PROTECTIVE OVERSIGHT OF BIOTECHNOLOGY: A DISCUSSION PAPER

John Steinbruner
University of Maryland
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Since the terrorist attacks of September 11, virtually all discussion of security policy in the United States has concentrated on the implications of those events. In the immediate aftermath, there was a riveting fear of further assault, and the counterattack against the Al Qaeda network, assumed to be responsible, was given overriding priority. Over its initial phase at least, that effort has been more effective than initially expected and has not generated the political backlash that was considered to be a significant risk. The sense of imminent threat has certainly not been eliminated, but it has been mitigated to the point that broader implications can legitimately command attention – in particular the chilling realization that the disaster would have been far greater had mass destruction technologies been effectively used. It is now embarrassingly evident that we should have been more careful about access to the controls of flying airplanes. By extension we need to be more careful about things that are a great deal more dangerous than airplanes. However successful the continuing suppression of terrorist organizations might be, it is yet more urgent to manage much better than we have both the materials that enable large-scale destruction and the knowledge out of which they arise.

That realization was powerfully reinforced by the subsequent experience with powdered anthrax sent through the United States mail system. As is now widely recognized, the material used in two of the four contaminated letters that have been identified could have been far more destructive had a more effective method of dissemination been used. The few grams contained in the letters could readily have endangered thousands of people, conceivably tens of thousands. A kilogram of that material effectively broadcast could kill hundreds of thousands. Authorities have not yet managed even provisionally to identify the person or group who sent the contaminated letters, let alone to determine any association with the Al Qaeda network. The difficulty of answering these questions after an attack underscores the futility of expecting intelligence, security, and law enforcement officials to identify and eliminate all potential terrorists before they strike. It becomes critically important therefore to enlist biologists, doctors, and other members of the scientific community in a comprehensive effort to monitor inherently dangerous materials, knowledge, and activities as carefully as possible.

While recent events have focused attention on preventing or responding to another deliberate bio-attack, they also underscore the need for care that legitimate research does not inadvertently create even more dangerous pathogens and delivery mechanisms, or unwittingly enable others to do so. It is equally important to avoid having stepped-up biodefense projects be mistaken for offensive programs, and to provide credible reassurance that former bioweapon scientists have not been tempted to abuse their expertise.

Nuclear weapons and the fissile materials that provide their explosive power have long been the primary instance of mass destruction technology, and from the outset their development was accompanied by elaborate efforts to control access and to prevent any form of misuse. The various provisions of managerial control that have evolved over half a century are not adequate

under current circumstances, particularly not in Russia, but they do reflect a sustained attempt to provide reasonably comprehensive protection. The degree of protection actually achieved defines the state of the art as it is currently practiced.

In stark contrast to nuclear materials, the handling of biological pathogens has largely been treated as a matter of safety rather than security, and the protection provided against deliberately malicious use or unintentional misapplication is primitive by comparison. Not so the inherent danger, however. Knowledge of biology has developed to the point that extremely consequential intervention in fundamental life process has become feasible, both for good and for ill. One can plausibly imagine the eradication of many historical diseases. One can also envisage the creation of new diseases that would endanger a larger portion of the human species than is currently threatened by nuclear weapons. With deliberate maliciousness so spectacularly demonstrated on September 11, some serious effort will undoubtedly have to be made to devise methods of protective management for biotechnology while also promoting its beneficial application.

The process of developing advanced measures for these purposes is likely to be both difficult and controversial. Protective measures will apparently have to subject the fundamental research process to forms of scrutiny that up to this point would have been heatedly resisted as inappropriate intrusion -- for reasons that have been transcended but have not disappeared. The looming dangers of biotechnology will not themselves generate an effective oversight design and do not guarantee that the familiar litany of perverse regulatory effects can be avoided. An oversight arrangement that will reliably do more good than harm in this situation is not yet available. Devising such an arrangement is likely to require major conceptual innovation, a substantial adjustment of prevailing political attitudes, and ultimately a creative synthesis of scientific judgment, advanced monitoring and data management technology, legal specification and institutional design.

Accomplishing all that will undoubtedly require time, extensive effort and very broad ranging discussion. In the course of such an effort, many of the original thoughts will presumably be substantially revised. Nonetheless even at the outset of this process, it is possible to envisage, in broad outline, a constructive outcome.

Essential Features of the BW Situation

Comprehension of the problem posed and visualization of a constructive response can both begin with a basic observation: the primary impulse in biotechnology comes from a globally distributed medical and agricultural research community. Most of the fundamental work is being done by people with unquestionably legitimate purposes in mind and is published in open literature at the rate of more than a million items each year. Dedicated weapons projects conducted in secrecy are a very small part of total activity and in general have not been the source of broadly significant scientific discovery. It is increasingly evident that the understanding of basic life processes emerging from this general research effort will enable the human species to intervene deliberately in the course of natural evolution, a development that certainly appears to be a watershed in all of history. Unfortunately that capacity is not matched by the ability to understand the full consequences of such intervention. The human species has

learned how to manipulate some of the basic rules of evolution but has a great deal to learn – virtually everything really -- about the extended consequences.

As a result of this situation it is prudent to assume that inadvertent effects of legitimate research are at least as great a danger as deliberate maliciousness and are probably in fact the greater danger. Those consciously dedicated to destruction are likely to choose instruments they understand, and their understanding is likely to be derived from widely accessible knowledge they did not themselves generate. Those probing the frontiers of knowledge are less likely to be willfully destructive but are more susceptible to unpleasant surprise, as compellingly illustrated by the recent mousepox experiment in Australia.[1] At the moment, there are no established criteria for identifying which lines of research are especially dangerous and deserving of special scrutiny. That determination must be made in highly detailed context and the appropriate response depends heavily on the intentions attributed to the people involved. Not even the very best of them can transcend the limits of what they know.

There are several major implications of this assessment.

First, it suggests that the most serious danger does not yet exist and can still be prevented. The human, animal and plant pathogens that have naturally evolved and are currently known are not as lethal as those that can now be imagined and potentially created. Those pathogens historically associated with biological weapons programs, ominous as they may be, are not as destructive as those that might be deliberately designed. Even the exercises in deliberate design attributed to the Soviet Union's weapons program by prominent defectors are not the worst that can be plausibly conceived. That fact is beneficial in the sense that systematic prevention can in principle be practiced. The monumental problems of eradication presented by massive nuclear weapons deployments have not yet emerged in biotechnology. It is above all important that the deliberate development of advanced pathogens for belligerent purposes not be legitimized.

Second, if unanticipated consequences are assumed to be a principal part of the problem, that presumption offers some important advantages in constructing oversight provisions. One can promote them without implying suspicion of criminal intent. One can design them on the assumption that most of the people affected are willing to comply as long as the rationale is understood and the procedures are not unduly burdensome. One can evoke as the basis for the arrangement the very powerful traditions of the medical community. The commitment of that community to the promotion of human health and its universally acknowledged injunction to do no harm are arguably the human values most capable of transcending the parochial conflicts of interest and identity that are usually used to justify deliberate destructiveness. If robust oversight practices were established among the vast majority of researchers whose purposes are legitimate, it would make willful violation much more difficult to accomplish than it currently is. It would also make timely detection and preemptive reaction much more feasible. More refined and better organized standards of behavior within the legitimate community would appear to be the single most effective means of providing protection against inadvertent destructiveness and are a necessary condition for dealing with deliberate maliciousness.

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[1] Ronald J. Jackson et al., "Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox," *Journal of Virology,* Feb. 2001, 1205-1210.

Third, if the scientific roots of dangerous application are so closely intertwined with legitimate ones that those most immediately involved can have difficulty applying the distinction, then a viable oversight arrangement must strike a balance between preventing danger and promoting opportunity. General research techniques that promise constructive applications will certainly be developed even if they do pose massive danger as well. And indeed the dangers will have to be directly investigated in order to understand their exact character and to assess the prophylactic or therapeutic actions that would be necessary if preventive measures should fail. The judgment required to balance these considerations must encompass the leading intricacies of fundamental science, the advanced practice of public health and individual medicine, major features of agricultural development, and areas of security policy that at best have been only provisionally explored.

There is no categorical escape from the problem posed. Fatal error is an inherent risk and recurring consequence of practicing medicine. Capacity for destruction is an inevitable by-product of knowledge. Belligerent impulses certainly appear to be an enduring feature of human societies. Since it is neither feasible nor desirable to reverse the momentum of biotechnology and since the dangers emanating from it will inexorably increase, probably quite dramatically, some method for managing the diverse consequences will presumably have to be developed.

Existing policies and institutional arrangements cannot plausibly claim to have the scope of responsibility or the established competence required to manage this situation. The most direct effort to date to create an appropriate oversight process was embodied in negotiations to provide a verification and enforcement protocol for the Biological Weapons Convention (BWC). Those negotiations have just failed with no formula for resumption visible as yet. The failure, moreover, is rooted in a deepening pattern of international suspicion in which the United States government is unavoidably implicated. The United States has issued blunt indictments against 13 countries -- not all of them specified -- who are alleged to be conducting offensive biological weapons programs in violation of the BWC, but it has refused to subject all of its own activities to international scrutiny. Some US government programs are credibly reported to be of the same character as those that form the basis of the proclaimed indictments. Although the reports do not contend that the United States is actually conducting an offensive program, it clearly is applying a more permissive standard to itself than it extends to other countries. Meanwhile US government activities are acknowledged to be to be a possible, even a likely source of the powdered anthrax maliciously sent through the American mail system.

Even under the most charitable presumptions in this situation, independent initiative will clearly have to be taken within the scientific community if an appropriate and generally accepted oversight process for biotechnology is to be devised. Such an initiative would be necessary regardless of the current background suspicion but is especially important given the fact of it, as responsible government officials should themselves recognize. It is certainly a strong interest and arguably an urgent duty for representative scientific organizations to address the problem.

Working Presumptions

A number of domestic regulatory provisions currently in effect in the United States have some relevance and provide some precedent to build upon. There are equipment requirements and procedural standards meant to assure adequate confinement of currently known pathogens at the laboratories licensed to handle them. There are provisions for review and prior approval of experiments on human subjects. The process of licensing drugs and vaccines for human use involves extensive documentation and regulatory review of virtually all of the associated activities. Registering, reporting and packaging requirements have been at least formally imposed since 1997 on individuals and institutions engaged in shipping dangerous pathogens from one place to another. Antiterrorism legislation proposed in the wake of September 11 is in the process of extending those regulations to cover possession of designated pathogens. Internal review procedures of basic research are said to be well advanced within the major pharmaceutical companies, although those procedures are not externally visible and are not subjected to outside review. A review of these domestic arrangements and an assessment of their effectiveness is being undertaken by the National Academy of Sciences, but pending the committee's judgment the presumption has to be that existing procedures do not provide comprehensive oversight at the critical stages of exploratory research, even within the leading countries, let alone for the world as a whole. If the inherent dangers of emerging biotechnology are as serious as they appear to be, then presumably some fundamental managerial innovations will have to be explored.

It seems evident that effective oversight could not be achieved by the categorical exercise of centralized authority. Whatever legal rules and regulatory guidelines might be promulgated, the success or failure of any arrangement will depend primarily on judgments applied in detailed context by the scientists directly involved and by qualified peers. The problem is to induce awareness of the necessary judgments, set applicable standards, and provide for the timely exchange of information that would allow the research community as a whole to shape the behavior of all of its members. That would necessarily be a distributed process, operating more by induced consensus than by imposed authority. Presumably it would require some legal specification and the exercise of formal authority, but it would primarily depend on spontaneous professional and social interactions – working scientists setting and enforcing standards for which they accept principal responsibility.

The critical element in such a process is a set of transparency rules designed to assure that no one could act outside the boundaries of reasonable common judgment without provoking corrective reaction. Transparency in this sense is not the same as unrestricted publication, but it does imply informed scrutiny by those qualified to exercise it. If that is to occur then relevant information has to be made available and the scientific community has to be organized to react to it. There has long been a rule that no single individual is ever allowed to exercise exclusive control over a nuclear weapon, and elaborate organizational procedures have been devised to assure that rule is upheld without exception. The corresponding rule would be that no single research team of whatever size or whatever institutional affiliation should conduct inherently dangerous experiments without independent, actively exercised oversight.

In order to be reliably effective, such an arrangement would have to be global in scope. A pathogen emerging in any part of the world would threaten the rest, even if that were not the deliberate intent. The relevant research process is not exclusively conducted in any limited set of countries. Standards set within the United States or among the OECD countries would not provide adequate protection unless they were generally applied. Although an advanced oversight arrangement would probably have to be initiated by a small number of leading countries, the ultimate requirement for global extension would have to be a major consideration at the outset. There is a presumption, therefore, that the process of designing an oversight arrangement would have to be broadly inclusive at the early stages.

Practical Problems

Some difficult practical problems emerge from these presumptions. Any exercise of judgment runs the risk of misjudgment. Systematic provision of detailed information designed to enable prudent oversight judgments could also stimulate malicious, hysterical or simply misguided interference with legitimate activity. Individuals engaged in leading edge research will generally insist on the right to explore any promising line of scientific inquiry. They will also want to assure personal credit for their accomplishments and the associated rights for commercial application. They are understandably inclined to avoid outside scrutiny until these rights have been adequately exercised.

For well-known reasons, commitments to narrowly defined interests are generally more intense and better organized than are commitments to broader interests. In this case that means that however imposing the general opportunities and dangers of biotechnology may be, intrusive oversight provisions undertaken on behalf of the human species as a whole would have to be carefully targeted against the small percentage of activity that meets agreed criteria for especially dangerous research and would need to be accompanied by very robust measures to increase positive incentives and minimize negative side-effects. In order to be acceptable, a protective oversight arrangement would have to demonstrate not only that on balance it does more good than harm but also that whatever harm it does would not be unduly burdensome to the individuals and institutions directly affected. That would require a much more refined definition of the respective interests than has yet been established, as well as more developed legal provisions for managing the competing claims.

If, therefore, the inherently sensitive information that an oversight arrangement requires is to be provided, the agreement or requirement to disclose information must be accompanied by credible reassurances. Rules of access and use must be set to protect the legitimate subordinate interests involved, and those rules would have to be enforced to a high standard. If there are to be legal sanctions against the deliberately malicious or irresponsibly careless application of biotechnology, then there must be corresponding legal sanctions against the mishandling of information disclosed in an effort to prevent dangerous misapplications. The familiar dangers of plagiarism, espionage, and mass media sensationalism would have to be adequately contained for any oversight arrangement to be enacted. Doing so appears to require substantial elaboration of existing law and existing institutions. It is doubtful that current law provides the legal specification that would be necessary to support advanced oversight provisions. It is virtually

certain that no existing institution has the technical capabilities for the sophisticated data management challenges that such a system would entail, let alone the political and scientific standing to be entrusted with a globally comprehensive oversight process.

In addition to avoiding perverse effects, an oversight arrangement would also have to provide demonstrable security benefits in order to be globally acceptable. Advocates of the arrangement would have to overturn the standard objection, especially prominent in the United States at the moment, that no arrangement that protects the interests of willing collaborators could also prevent dedicated violation. The contention is that bad guys cannot be stopped and that good guys therefore should not be bothered. It has been difficult enough to set reasonable standards of compliance for arms control agreements that establish quantitative force limits or prohibit specific activities, such as conducting nuclear explosions, regardless of whether they are undertaken for military or peaceful purposes. It will be particularly difficult to agree on reasonable compliance standards for an arrangement designed to prevent the misuse of biotechnology because there is no threshold below which certain activities would be deemed "safe," yet these dangerous activities can not be reliably differentiated from legitimate ones without addressing the inherently ambiguous problem of imputed intentions. At least in the United States it will take a major change in prevailing political attitudes to establish the central principle that advanced oversight among the willing is a necessary condition for detecting and reacting to willful violations.

For many people-- perhaps most people at this point -- the practical problems are grounds for summary rejection of the entire idea of protective oversight for biotechnology. The necessary revision of prevailing political attitudes, the elaboration of applicable law, and the creation of a new organization without any close precedent is more than they care to try to imagine. Understandable as that assessment is, however, the world as a whole and the scientific community in particular cannot afford for everyone to indulge in it. The topic needs some venturesome pioneers.

An Imaginable Outcome

Despite the formidable problems, moreover, it is not difficult to visualize a comprehensive oversight arrangement once the compelling need for it is admitted. The basic elements would be as follows:

1. A substantially enhanced international program to control infectious disease generally. That would provide a strong positive incentive for participation, especially for those parts of the world already being ravaged by naturally generated pathogens.

2. A widely accepted determination of the set of especially dangerous pathogens and related research activities. This would have to be an open designation to which new pathogens and new research activities are added as they become identified. The basic idea, however, would be to specify a relatively restricted set of activities to which special rules would apply.

3. A set of requirements for registering and licensing individuals and research facilities involved in the especially dangerous class of activities. It would be illegal for any unlicensed individual or facility to possess pathogens or engage in scientific research in the designated class.

4. A set of reporting requirements for licensed individuals and facilities documenting their basic purposes, their research results and the population of pathogens in their possession. All experiments would be reported in advance. All strain variations of the pathogens would also be reported.

5. An international governing body authorized by appropriate majority voting rules to set priorities for the general effort to control infectious disease, to establish protocols for reaction to disease outbreaks of international concern, to designate the class of especially dangerous pathogens and related research activity, to determine basic reporting requirements including rules of access to the information reported, and to provide financial support for institutionalized implementation of disease containment and dangerous pathogen oversight.

6. An international scientific commission established by the general governing body to conduct the infectious disease program, to issue the required licenses, to receive the required reports, to organize scientific oversight, to enforce access rules regarding the reported information, to support legitimate research in the area of concern, and to perform routine auditing of compliance. The commission would periodically submit a budget for its operations to the convention for approval. In effect this would be an extension of scope and an institutionalization of the peer review process that is already established scientific practice.

7. A set of formal inspection and enforcement provisions -- along the lines of those proposed for a BWC protocol but more comprehensive -- to be evoked in response to questionable activity that cannot be clarified by routine auditing of the scientific commission.

In this scheme the international governing body and the scientific commission would basically set disclosure rules and provide financial incentives for compliance, leaving somewhat open the question as to how standards of behavior would be set and how they would be harmonized across individuals, institutions and countries. If it proves to be possible to achieve progressively converging judgment on those matters without vesting central institutions with the authority to impose it, most members of the relevant scientific communities would presumably prefer that arrangement. If consensus does not spontaneously arise under conditions of enforced transparency, however, then the forms of determinative authority the governing body and the scientific commission might reasonably be given would have to be explored. The ability to withhold financial support and training opportunities is implicit in the scheme. The ability to deny approval for publication might naturally be added. Beyond that it gets more difficult, however, and creative thought about incentives for cooperation will be required. To the extent that one worries about willfully malicious and systematically devious violation and therefore seeks to give the governing body and the implementing commission authoritative powers, one

also increases the potential for objectionable intrusion in normal scientific activity. Requiring that the governing body make substantive decisions by consensus would protect against an overly powerful international organization, but would produce lowest-common-denominator solutions and would preclude timely adaptation to rapid advances in biotechnology. At any rate it would clearly be important to work out an appropriate and presumably evolving balance of capacity and restraint.

Incremental Steps

In the initial stages, discussion of a comprehensive program to control existing infectious diseases and to prevent emergent ones would primarily be a constructive means of exploring the fundamental problems posed by biotechnology. Even for those most responsive, a viable global oversight arrangement is likely to be seen as a distant prospect of questionable probability. It is also important therefore to identify partial measures that would be constructive by themselves and would contribute to a comprehensive arrangement without imposing the full burden of development at the outset. There are a number of partial measures that might play this role.

Serious effort to complete a verification and enforcement protocol for the BWC would be the most obvious partial measure and arguably also the most critical. The failure of long running negotiations on that subject will inevitably degrade perceived international commitment to the core principles of the convention. Whatever else is done, that effect will have to be reversed and commitment to the convention reaffirmed among those willing to uphold it. If the central provision of the convention is to survive – that is, the prohibition of offensive weapons activities – then the adherence of major countries to that principle will have to be less ambiguous and more credibly conveyed than it currently is, especially for the United States, Russia, and China. In particular that means that reporting, visitation and inspection requirements must be established to some meaningful extent and that they must be applied to all relevant facilities of whatever size. Even if such requirements cannot alone provide high quality protection against competently concealed violation, they are important, indeed vital in setting standards among the compliant states. Actively enforced standards are necessary for detecting and prosecuting violation even if they are not sufficient. The appropriate criterion for assessment is not whether formal inspection arrangements can preclude all willful violation but rather whether they are adequate to prevent or to resolve residual suspicion among genuinely complaint parties. If that much is established, then supplementary actions could be taken in truly troublesome cases. As a practical matter, rogues cannot thrive if the legitimate community is adequately organized, and demonstrating compliance with unambiguous standards is the first step in being adequately organized. At a bare minimum, meaningful negotiations on this subject must be regenerated.

Similarly it is important for the major institutions of the scientific community to initiate discussion of oversight procedures that might be enacted voluntarily and it would certainly be desirable if some exploratory efforts were organized. Scientific discussions, voluntary transparency visits to sensitive locations, and cooperative threat reduction activities have provided some useful insights and could be expanded further. Given the magnitude and character of the potential danger, there will be an inherent question whether voluntary arrangements can provide adequate protection, but they certainly cannot do so if they are not developed. It is

incumbent on those who object to the idea of a fully comprehensive arrangement to nominate a partial one that might provide adequate protection.

Finally, as a substitute for continued negotiations on a protocol to strengthen the BWC, the United States government has suggested a dialogue among selected countries that is apparently intended to improve national regulations of existing biological agents. That too should be explored as a partial measure, but the suggestion would have to be extensively developed in order to make a meaningful contribution. As originally presented it would be confined to regulations applied to the possession and transport of designated agents. It would not address the research process capable of generating yet more dangerous agents.