The Argument for Oversight

Panel on Biosecurity Challenges in the Post 9/11 World
American Association for the Advancement of Science
February 18, 2006

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The Fundamental Problem

• Rapid progress in basic molecular biology is apparently enabling extraordinarily consequential applications, including in principle deliberate intervention in the process of evolution.

• The same basic science simultaneously identifies both therapeutic and destructive possibilities.

• The extended consequences of this situation cannot be determined with confidence.

• Those consequences will assuredly involve social dynamics as well as basic science.
• Recent reconstruction of the 1918 influenza virus is currently the leading instance of the more general problem.
  – Work actually motivated by “historical curiosity” but does have potentially important therapeutic implications.

  – Degree of oversight and containment applied does not appear commensurate with the magnitude of risk entailed.
    • Reconstructed strain is substantially more virulent than standard reference strains.
    • SARS has escaped BSL 3 containment at least 3 times.

  – Decision on publication made with no intermediate option available.
Evident Implications

• The scale and character of potential consequences mandate more advanced protective procedures than have yet been devised.

• In principle appropriate procedures should:
  – Prevent the deliberate or inadvertent creation of pathogens more destructive than those that have naturally evolved.
  – Assure prudent exploration of protective and therapeutic applications.
  – Assure equitable access to all constructive applications.
The Basic **Principle** of Protection

- Since the potential for constructive and destructive application of biotechnology cannot be categorically disentangled, effective protection depends on reinforcing and existing behavioral rule:

  **Biotechnology must not be used to do deliberate harm under any circumstance for any reason**

- Categorical rule must be adapted to specific context to be meaningfully applied.
• That basic principle is reasonably well established as a universal norm.

• Has been authoritatively articulated:
  – The Hippocratic Oath.

• Is broadly upheld and not expressly rejected.

• Nonetheless it must be substantially strengthened if it is to be the practical foundation for protection.
The Basic **Method** of Protection

• In most other areas of high potential consequence independent oversight is used as the fundamental method of protection.
  – Auditing of financial transactions.
  – Multiple person access rules for handling nuclear weapons and related explosive materials.
  – Peer review for publication of scientific results.

• It is prudent to assume that the principle of independent oversight will have to be applied to inherently dangerous areas of biological research.
Essential Features of Protective Oversight

• Adequately effective oversight of fundamental research would have to be:
  – Global in scope of application – all parts of the world.
  – Comprehensively inclusive – all relevant research activities.
  – Credibly focused.
  – Legally mandatory.
  – Actively practiced.
  – Efficiently organized.
  – Appropriately constrained.
Illustrative Design

- An oversight process meeting those criteria might operate in three tiers:
  - International jurisdiction over research activities of **extreme concern** that might generate pathogens more lethal or otherwise more consequential than those currently extant in nature.
  - National jurisdiction over research activities of **moderate concern** – the more lethal of currently regulated agents.
  - Local jurisdiction over activities of **potential concern** involving agents that might be elevated to moderate or extreme categories by use of advanced manipulation techniques.
• Such an arrangement:
  – Would license individuals and research facilities.
  – Would subject individual projects to prior review.
  – Would set conditions for the conduct of research and for the dissemination of results calibrated to the degree of danger involved.
  – Would initiate procedures of harmonizing the review judgments made in separate jurisdictions
Determination of Danger

• Criteria for Oversight Jurisdiction:
  – Activities of Extreme Concern (AEC):
    • 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/ABSL 4 level of containment,
    • De novo synthesis of any agent matching the above characteristics,
    • Expanding the host range of an agent or changing the tissue range of an 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.
Activities of Moderate Concern (AMC):

- Increasing virulence of listed agent or related agent.
- Insertion of host genes into listed agent or related agent.
- Increasing transmissibility or environmental stability of listed agent or related agent.
- Powder or aerosol production of listed agent or related agent.
- Powder or aerosol dispersal of listed agent or related agent.
- De novo synthesis of listed agent or related agent.
- Construction of antibiotic- or vaccine-resistant related agent.
- Genome transfer, genome replacement, or cellular reconstitution of listed agent or related agent.
– Activities of Potential Concern (APC):

- Work with listed agent—or exempt avirulent, attenuated, or vaccine strain of select agent—not covered by AEC/AMC.
- Increasing virulence of non-listed agent.
- Increasing transmissibility or environmental stability of non-listed agent.
- Powder or aerosol production of non-listed agent.
- Powder or aerosol dispersal of non-listed agent.
- De novo synthesis of non-listed agent.
- Genome transfer, genome replacement, or cellular reconstitution of non-listed agent.
A survey of US grant applications and research publications 2000 – 2005 indicates that under these criteria of jurisdiction a total of 310 research facilities and 2,574 individuals would have been subjected to oversight, of which:

• 12 facilities and 185 individuals would have been assigned to international oversight;
• 14 facilities and 133 individuals would have been assigned to national oversight.
• 231 facilities and 2,119 individuals would have been assigned to local oversight.
• 53 facilities and 137 individuals would have encountered multiple jurisdictions.
• Criteria for project evaluation:

  – Spontaneous transmissibility =
    capacity to propagate between hosts under standard conditions.

  – Infectivity =
    capacity to penetrate a host and reproduce.

  – Pathogenicity =
    capacity to generate a lethal or otherwise hostile effect within an infected host.
Conceptual Parameters of Danger
Assessment of Operational Danger

• Immediate terrorist threat is comparable to or less than the natural incidence of infectious disease.

• Hostile competition among national threat assessment programs is a more serious immediate concern.

• Exclusive subordination of national threat assessment activities to public health jurisdiction and transparency rules is an urgent priority.