive applications of extraordinary potential consequence. But, second, no one is able to judge with assurance the exact character or extent of those consequences. Speaking of the human species as a whole, we have collectively initiated the acquisition of knowledge whose ultimate consequences we cannot determine. We have therefore created problems of prudential management we are not as yet either conceptually or institutionally prepared to handle. I understand this forum to be a welcome and important instance of the presumably lengthy effort that will ultimately be required to respond to this situation.[1]

Admittedly technical capability, particularly destructive capability has often exceeded understanding over the course of history, and one can plausibly argue that situations of that sort are a recurring feature of the human condition. Nonetheless this situation does appear to be unprecedented both in character and in magnitude. For the first time in all of history, one species has identified the dynamics of basic life processes in sufficient detail to be able to intervene with some degree of deliberateness in the process of evolution itself. But that capacity is not and will not be accompanied by an ability to understand all the implications. It already seems evident that hundreds of millions of individual lives might in principle be enhanced, salvaged, degraded, manipulated or terminated depending on how advanced knowledge is applied. It is conceivable that the viability of the human species as a whole and of the global ecology on which it depends might be at stake. In the end that may not prove to be correct, but it is prudent to assume that it could be.

If we admit that much, as I believe we are obliged to do, then we are also obliged to imagine a constructive response to the situation. And in doing so we are justified in assuming that the magnitude of potential consequence might eventually induce much more substantial innovation than we would be inclined to expect if current attitudes and institutional arrangements were the exclusive source of guidance. With those observations in mind, I want to outline the criteria required both to establish effective protection against the destructive potential of biotechnology and also to assure full development of its benefits with reasonably equitable access to those benefits. I believe those two purposes – effective protection and equitable access – ultimately depend on each other, despite the natural inclination to purse one at the expense of the other.

[1] My comments are derived from a working paper, Controlling Dangerous Pathogens: A Prototype Protective Oversight System, prepared in collaboration with Nancy Gallagher, Elisa D. Harris and Stacy Okutani at the University of Maryland. See also John Steinbruner and Stacy Okutani, "The Protective Oversight of Biotechnology", *Biosecurity and Bioterrorism*, December 2004.

The Basic Principle

Since the potential for beneficial and destructive application of biotechnology cannot be categorically disentangled, organized protection depends on reinforcing a fundamental principle of behavior already widely supported: namely, that biotechnology should not be used to do deliberate harm under any circumstance for any reason. That prohibition would apply not only to lethal applications but also to non-lethal uses undertaken for coercive purposes. It would also apply to stealthy manipulation. Do no harm is the core principle of the Hippocratic Oath that has been recognized since ancient times. It is also the core principle that underlies prohibition of the use of biological weapons promulgated in the 1925 Geneva Protocol and of the possession of such weapons embodied in the 1972 Biological Weapons Convention. Although neither of those agreements enjoys universal legal adherence, no country currently proclaims the right or the intention to deploy biological weapons. Some have refused to renounce that right as long as nuclear weapons are deployed, but that is not the same as asserting it. The basic principle is already in practice a universal norm, and it could be substantially strengthened with a dedicated effort to do so.

Procedural Rules

The principal method for assuring compliance with the basic principle is also well established. In virtually all areas of human activity where misapplication of significant capability is a serious concern, requirements for independent oversight are imposed. Banks are audited so that they do not divert the money they are entrusted to manage. As best we can judge, no single individual anywhere in the world is ever allowed exclusive control over a nuclear weapon. The leading scientific journals do not publish research results without independent review of their credibility. The degree of vigor with which independent review is exercised is generally related to the degree of concern over misapplication, and that concern, of course, reflects judgments both of probability and of the magnitude of consequence. In some areas of biological research the magnitude of potentially destructive consequence is truly enormous, unprecedentedly so in fact, and the probability of occurrence, however it might be discounted, cannot be determined to be negligible. That almost certainly means that very vigorous oversight procedures will have to be applied to those areas of research.

Since independent oversight is never intrinsically welcome and can itself have perverse consequences, there is and will continue to be strong resistance to applying it to areas of fundamental scientific inquiry where individual autonomy has been highly valued for the best of reasons. Scientists are accustomed to review of scientific merit before they publish their results. They are not accustomed to review of potential social consequence before they initiate the work expected to yield results of scientific merit. Although there are precedents and procedures that can be applied and limited initiatives that can be seen as precursors, there is as yet no review process anywhere in the world comprehensively and systematically assessing inherent social danger with a degree of vigor commensurate with the apparent problem. Eventually, however, despite predictable reluctance, a process that is commensurate with the underlying problem will certainly have to be considered and probably attempted.

If it is to be adequately effective, an independent review process addressing potential social consequence in advance of scientific experimentation would have to operate on a global scale. The remarkable momentum of discovery in molecular biology is the result of widely

dispersed research in the biomedical community, virtually all of it undertaken for compellingly legitimate reasons. The dynamics of infectious disease that pose the primary source of threat are inherently global in character, as has long been recognized. Under these circumstances no oversight process confined to national jurisdiction can aspire to offer adequate protection. Moreover, an adequately effective oversight process would also have to be actively practiced and comprehensively applied in the sense that all relevant areas of research would have to be subjected to the same procedures utilizing consistent criteria of judgment. That almost certainly means that the process would have to be legally mandatory. Voluntary arrangements do not command the commitments of time or the allocation of resources necessary to assure effective performance. Nor by definition do they have the authority necessary to assure compliance.

An oversight process meeting these standards would subject relevant areas of biological research to a degree of independent scrutiny calibrated to the degree of social danger posed. That would require robust and widely accepted determinations of what research is relevant and how degree of danger should be assessed. Achieving effective global consensus on those determinations and their operational implications would undoubtedly be a very demanding venture, but one can nonetheless plausibly imagine how it might work out. The most extreme category of danger, for example, would be reserved for those research activities that might reveal in specific detail how pathogens more lethal or otherwise more objectionably consequential than those that have naturally evolved might be created. All projects of that sort would have to be reviewed in advance at an international level of jurisdiction by people competent to judge both the science involved and the potential social consequence of its application. If approved, implementation of those projects would be monitored, and knowledge of their results would be restricted to globally authorized individuals with legitimate reasons for having that knowledge.

Under such an arrangement, most research with the more dangerous of the currently known pathogens would be assigned to a second tier category of danger, and active oversight would continue to be handled through national jurisdiction. Active international efforts would be undertaken, however, to upgrade national oversight arrangements according to agreed standards and to harmonize the judgments made within separate national jurisdictions. A third tier category would be defined for research activities that are of less immediate concern but might nonetheless create more dangerous pathogens through the application of advanced research techniques. Projects in that category would be subjected to local oversight entities whose review process would be regulated and harmonized by the relevant national review bodies. Most biological research activities would fall outside these categories and would not be subjected to this form of independent review, but efforts would be made to assure general knowledge of the requirements and submission to those requirements at any point when research results appear to require it.

Establishing review procedures of this sort would not provide absolute protection against the deliberately or inadvertently destructive application of biotechnology. It would provide a much more advanced standard of protection than currently exists, however, and would be a necessary foundation for any yet more assertive effort.

Defining Danger

Any serious effort to develop a global oversight process would undoubtedly require considerable conceptual, legal, institutional and political innovation and would involve very substantial adjustment of prevailing public health and national security practices. I will not attempt to assess all that might be entailed, but I would like to emphasize the importance both of devising a viable definition of technical danger and of making a prudent judgment about its

immediate operational character. A credible definition is essential to designing a globally acceptable oversight arrangement. An accurate judgment of immediate threat is critical to the design as well but also to any hope of initiating productive official discussions of the topic.

There are two functional purposes that a definition of technical danger must achieve. It must determine in a generally understood and accepted manner what persons and what projects are to be subjected to what level of oversight. It also must provide a coherent basis for exercising independent judgment in the course of oversight. Those purposes are sufficiently different to affect the nature of the definition advanced. A procedural definition is appropriate for determining oversight jurisdiction. A substantive definition is necessary for making oversight judgments.

In implementing this distinction, the first tier categorization of danger requiring international oversight jurisdiction might be applied to any proposed research with any of the following characteristics:

- Any work on the variola virus (smallpox) or a comparably virulent agent that has been eradicated in nature,
- Any spontaneously infectious agent requiring BSL 4 level of containment,
- Synthesis of any agent matching the above characteristics,
- Expanding the host range or tissue range of any agent that would otherwise be assigned to a lower tier category,
- Constructing vaccine resistant or antibiotic resistant strains of agents that would otherwise be assigned to lower tier categories.

In effect those provisions would formalize and generalize current arrangements for international scrutiny of smallpox research.

With jurisdiction so determined, guidelines for the exercise of international oversight would be based on the intrinsic properties of the pathogens proposed to be either the subject or the product of the research submitted for review; notably, their transmissibility, infectivity and pathogenicity. Transmissibility refers to the ability of a pathogen to propagate spontaneously from one host to another; infectivity to its ability to penetrate a new host and reproduce within it; and pathogenicity to the incidence and severity of the diseases it causes. Of these transmissibility is of particular concern from the perspective of social impact. The ability to threaten large numbers of people, plants or animals in a short period of time essentially depends on a highly transmissible pathogen. Unfortunately the determinants of transmissibility are not well understood or well measured, but that means there is reason to be especially careful.

The operational judgment of immediate danger has to do with assessing the most likely source of destructive application. Deliberate terrorism is clearly the most frequently mentioned candidate, but it is not, I would argue, the most imminent threat. The greater problem arises from national government programs conducting threat assessment activities that are protected from international scrutiny by national security classification. There has been a surge of such activity in the United States in reaction to the malicious use of anthrax in 2001, but other governments are undertaking apparently similar efforts. That process generates reverberating suspicion and creates conditions under which competitive national government programs might create the threats they imagine they are attempting to defeat. The best protection against that danger is to conduct all threat assessment research under public health jurisdiction and rules of transparency. That would be my most urgent immediate recommendation.