In my talk today, I'd like to proceed backwards, like one of those movies that starts with the concluding outcome and works through hindsight to unfold how the plot reached its end -- its denouement.

So, the last question is: how might a bio-attack occur. No one knows, and we all desperately hope that it does not happen at all. In my estimation, it will be engineered flu, probably an H5N1 derivative. The flu must not be taken lightly; history's most catastrophic pandemic was the 1918 "Spanish Flu" that took at least 40 million lives, perhaps as many as 100 million. It did it when humanity was 1/3 of its current number and when trans-national travel was far more limited than today.

Today, we must contend with an avian flu that is no less lethal but far less contagious. How difficult would it be insert or modify genetic sequences of the avian flu to add characteristics of high contagion? The answer is that it would be trivial to add such sequences; we know an enormous amount about the flu virus – one of nature's simplest. What we don't know is how the resulting genome would behave. Would it be stable if released in natural conditions? Would all if its parts work together to sustain a pandemic? Today, there are a few scientists who could figure all that out successfully, but the chances of someone doing that precisely correctly without anyone noticing are, today, in question.

Likely, the bug will not be the best that science can produce. It will lack some substantial degree of lethality or contagion. It will be an amateurish concoction. The perpetrator will make up for its shortcomings by strategically diversifying the attack. For one thing,

he'll hide it behind other agents. An anthrax attack, even having limited consequences, will wildly distort public health response capabilities and provide perfect cover for spreading a contagious disease which might not even be recognized as a distinctive event. Even better, he might take advantage of a natural flu epidemic – what better cover to disguise an intentional and lethal variant than its far less cataclysmic cousin.

I doubt he'll attack London or New York or Washington. Why go where law enforcement and public health are at the top of their game? Can we identify some cities that are: (1) key population centers of nations with strong ties to the U.S. and U.K.; (2) have teeming populations with wholly inadequate public health infrastructures; and (3) are international transport hubs: Calcutta, Cairo, Caracas. Envision a series of attacks against these developing urban centers, perhaps timed to follow local officials' expressions of friendship to visiting U.S. dignitaries. The attacks could carry a well-publicized yet simple warning: "If you are a friend of the U.S. or U.K., receive its officials or support its policies, thousands of your people will get sick." How many attacks in how many such cities would it take before international diplomacy, to say nothing of international transit, comes to a crashing halt? How many attacks that cause how many victims would it take before panic and interruptions of international trade provoke officials to close stock markets? At some point, even if not a single American or Englishman is actually sickened, the West's economy and political leadership would be near collapse.

Now, let's work backward. What would our perpetrator have to do. The good news is that an attack of real magnitude with dire strategic implications is harder to execute than the media suggests. To develop substantial quantities of multiple agents with even approximately desired properties takes a supply of pathogens, some decently sophisticated equipment, a lot of know-how, control systems to handle the agents and protect against their premature release, and a dedicated cadre to put the plan into motion including, with regard to contagious agents some suicide bio-bombers to ignite the spread. It's a challenging operation that has eluded even well-financed cults like Aum Shinrikyo.

Could it be done today? We know that the directional signals are all pointing the wrong way. Advancing bio-science is, every day, making it easier for an ever-smaller group of individuals to inflict ever-greater harm against an ever-expanding victim population. Whatever capabilities are speculative today will be potentially available in a short time and pedestrian within a few years after that.

So let's step further backward. Knowing something about what he needs to inflict a catastrophe, how should we stop him. There is no single answer. Of course, counter-terrorism efforts including good intelligence are critical, but there are few if any experts that expect these efforts to ferret out malevolent groups that may number a dozen or less. Prevention must be made or sterner stuff.

First, it should be hard for a bio-offender to get what he needs to commit bio-violence. He needs pathogens and a capability to weaponize

them. If he can pick up refined pathogens and readily work with them using sophisticated equipment and facilities, he will be more likely to succeed than if his preparations are unremittingly difficult. If bio-violence is too complicated, it is likely that he will take his resources and evil intentions in other directions.

Especially lethal pathogens need to be controlled; only scientists who have a demonstrable research need should have access to them, and their access should be declared to responsible officials. Pathogens should be genetically marked so that their legitimate sources can be tracked with movements accounted for. Bio-equipment is far too ubiquitous to strictly regulate, but we can require that, as of now, all high-end equipment be tagged with locational devices, enabling us to know if it is being used in a legitimate research facility or in some Afghan cave.

Global implementation of denial measures that complicate some of the easier and more straightforward ways to commit bio-violence will compel the bio-offender to pursue more technically challenging routes, raising his costs as well as the odds of botching his plans. Correctly structured denial measures should therefore be linked to observable signals so that an offender trying to leap those hurdles will be more likely to make a mistake and tip his hand and alert law enforcers.

This is how interdiction measures can be beneficial. Law enforcers (police, customs and border control officials, regulatory inspectors, etc.) should be authorized, trained and equipped to look for such indicative behavior so that they can stop a bio-offender before he has a chance to

carry out his plans. Interdiction measures are intimately linked to denial measures: we set up hurdles that a bio-offender will have to leap over in order to prepare a bio-violence attack, then we make sure that law enforcers are observant of leapers and can quickly move against them.

The key challenge facing law enforcers is to know where and at whom to look. It is important to gather detailed data about legitimate bio-science so that we gain some insight about who is engaged in illicit activities and where they might be carrying out those activities. By knowing the locations and traffic in legitimate science, law enforcers can look for anomalies, *i.e.*, bits of information that might seem incidental but which, to a trained observer, suggest attempts to camouflage covert activities. With this information about bio-science, offenders will stand out, enabling law enforcers to optimally focus scarce resources; absent that information, the movement of pathogens and access to laboratories, etc. will be just a blur. There is a double benefit here: by reporting relevant data, legitimate bio-science can help law enforcers to leave them alone and focus scrutiny on identifying outlaws.

The value here is not to create a foolproof system; it is that by marking pathogens and tagging equipment, we compel legitimate users to disclose their location and, more important, we convey to perpetrators that their use might give away their plot. Moreover, by having a very clear picture of where legitimate bio-science is taking place and what is being done and putting that information together with extensive law enforcement databases, we can detect bits of suspicion that things don't make sense and where more investigation is appropriate.

But what is the current reality? There appear to be huge opportunities for bio-offenders to gain lethal capabilities. Getting sophisticated equipment is trivial, and there are an untold number of bio-laboratories containing refined pathogen seed stocks. How readily might any of these labs deliver pathogen samples in response to a fraudulent request? How many labs have appropriate safeguards for complicating diversion of pathogens or wrongful use of facilities? Maybe there are many; maybe only a handful. No one knows for sure. Rumors abound, but we know one thing for sure: in most places around the world, if pathogens are diverted or if labs are malevolently used, it is extremely unlikely that law enforcers would find out in time to stop a catastrophe! Like the rest of us, the police will find out after the attack is carried out and the victims pile up.

It is alarming that we do not know where are these pathogens and laboratories. More precisely, we know an enormous amount about where some of these pathogens and labs are; it's the ones that we do not know much about that are most worrisome. And the list of what we don't know about gets ever longer due to the rapid global proliferation of bio-science. Today, as bio-science increasingly permeates regions near and far, we have no real idea of what we do not know.

It gets worse: most States outside of North America and the European Union have not legally restricted accumulation of bio-agents or critical equipment that bio-offenders might need nor fully authorized official supervision of these items. In most States, cultivation or transfer of deadly pathogens is not a criminal act. It is perfectly legal to obtain

the most lethal agents and the equipment with which moderately-trained scientists could assemble a functional bio-weapon. A bio-offender can prepare, transport, and even export biological agents that could be catastrophically misused without running afoul of any legal constraint. Nor is preparing pathogens for lethal dissemination prohibited. Only the final act – the actual commission of an attack – is a crime. In all but a handful of nations, no law authorizes law enforcers to detect or interdict preparation of bio-weapons. In most nations, even if police learn that someone has an amateur laboratory, they would not be able to inspect much less stop it because that laboratory violates no law and the police lack authority to investigate amateur bio-science activities.

This is irresponsible. We would not accept a system where anyone could fly a commercial airplane virtually anywhere without disclosure or compliance with safety standards. We would not accept a system where nuclear laboratories have open doors that might allow anyone to carry materials or equipment in and out. And we most certainly would not accept a system where, despite knowing that there is potential for criminality, law enforcers are incapable of doing much to prevent a most horrible crime. Most of us respect the need for scientific freedom, but there has to be a difference between freedom and anarchy, especially when the consequences of misuse could be cataclysmic.

Bio-scientists are not to blame for this condition, although some scientists are perhaps too complacent about the potential for bio-violence. At root here are legal gaps throughout major regions of the world and ignorance about what is going through those gaps. Some

States enforce relevant standards, most do not. Cavernous holes in national legislation undermine enforcement of basic security standards. And holes in nations' laws are magnified by the legal void at the international level. There is no authoritative system for keeping records and no way to know if enacted laws are actually enforced. There is no coherent international oversight structure that can make fine, nuanced decisions much less determine compliance with those decisions.

Most important, there is no mechanism whatsoever for detecting bio-science activity that is intentionally evasive of standards, *i.e.* criminal bio-science. While bio-offenders are becoming more focused and organized, policies to deny them the capabilities for bio-violence are vague, gap-ridden, backward-looking, unsupervised, and largely inattentive to the threat posed by intentional malefactors. More dismayingly, there is no process whatsoever to anticipate the policies that might suitably cope with tomorrow's challenges. The crisis here is not in science -- the crisis here is in law. There is a systemic failure to clarify and enforce even rudimentary legal obligations that could make it harder to commit bio-violence.

But we must be forthright: law is very expensive, and throughout the world today, there are natural disease crises that wholly surpass the threat of intentionally inflicted illness. To detect illicit activities, to implement biosecurity, to enhance law enforce capabilities, to sustain attention to risks of bio-science research, to promote bio-defense consistent with prohibiting bio-offense – all these endeavors are burdensome, especially for developing nations.

And the absolutely inescapable reality of our era is that in this month, nearly one million children under the age of five will die from preventable or curable conditions. Next month, nearly one million more children under the age of five will similarly die. The month after that … Simply stated, it is illegitimate to compel global pursuit of policies for preventing bio-weapons proliferation in isolation from the far more gripping pursuit of policies to combat pandemic disease. Strengthening public health is part of the answer, yet it is essential to consider how to strengthen indigenous bio-science capabilities.

The Millennium Development Goals call for collective efforts to advance science and technology for development. Indeed, policies should encourage the global spread of legitimate bio-science. These policies and the opportunities for bio-science development they bring should be linked to fulfillment of bio-security obligations: development funding in bio-science activities should be contingent on implementation of security controls; correspondingly, pro-active implementation of specific controls and cooperation with relevant international organizations should encourage developmental support.

So here is the challenge for international law, perhaps its most important current challenge:

- **Can we construct a system that reflects the global and wholly trans-boundary essence of the threats and the measures to reduce those threats?**

- **Can we promote bio-science, especially throughout the developing world, while sustaining a vigorous discussion about how to prevent the misuse of that science?**
- **Can we define rules governing access to pathogens, critical equipment, and laboratories based on sound science and due process of law and that satisfy our common aspirations for transparency and reviewability?**
- **Can we develop information retrieval and analytical databases that are sufficiently selective to provide indicative data without jeopardizing privacy or proprietary rights?**
- **Can we prescribe modalities of investigation and trans-national legal cooperation to cope with what we hope and believe will be the exceedingly rare situations that demand intense inquiry?**
- **Can we build bridges among bio-scientists, law enforcers, and promotes of sustainable development that builds capacity to address malevolent threats in harmony with capacity to address ubiquitous natural disease threats?**