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Biodefense: Next Steps

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Thank you for the opportunity to submit this testimony for the record.

My name is Meryl Nass, M.D., and I have worked for the past twenty years as an emergency physician and internist in community hospitals in the northeastern US. I have also studied many aspects of bioterrorism since 1989. I am the person who first demonstrated, in 1992, that one could investigate an epidemic retrospectively, and prove that it was due to biological warfare, using Rhodesia's 1978-80 anthrax epidemic as a model.¹

Since then I have authored and coauthored numerous documents on the subjects of preventing, investigating and ameliorating the effects of a bioterror attack. These included recommendations to the Biological Weapons Convention Review Conference of 1996,² and four Congressional testimonies, including one specifically on the best medical responses to bioterrorism, in November 2001.³

Because I continue to practice medicine, have a strong background in biological warfare, and do not consult for the drug industry, my concerns may differ from most Congressional witnesses. They are:

- 1) to achieve maximal readiness at the local level
- 2) to assure the development and availability of safe and effective measures, especially drugs and vaccines, to protect our citizens, and
- 3) to urge a much stronger focus on prevention of bioterrorism. Although it is a truism that it is impossible to fully protect our population against this form of attack, in our rush to buy protections we seem to ignore their limitations. The ability of an enemy to defeat our preparations will increase in future. Furthermore, the potential for biowarfare to destroy whole species or even end life as we know it is not inconsiderable.

I'd like to briefly cover these three issues. With respect to local readiness:

Through state and federal grants, hospitals have been given antidotes for chemical agents,

¹ Nass M. [Anthrax Epizootic in Zimbabwe 1978-1980: Due to Deliberate Spread?](http://www.anthraxvaccine.org/zimbabwe.html) PSR Quarterly, 1992; 2: 198-209. <http://www.anthraxvaccine.org/zimbabwe.html>

² Report of the Subgroup on Investigation of Alleged Use or Release of Biological or Toxin Weapons Agents. Federation of American Scientists Working Group on Biological Weapons Verification, April 1996.

³ Preparing a Medical Response to Bioterrorism. Written Testimony of Meryl Nass, MD. House Committee on Government Reform hearing, November 14, 2001: Comprehensive Medical Care for Bioterrorism Exposure. <http://www.anthraxvaccine.org/response.htm>.

and other appropriate drugs for use in a limited chemical or bioterrorism event. Hospitals do not have sufficient stockpiles of these substances to care for more than a tiny percentage of the population, should a massive event occur. We have even fewer people at the state or local level with the knowledge and experience to take charge of the situation appropriately, should a terrorism event occur. We lack sufficient gloves, gowns and masks on site in our hospitals to handle a sustained infectious catastrophe.

Our practice and knowledge of infection control needs to be improved. During the past month my hospital had several cases of hospital-acquired influenza in both staff and patients, despite following CDC-specified infection control measures. This occurred, in my opinion, because CDC did not pay adequate attention to transmission of the virus by fomites (inanimate objects that harbored transmissible virus) and because we had patients who were spreading virus prior to being diagnosed with the infection, i.e. before appropriate control measures were instituted, because it took up to 24 hours to get lab confirmation of the diagnosis. As most of the flu cases I cared for had received flu vaccine, flu was not suspected initially. Yet the vaccine apparently failed to protect them.

Attention to improving our understanding of infectious disease management will yield great dividends in helping us control a bioterrorism event. I am simply repeating what many others have said: the public health system has been a poor stepchild of the medical system for decades, generally relegated to providing a modicum of care for those who cannot pay, and handling conditions like tuberculosis and sexually transmitted diseases. It needs to further expand its horizons, and should become fully integrated into the practice of American medicine.

My second concern is that the provision of safe and effective drugs and vaccines to our population is of utmost importance. However, we cannot develop and manufacture a vaccine or antidote for every possible infectious agent for compelling reasons:

- a) we do not yet know how to do so (witness the lack of an AIDS vaccine or an effective drug for viral hepatitis or leishmaniasis)
- b) the number and variety of potential pathogens is infinite, so we cannot predict or identify all the pathogens that might be used as weapons, which makes finding treatments difficult or impossible
- c) the cost of developing and producing even one drug or vaccine for the entire population is likely to range from one to many billion dollars.

At this point, the United States has not even begun to develop a surge capacity for manufacturing such products, although it is clear this is what is required. My 2001 Congressional testimony (<http://www.anthraxvaccine.org/response.htm>) included many suggestions for rapid development of effective drugs and vaccines, so I will not belabor those points today.

What is urgently needed by the nation is for a group of knowledgeable, nonpartisan

experts in and out of government to review our weaknesses and strengths, and plan an overall approach to the problem of bioterrorism, while avoiding measures that could increase the threat. Until now, we have put the cart before the horse, purchasing a few drugs and vaccines (that may in fact be unusable due to safety problems that are only now being identified), without any overall program to protect the nation from the range of threats we face. Instead, there has been great duplication of efforts by agencies with overlapping responsibilities, but little attention to systematically plugging the gaps in our preparedness.

NIAID was given a large amount of money in 2002 to allocate to bioterrorism preparedness, and elected to use much of it to support building new high containment laboratories around the country. Although some additional capacity was needed, much of the additional capacity appears at this stage to be superfluous. More worrisome than wasteful, however, is the fact that the new labs will employ thousands of scientists with new careers in bioterrorism, who will study weaponizable pathogens, thus proliferating knowledge about these microorganisms. This could lend itself to serious blowback in the future, were this knowledge to be acquired by an enemy. We have no systematic mechanisms in the civilian sector to screen these scientists and other new biodefense employees, nor have we the means to prevent researchers from taking miniscule samples of pathogens out of the lab, nor to follow their activities once they leave our research centers. Nor do we have foolproof systems to maintain the security and safety of the labs. An electrical failure with loss of generator capacity at Plum Island, New York two years ago graphically demonstrated that even redundant systems can fail, and that one may not always be able to keep dangerous pathogens safely confined. It is simply not possible to have a fail-safe system. Researchers can become infected and bring their illness to the community; cultures thought to be dead or attenuated are found to be virulent.

Plum Island was chosen for biodefense work decades ago because there was no land link to Long Island or the US mainland. This was a powerful safety measure that we are now ignoring at our peril. There cannot be a sufficient rationale for siting biodefense laboratories in heavily populated areas, even if this makes attracting quality staff easier. The hubris of assuming that nothing can go wrong does not augur well for the scrupulous safety planning that should be taking place, particularly in light of accidents at these very same labs in the recent past. (Three researchers at Boston Medical Center developed tularemia and one researcher at Fort Detrick developed glanders recently as a result of working with the organisms; in each case, it was not suspected until late that they were ill due to occupational exposures.)

How do we best get safe new drugs and vaccines to the population? I would venture to say that when government has employed medical therapies for theoretical threats, rather than for a demonstrated medical need, the strategy often backfires. Using the techniques of public relations to create a need for medical treatment in the public's mind is another dangerous strategy with a tendency to backfire, as the public learns to mistrust the medical pronouncements of government. This may account for why we have a flu

vaccine surplus today, despite what was touted as a dangerous shortage only weeks ago.

The swine flu vaccine program of 30 years ago failed because vaccine was made and Americans vaccinated for the theoretical risk that an outbreak of swine flu at Fort Dix might be comparable to the 1918 influenza pandemic.⁴ This was a reasonable concern when the Fort Dix outbreak began, but made no sense six months later when vaccine became available, because the outbreak never left the base, had already died out, and there had only been one death. In order to get rapid production of vaccine by industry, the federal government assumed the liability for vaccine-induced injuries, and paid for hundreds of cases of neurological illnesses and some deaths. Americans learned for the first time that serious adverse events, especially Guillain-Barre Syndrome, could be caused by vaccines.

The important lesson for today is that once a massive program has been put in place to create a new drug or vaccine for an imminent threat, the program's momentum will likely lead to use of the product when available, whether or not it is needed at that time.

In 1998 the anthrax vaccine was rolled out as the first immunization in a potentially large program of vaccinations to protect the military from biowarfare threats. Again the federal government, in the person of the Secretary of the Army, indemnified the manufacturer against all liability from adverse effects or product failure. This measure was reportedly designed to reduce vaccine costs, but may become quite costly, due to ongoing litigation about the vaccine's safety and efficacy. The vaccine's license for prevention of inhalation anthrax was removed in October 2004 by Federal Judge Emmet Sullivan.

The fact that federal agencies have been able to shift the costs of product indemnification to other federal agencies probably worked to make indemnification attractive. For example, although it was the Army that indemnified the anthrax vaccine manufacturer (reducing the manufacturer's need to produce a quality product), soldiers who become disabled as a consequence of anthrax vaccination are paid primarily by the Department of Veterans Affairs and/or Social Security Disability. So far there has been little impact on the Army's budget from its decision to use a poorly tested and manufactured vaccine.

In late 2002 the federal government initiated the smallpox immunization program, with plans to vaccinate, stepwise, ten million first responders and medical personnel. The original manufacturer, Wyeth, had turned over its smallpox vaccine stockpile to the federal government two decades ago, and it too received federal immunity from liability claims. Due to a poor initial uptake of smallpox vaccine by volunteers, Congress crafted a plan to insure vaccine recipients against death or disability, with a maximum payout per recipient of \$262,100. However, despite this guarantee, higher than expected rates of

⁴ Hilleman MR. Cooperation between government and industry in combating a perceived emerging pandemic: The 1976 swine influenza vaccination program. *JAMA* Jan 17, 1996. Vol 275, no. 3. Pages 241-3.

cardiac complications caused the pool of volunteers to dry up. The civilian smallpox vaccine program withered on the vine in late 2003, but mandatory military smallpox vaccinations continued, perhaps helped along by shifting the costs of the programs' adverse medical consequences to other agencies.

In November 2004, FDA added a "black box" warning to the smallpox vaccine label, limiting use to only those at high risk of smallpox, and indicating that myocarditis (heart muscle inflammation) was occurring approximately 100 times more often than initially reported: one in every 145 vaccine recipients had developed this complication in a clinical trial conducted by industry. The military smallpox program continues nonetheless, reporting much lower rates of this complication than seen in civilian studies.

A historical lesson that industry may not want to acknowledge is that when the removal of manufacturers' liability is sought and obtained, the resulting products have usually been associated with serious safety issues. And when the government assumes the liability, it has a strong disincentive to perform appropriate scientific studies that will identify and quantify the health risks of such products. Thus we still lack reliable statistical data on the types and rates of adverse reactions for anthrax vaccine. And despite CDC surveillance of 40,000 smallpox vaccine recipients, we remain in the dark about the rates of other vaccine complications, apart from myocarditis and certain skin conditions.

The Food and Drug Administration used to be the preeminent agency in the world for protecting citizens from bad drugs. Unfortunately, this began to change in the early 1990s, spurred by two Congressional-FDA initiatives: the 1992 Prescription Drug User Fee Act (PDUFA) and the 1997 Food and Drug Administration Modernization Act.

Encouraged by the Executive branch, FDA came to view industry as its primary client, rather than the public, and focused more on rapid drug approvals than on assuring safety of drug products. In fact, the fees FDA obtained from PDUFA were prohibited from being used to review safety. Guidelines issued in 1997 for broadcast advertising have further damaged the agency's reputation, as this form of consumer advertising is not permitted in other countries. This advertising makes it harder for physicians to prescribe medicines cost-effectively. Ignoring serious bacterial contamination in 2004 at flu vaccine manufacturer Chiron Corporation, FDA demonstrated a willful failure to carry out its responsibility for assuring the safety of the US drug supply.

Things have gone from bad to worse at FDA lately. The large number of recent drug withdrawals, the continuing series of scandals involving FDA's connivance with industry to hide serious adverse drug effects, and widespread loss of trust – by its own employees -- that the FDA can do its assigned job grace the pages of our newspapers daily. The fact that the American Medical Association recently recommended that assessment of drug safety be performed by a separate agency confirms that the credibility of FDA has dropped to a critical level, and serious reforms are way overdue.

It is this flawed, unreliable FDA that is now charged with approving new drugs and vaccines for bioterrorism: products likely to receive less testing, using new fast-track procedures, than for standard drug approvals. This FDA also approves the use of *unlicensed*, investigational products under certain circumstances, and has just done so for the military, so that it can keep using anthrax vaccine despite a judicial ruling that removed the vaccine's license.

Given FDA's ongoing credibility problems, the procedures currently in place to assure that American citizens obtain safe and effective products to prevent and treat diseases due to bioterrorism are inadequate. We are talking, after all, about drugs that cannot be tested for efficacy in humans: potentially the entire nation could receive such drugs or vaccines that have had only rudimentary human testing. And animal testing is uniformly acknowledged to be incapable of predicting human safety.

Americans cannot currently rely on FDA to guarantee quality manufacturing, testing, safety and effectiveness of these products. Because these drugs are likely to be used all at once, i.e., the entire nation might be treated during the same week, we will have only very limited information about the drugs' side effects and effectiveness when the decision to use them is made. We will not have acquired the clinical familiarity and longer term data that accrue over the first year or two of a new drug's use, and upon which most physicians rely.

As a clinician, I consider this entirely unacceptable. Such drugs need more attentive oversight than ordinary drugs, not less, before they are approved for use. A reliable track record must exist before I can prescribe a drug or vaccine to one person. What evidence should a drug have before it is prescribed to the entire nation?

Because all drugs cause adverse reactions in some recipients, and the administration of every drug involves a risk-benefit calculation, their appropriate use requires care and skill. No one should decide to prescribe for the nation without the availability of reliable information on the drug to be used. Yet current law permits the Secretary of HHS to do so, even if that person has no medical training. He may consult with the FDA Commissioner; but the current Acting Commissioner is a veterinarian. HHS may shoulder no financial liability if the drug turns out to be more dangerous than anticipated.

Of course industry needs incentives in order to develop and produce useful products. I submit that current patent protections for industry should be changed. Why should the clock start ticking on a drug patent the day the patent is issued, even though this is years before FDA approval is obtained and the product can be manufactured? The ticking clock forces FDA to eschew safety considerations for speed.

A preferable alternative would be, for example, to extend patent protection based on the date of FDA licensure. This would give FDA and the manufacturer breathing space,

allow for clinical safety trials of longer duration, and give the manufacturers a reasonable incentive. In order to speed new drug development, the length of patent extension could also become a function of how quickly the new product is developed. Another advantage to this proposal is that it would remove the incentive manufacturers now have to rush out drugs before they are well understood.

Other incentives for industry have been discussed elsewhere, but should not be used if they are associated with significant potential safety risks. Industry may wish to use certain products, such as currently unlicensed vaccine adjuvants, in vaccines designed for bioterrorism because they improve efficacy. Possibly this back door approach would help them move these adjuvants toward licensure. However, given the known risk of these products to induce autoimmune disorders in susceptible recipients, the threat of bioterrorism must not become the excuse to initiate their widespread use in humans.

My final point is that prevention of bioterrorism should be the top priority of Bioshield legislation. Because we cannot afford to protect against all potential pathogens, because we cannot even predict the potential pathogens we might face, and because the minute size of microorganisms makes bioagent proliferation extremely easy, it should be clear to all that we will never be able to purchase adequate protection from bioterrorism, no matter how many resources we expend. Therefore, finding ways to maximize international cooperation in the development of countermeasures, in inspections of biological research and manufacturing facilities, in sanctions for failure to comply with treaty obligations, and in preventing the proliferation of bioweapons scientists and knowledge should receive our full attention and resources.

It is hard to understand why successive US administrations have failed to embrace the value of this approach, and why diplomatic measures, such as strengthening the verification provisions of the Biological Weapons Convention, have not received strong support from the US government. This is a low cost approach that can be undertaken in tandem with all the other measures designed to boost protection for our population. Although industry had reservations about inspections in the past, because of the potential loss of trade secrets, PhRMA now supports strengthening the Biological Weapons Convention with inspections and other efforts.

The clock is ticking for our species and planet. We can throw money scattershot at this problem and move on, or we can give it the prolonged attention and effort it deserves, and ask some of our strongest scientists, engineers, and statesmen to help think through the overall problem of readiness and appropriate preparation. If we are to take the threat seriously, we must maximize our resources on the local and global levels. So far we have not done so.

Thank you.