The Argument for Oversight

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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.
  - The 1925 Geneva Protocol.
  - The 1972 Biological and Toxin Weapons Convention.

- 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.

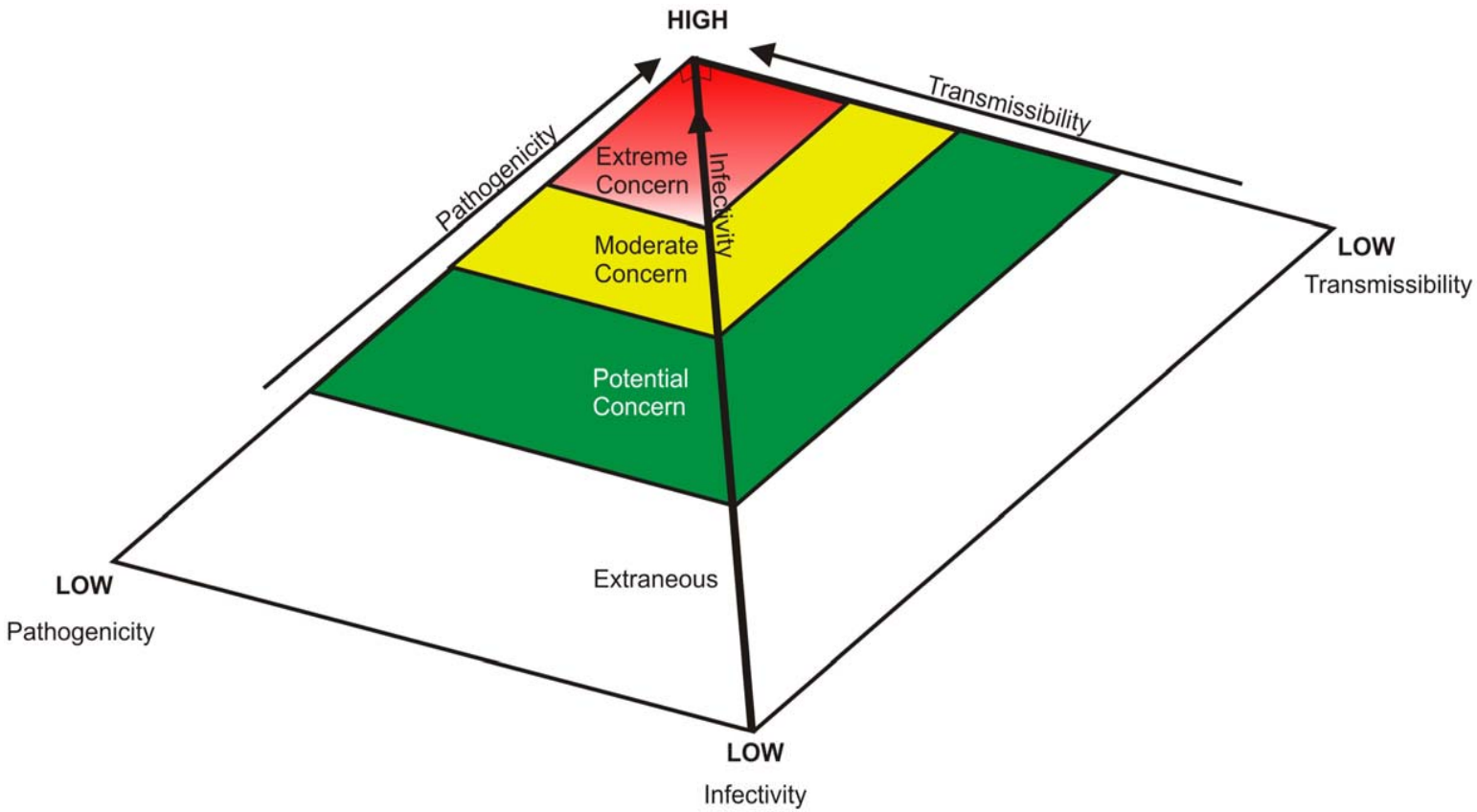
  - Infectivity =

    capacity to penetrate a host and reproduce.

  - Pathogenicity =

    capacity to generate a lethal of 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.