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February 18, 2013
Amy Gutmann, PhD, Chair
Presidential Commission for the Study of Bioethical Issues
President, University of Pennsylvania

Dear Dr. Gutmann:

RE: Ethical Issues Associated with Countermeasures for Children:
Proposed Government Experiment to Test Anthrax Vaccine on Children

This Presidential Commission spent 4 meetings and the greater part of a year deliberating about the ethics of testing the anthrax vaccine on children, but somehow ignored the most basic information about the vaccine: its effectiveness after exposure to inhalation anthrax is unknown, and the lack of a reliable animal model makes any calculation of effectiveness and dosing impossible. What is known is that *BioThrax* is a dangerous vaccine. The FDA-approved 2002 label[1] states: 5% to 35% of adults who were vaccinated suffered adverse events. Those adverse events encompass local adverse reactions—such as, bruising, inflammation, swelling, pain, and fever; systemic reactions—such as, muscle aches, joint aches, headaches, malaise, rashes, chills, fever, nausea. The FDA-approved 2012 label[2] states:

> *"acute allergic reactions, including anaphylaxis…Stevens Johnson syndrome have occurred with BioThrax… [and] BioThrax can cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while ta king this drug, the patient should be apprised of the potential hazard to a fetus."*

A "pivotal safety / immunogenicity trial" conducted by the Centers for Disease Control reported in the *Journal of the American Medical Association (JAMA*, 2008)[3] that 12% of the adult subjects suffered "serious adverse events" (SAE) during the 43 month trial. SAEs are defined as *"death, life-threatening*

events, initial inpatient hospitalization or prolongation of hospitalization, significant or persistent disability or incapacity…"

The following presentation is made on behalf of **The Alliance for Human Research Protection (AHRP)**, a national 501-C3 human rights organization dedicated to advancing responsible and ethical medical research practices. We will make the case that the proposed pediatric anthrax vaccine trial and broader non-specific "countermeasures research" in children, involving greater than minimal risk is unethical and unapprovable in the absence of a clear and present danger to children.

At the close of the Commission's May 17, 2012 meeting, you pinpointed[4] precisely the two most important factors for the Commission to consider when developing its recommendations. First, it needed to consider the relevant scientific facts and the state of knowledge relating to the issues involved in pediatric "countermeasures research":

> *"To say that research on one vaccine should go forward really requires having facts, not just the framework….I would definitely agree you can't come to a decision in this matter without having the facts…I would request that all of you who work in the domain of the facts get us the relevant facts -- all of the relevant facts that are known or any that are unknown-- that would need to be gotten… that would have to be known before a final decision should be made on specifically a vaccine, an Anthrax vaccine for children... it's really important for us to know what is the state of knowledge of the facts in this matter…"*

You also pinpointed the most important ethical consideration which is tacitly overlooked by many IRBs: whose children would be the subjects of countermeasures research?

> "…if the people who are in favor of this would feel that it was the right thing to do to volunteer their children, that would send a very strong signal about the confidence in the rightness of doing this."

Unfortunately none of the invited presenters at the Commission's subsequent public meetings provided "the facts." No one even referred to the disclosures contained in the FDA-approved vaccine label which explicitly states: *"The safety and efficacy of BioThrax in a post-exposure setting have not been established."*[5] And no one ever mentioned volunteering their own children for such a study.

The purpose of this letter is to apprise you of the essential scientific, contextual, historical, and statutory facts—including judicial rulings about the ethical standards for research involving children—in particular, nontherapeutic research with no direct benefit to those children. In a word, we provide

the relevant facts—both "the known and unknown facts"—that you, Dr. Gutmann acknowledged the Commission must consider before making a final decision.

We, of **the Alliance for Human Research Protection** submit to you and your Commission the following:

1. How significant is the anthrax threat to Americans?

In modern times no foreign enemy has used biological weapons against Americans—neither against military personnel nor civilians. The only possible exception was the anthrax –laced mail attack on civilians in October, 2001. But unlike the September 11, 2001 terrorist attack by foreigners, the FBI determined that the anthrax spores in the letters emanated from a US military laboratory at Ft. Detrick, and the attacker was the scientist in charge of anthrax vaccine testing—**who is now dead.**

Since 2001 there have been no credible reports about an anthrax threat. In 2002, the GAO[6] reported that DOD determined "The Anthrax Threat Has Been Limited and Stable Since 1990." Nevertheless, in October 2008, Michael Leavitt, Secretary of Health and Human Services (DHHS) invoked his extraordinary authority under the Public Readiness and Emergency Preparedness Act (PREPA, 2005) and declared an anthrax public health emergency, to be in effect through the end of 2015.[7] [See section 12 below]

That declaration by DHHS' Secretary granted unprecedented, broad immunity from all legal liability to the manufacturer, the government program planners, healthcare and other providers—everyone involved in every aspect of an anthrax vaccination program. The declaration bars any persons injured by the anthrax vaccine from seeking damages through the judiciary.

- ***"How do you decide there is an emergency when there is no evidence of one?"***

  That question was posed at the time by one of us, Dr. Meryl Nass, an internal medicine physician who identified the first modern use of anthrax as a weapon of war in Zimbabwe, from 1978-1980.[8] She has also treated many patients with anthrax vaccine-related illnesses.

  Neither DHHS nor anyone in government has cited any evidence to support the declared "public health emergency." The question is especially germane in light of the written response by Michael

Chertoff, the Secretary of Homeland Security (Sept. 23, 2008), to Secretary Leavitt's inquiry as to whether the threat of anthrax met the legal standard for declaring a state of emergency:

> *"There is not currently a domestic emergency involving anthrax. Additionally, there is not currently a heightened risk of an anthrax attack. We have no credible information indicating an imminent threat of an attack involving Bacillus Anthracis."*[9]

FACT: No bioterrorism events have happened since 2001, due to anthrax or any other biological agent. Anthrax is only one of dozens of possible agents that could be used as biological weapons by terrorists or foreign militaries—or only one of hundreds more that could be genetically engineered.

No evidence of an impending anthrax threat has been offered that might conceivably justify extraordinary government measures suspending democratic safeguards and citizens' legal rights. The likelihood of an anthrax terrorist attack is a matter of sheer speculation.

DHHS officials invoke specters of anthrax clouds to rationalize violating federal child protection regulations. A "tabletop exercise" or war game titled *"Dark Zephyr*" is said to have convinced federal officials of a need for testing and treating children with anthrax vaccine. The game simulated a hypothetical anthrax attack on San Francisco, one of the sites of notorious military mock spray germ attacks in the 1950s and 1960s.[10] However, the value of *BioThrax*, the anthrax vaccine, as a treatment in such a post-attack scenario remains speculative and unproven, as is explicitly stated in the FDA-approved label.[5]

Fact: of many thousands of people exposed to anthrax spores in 2001, antibiotics prevented illness in 100% of those treated after exposure. Five people died, their cases unrecognized until very late. There was no additional benefit from anthrax vaccine, which was accepted by less than 2% of those who used antibiotics.

This reassuring fact—that antibiotics proved to be 100% effective—is being ignored, while an adult war game is cited by DHHS officials as the persuasive reason to sacrifice children's health and well-being in a dangerous vaccine experiment that—as will be documented below—is doomed to generate no useful data of any kind. The conduct of such an experiment on children is explicitly prohibited under Federal law.[11]

2. How effective would the vaccine be in an anthrax attack?

BioThrax (a.k.a. AVA or Anthrax Vaccine Adsorbed), the vaccine manufactured by Emergent BioSolutions (formerly BioPort) **has never been proven effective in humans against weaponized (inhaled) anthrax—and is not licensed for post-exposure use, not even for adults.**

FACT: Efficacy studies of *BioThrax* have only measured antibodies: but whether vaccine-generated antibodies will protect people who are exposed to inhaled anthrax from death remains unknown, which is why the vaccine has never been approved for such use by the FDA.

It takes about 40 days after starting 3 inoculations before—what is hoped to be—a sufficient immune response develops. However, after decades of research, there is still no evidence that any antibody level in humans will prevent them from getting inhalation anthrax.[12]

A long history of anthrax vaccine research acknowledges that immunogenicity data do not provide evidence of vaccine effectiveness.[13] In December, 2001, Anthony Fauci MD,[14] Director, National Institute of Allergy and Infectious Diseases, of the NIH, stated on National Public Television:

> *"Since the scientific data, particularly in animal models, do not indicate one way or the other whether or not that this is going to be helpful, in fact the data in monkeys indicate that there really was no difference between monkeys who received the antibiotics plus the vaccine versus the antibiotics alone"*

Indeed, FDA's Regulatory Action, May 17, 2012, acknowledged that data in support of the vaccine's efficacy following inhalation exposure was still lacking:

"...In the absence of data establishing a threshold level of antibody needed to protect against the development of anthrax disease following inhalational exposure..."[15]

Two papers published in 2012 by top anthrax vaccine scientists confirm this point. Copies of both papers were sent to your Commission by one of us [MN].[8] The first, by Ingram and Baillie[16] noted that,

> *"the protective efficacy [of licensed human anthrax vaccines] has yet to be comprehensively demonstrated against the exposure route likely to be encountered during a bioterrorist attack." Furthermore, "concerns over the immunogenicity, safety and reactogenicity of these [currently licensed] vaccines...have driven efforts to develop side effect-free, fully defined, second-generation vaccines capable of stimulating protection following minimal dosing."*

The second paper, by Bellanti, Robbins and Schneerson et al,[17] made this same point:

> *"Spore challenge studies in rabbits showed protection with PA antibody levels of 50 to 100 mcg/ml, (14, 16)* ***but a protective level in humans is unknown. Even less can be surmised about the level needed to protect from a bioterrorist attack, making assessment of the responses to the different vaccines and schedules difficult."***

Instead of facts, several invited witnesses provided misleading testimony to the Commission about the safety and efficacy of the vaccine. Several witnesses conflated immunogenicity (stimulates the production of antibodies and/or T cells) with efficacy (prevents human infection and death).

FACT: Though it might seem counter-intuitive, scientists have never been able to establish an animal model that can bridge survival data from vaccinated experimental animals to survival in humans. The inconvenient truth is that due to lack of an animal bridging model for anthrax vaccines, there are only immunogenicity data in humans, not human efficacy data. Immunogenicity data cannot reliably predict efficacy for this vaccine, either in adults or children.

It is, therefore, not possible to derive effectiveness data for children from any anthrax trial that DHHS may propose. Neither can useful dosing information be derived from a child study.

- **What then, is the justification for performing a pediatric trial?**

3. What is the most effective treatment after exposure to anthrax, and would the current vaccine provide additional benefit for someone taking antibiotics?

Effective emergency treatments for anthrax exposure include antibiotics (antimicrobials), monoclonal antibodies, and anti-anthrax antisera, all of which have been stockpiled by the US government. The consensus among medical experts is that antibiotics are the recommended treatment for those exposed to anthrax spores to prevent even the most lethal (inhalation) form of the disease.

FACTS: This consensus is based on evidence that those who were promptly treated with antibiotics after exposure to anthrax—both humans in 2001 and monkeys in the lab—did not come down with the disease. Possibly 30,000 people were exposed to spores from the anthrax letters in 2001. Most took antibiotics alone; only 198 accepted vaccine. Indeed, according to the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control (CDC):

"No cases of anthrax have been detected among persons recommended to take antimicrobial prophylaxis after the terrorist attacks of 2001."[18]

- **Antibiotics (antimicrobials) were 100% successful at preventing anthrax in those who were treated for an exposure to the anthrax-laced letters in 2001.**
- Homeland Security Secretary Chertoff,[9] recommended antimicrobials in the event of any possible future threat—*"those exposed to Bacillus anthracis need to take appropriate antimicrobials rapidly after exposure to avoid contracting anthrax."* He did not recommend, or even mention, the anthrax vaccine.

- The bipartisan WMD Terrorism Center stated in its "Report Card" (October, 2011): *"Currently, the SNS [Strategic National Stockpile] maintains a sufficient supply of oral antibiotics to provide approximately 60 million individuals with a 60-day course of treatment. The oral antibiotics in the SNS could also be used for response to attacks with likely bacterial agents."* [19]

In November 2012, an FDA advisory committee voted to approve the monoclonal antibody Raxibacumab,[20] for post-exposure use to prevent or treat inhalation anthrax. FDA has never granted the vaccine *BioThrax* an approval for this use.

Raxibacumab is administered in a single 2-hour intravenous infusion, and it works immediately—not 40 days later. The drug is said to be effective in later-stage infection and for antibiotic-resistant anthrax, and is already included in the US stockpile.

FACT: The efficacy of antibiotics following exposure to inhaled anthrax spores is undisputed: whereas anthrax researchers have expressed reservations about the vaccine's efficacy.

You and the Commission would gain insight into the science by examining the transcript of **FDA's vaccine advisory meeting**,[21] November, 2010, which focused on the difficulties that prevented properly testing the vaccine's efficacy in humans following exposure. Below are excerpts from the Committee discussion during its open session:

> DR. DRUSILLA BURNS (FDA-CBER): "*In a bioterrorism event, exposure would likely come without any warning, and a full course of antibiotics—would be initiated as quickly as possible. Then the vaccine would be administered on an accelerated schedule… concomitant antibiotics therapy with the vaccine. This is a component which has not been studied, to our knowledge, for this vaccine."*

"Human efficacy studies are not feasible because human challenge studies would not be ethical…"

"I think it's pretty clear that antibiotics are very, very effective against the disease, while they are being given. Would the vaccine provide anything beyond that? I'm not sure…."

DR. FERRIERI: "*This is an extraordinarily difficult disease to develop a vaccine for, given that you can't test it out in the field with thousands of kids or other population groups. None of the scenarios and models that have been presented really deal explicitly with what the human situation would be—the unpredictability of mass exposures, for example."*

DR. BURNS: "***I think from the data in the literature from other animal studies, it's pretty clear that vaccine by itself is not going to protect. That is probably a given. So what we are talking about is perhaps shortening the course of antibiotics."***

DR. JACK STAPLETON: "*the post-exposure prophylaxis studies are very difficult, given the severity of the infection. Therefore, while they are helpful to show that it doesn't interfere with the antibiotics and that there may be some additive benefit, I don't know that they are as helpful as we would have liked."*

DR. DURBIN: *I have a question on the nonhuman primate study, just to clarify. In the 1-to-10 human dose, there was an excellent boost at challenge, but I believe 40 percent of the animals died. Was there any significant difference between the boosted antibody titers of those animals that survived and those that died?*

DR. QUINN: *Those data are for the survivors only, because the macaques go down in two to three days, before we can take samples for antibody measurement. Where we have been able to take measurement, there has been no measurable onset of antibody. Basically, the animals die too quickly.*

DR. STAPLETON: *"I want to announce that for this session the questions and answers should not cover material that will be discussed in the closed session."*

- In 2002, the **Institute of Medicine** issued a report[22] stating that:
  "*A new vaccine, developed by more modern principles of vaccinology, is urgently needed….a new vaccine should require only two or three injections, elicit protection within 30 days that lasts for at least a year, and remain potent for a long period of time so that it can be stockpiled to ensure ample supplies when needed."*

- **When the appropriate treatment for anthrax exposure is antibiotics, why the urgency to test an outmoded, inferior treatment in children? Why now?**

Another justification that has been put forward for vaccination after exposure is to allow people to continue to inhabit an area contaminated with anthrax spores. But given the unpredictable efficacy of the vaccine and rapid drop off in antibody titers, relying on vaccine protection for continuing

exposures would be foolhardy. Would rational people whose vaccine-induced immunity was uncertain, continue to live in a contaminated area where their pets, wild animals and livestock would be dying, frequently and unpredictably?

CDC Officials have arbitrarily selected 60 days as the cut-off for antibiotics after exposure, asserting that the risks from longer-term antibiotic use are greater than from the vaccine. But there is no evidence for this claim. Doxycycline—the major prophylactic antibiotic used for anthrax exposures—is taken by patients for years, to prevent acne, without major problems. Tuberculosis patients take multiple antibiotics for 6-12 months or more. Maintaining antibiotic treatment for longer than 60 days would provide reliable protection with minimal risk.

4. How safe is the current anthrax vaccine?

- The 2002 vaccine label indicates that 5% to 35% of vaccine recipients developed systemic adverse events. "*Approximately 6% of the reported events were listed as serious. Serious adverse events include those that result in a birth defect, death, hospitalization, permanent disability or are life-threatening."*[1]

- *"A comprehensive review of VAERS AVA data in 2004 demonstrated that women were 3 times more likely than men to have or report an adverse event."*[23]

- The Government Accountability Office (GAO)[23] reported to Congress in 2007 that: *"Officials from the VHC [Military Vaccine Healthcare Centers] Network and CDC estimate that* ***between 1 and 2 percent of immunized individuals may experience severe adverse events, which could result in disability or death."***

- A 2010 CDC review of FDA's Vaccine Adverse Event Reports (VAERS) found that 600 of 6,015 (9.9%) nonduplicative reports *"were categorized as serious events (i.e., events resulting in death, hospitalization, or permanent disability)."*[24]

- A detailed review by the Military Vaccine Agency[25] (2012) that was designed to assure readers of the anthrax vaccine's safety, noted: *5% to 35% will notice rashes (16%), headaches (14% to 25%), joint aches (12% to 15%), malaise (6% to 17%), muscle aches (3% to 34%), nausea (3% to 9%), chills (2% to 6%), fever (1% to 5%).*

- The FDA-approved 2012 label pregnancy warning states:

  "*Of women who received vaccine within 90 days of the estimated conception (n= 14), 2 spontaneous abortions and a first trimester intra-utero fetal death were reported, along with one report of 'healthy' term infant with mild right clubbed foot abnormality."*[2]

- **How can the severity and magnitude of such risks be justified under a United States statute[11] that requires children be exposed to no greater than a "minor increase over minimal risk"?**

5. Why has this vaccine been the center of much heated controversy for over 15 years?

In 1998, US Department of Defense (DoD) launched a mandatory Anthrax Vaccine Immunization Program, which became a source of heated debate and disagreement. Inasmuch as no army anywhere has ever been attacked with anthrax, calling into question the need for vaccination, the vaccine's safety hazards generated impassioned controversy. Hundreds of high-ranking soldiers revolted, refusing to be vaccinated: hundreds of National Guard and reserve pilots left the military and over 100 soldiers were court-martialed for refusing to be vaccinated for fear of incapacitating adverse vaccine effects. These resulted in several lawsuits and a dozen Congressional hearings.[26]

After holding a series of hearings on the anthrax vaccine program, the House Committee on Government Reform issued a critical report titled *"The Department of Defense Anthrax Vaccine Immunization Program: Unproven Force Protection,"*[27] suggesting the vaccine only be used as an experimental product, with medical follow-up for each recipient.

FACT: No other country in the world mandates that its troops be vaccinated with anthrax vaccine. Canada, Australia and the United Kingdom all began anthrax vaccinations of their troops– but all three programs were soon cancelled.

- In the UK, boxes of vaccine were discovered washing up on beaches, after shipboard troops threw boxes of the vaccine overboard.[28] Vaccinations are not mandatory in the UK; a low voluntary vaccination rate ended its program.

- Australian troops too rebelled against the vaccinations.

    - *"Defense officials in Australia admitted Saturday to keeping secret a variety of side effects associated with the anthrax vaccine administered to Australian troops bound for Iraq, according to the Canberra Times (see GSN, Dec. 29, 2003). The Australian military's anthrax vaccination program was suspended for two months in 2001 after personnel headed for Afghanistan suffered side effects. Confidential defense documents released in Australia revealed that nearly 75 percent of troops receiving the injection experienced side effects*

ranging from swelling in the injected arm to flu-like symptoms."[29]
The program was later cancelled permanently.

- Canada's highest military judge, Guy Brais, ruled in 2000 that giving the vaccine to troops contravened Canada's 1982 Charter of Rights and Freedoms, permanently ending the vaccinations:

  - *"It was sufficient and the court is satisfied on the balance of probabilities that the defense has successfully demonstrated that* ***the anthrax vaccine contained in lot 020 was unsafe and hazardous and could be responsible for the important symptoms reported by so many persons who received that vaccine…"***

  - *"In those circumstances, the court concludes that the accused's right to life, liberty and security of the person in section 7 of the Charter of Rights and Freedoms were infringed. And as the court stated earlier, the government, through its Department of National Defense and the Canadian Forces, could never be justified to impose inoculation of soldiers with an unsafe and dangerous vaccine as a limit of their rights under section 7."*[30]

Israel tested both the US and an Israeli anthrax vaccine on troops, many of whom subsequently sued the government over resultant injuries. The Israel Medical Association issued a report calling the experiments "scientifically unjustifiable and in violation of the Helsinki Accords."[31]

- Will parents be informed about the vaccine's true risks, pain, and discomfort?
- Will a responsible parent then volunteer their child for this government experiment?

6. Safety data from "pivotal safety / efficacy trial" conducted by CDC at taxpayer expense has been withheld from the public—Why?

Dr. Gutmann, at your May meeting you asked to be provided with the *"known and unknown"* facts about the anthrax vaccine. Although some of the safety risks of this vaccine for adults are disclosed in the *BioThrax* package insert, and in FDA, CDC and GAO documents—this Commission has never discussed these "known" vital facts.

Have you been briefed about the Congressionally mandated CDC *"pivotal safety and immunogenicity trial,"* a randomized, double-blind, placebo-controlled clinical trial testing the anthrax vaccine's safety / immunogenicity / and dosing regimens in 1,563 adults?

The trial duration was 43 months, and involved at least 25 clinic visits per subject. This "pivotal trial" was conducted at five clinical sites in the US—Walter Reed Army Institute of Research, Baylor College of Medicine, University of Alabama, Emory University, and the Mayo Clinic—from 2002-2007.

Partial findings from the first 1,005 subjects during the first 7 months of the 43-month trial duration were published in the *Journal of the American Medical Association*, on October 1, 2008, and the complete dataset was submitted to the FDA in 2009.

The **CDC authors of the trial reported in *JAMA*[3] that 186 people suffered 229 *"serious adverse events"[SAEs]* during the trial with 7 deaths—that is, 12% of the subjects suffered SAEs.**

> *"The following AEs were classified as serious (SAE), consistent with US regulations: death, life-threatening event, initial inpatient hospitalization or prolongation of hospitalization, significant or persistent disability or incapacity, congenital anomaly or birth defect, and a medical event that required medical or surgical intervention to prevent one of the other outcomes."*
>
> *"Since enrollment began, there have been 229 SAEs in the entire 1563 participant cohort involving 186 participants, with 7 deaths. Causes of death included atherosclerotic cardiovascular disease, intracranial aneurysm, motor vehicle accident, suicide, AIDS-related illness, accident, and gunshot wound. Nine SAEs (involving 7 participants) were rated as possibly related to the study agent (Table 7). All other events were considered unrelated or unlikely to be related to the investigational agent.* ***A complete and unblinded analysis of SAEs will be conducted at the study conclusion when all participants complete the 43-month visit.***
>
> **"*...The data from the remaining 559 participants […] will be included in the analyses at the end of the study in 2009.*"** [emphasis added]
>
> The **JAMA** Network **TABLE 7 describes 9 Serious Adverse Events suffered by 7 people.**

Table 7. Serious Adverse Events Rated as Possibly Associated With the Study Agent Since Study Initiation

Participant	Description of SAE	Status	Outcome	Medical Monitor Causality Assessment[a]
1	Tear of supraspinatus tendon	Study injections discontinued; continuing follow-up	Symptoms resolved after surgery and physical therapy	Possible
2	Generalized allergic reaction	Study injections discontinued; continuing follow-up	Resolved	Possible
3	Bilateral pseudotumor cerebri with bilateral disc edema	Study injections discontinued; continuing follow-up	Treated and improving	Possible
4	New onset of generalized seizure; hospitalized for generalized clonic seizure; MRI confirmed hydrocephalus consistent with aqueductal stenosis; hospitalized endoscopic third ventriculostomy secondary to aqueductal stenosis	Study injections initially suspended and then later discontinued; continuing follow-up	Discharged in stable condition	Possible
5	Bilateral ductal carcinoma of the breast	Completed study	Undergoing further testing (at time of report)	Possible
6	Onset of new bilateral arthralgia of the metacarpophalangeal joints; ANA positive	Completed study	Continuing treatment	Possible
7	Invasive ductal carcinoma of the breast	Study injections discontinued; continuing follow-up	Positive outcome reported by participant following mastectomy and chemotherapy treatment	Possible

Abbreviations: ANA, anti-nuclear antibody; MRI, magnetic resonance imaging; SAE, serious adverse event.
[a] Blinded review using World Health Organization causality assessment criteria.

However, the complete safety findings from this "pivotal trial" have never been published or publicly disclosed.

Except for Table 7 which describes 9 SAEs suffered by 7 adults, and the seven deaths, the nature of the remaining 213 SAEs suffered by 172 subjects has been withheld—even when requested by one of us (MN) under the Freedom of Information Act several years ago.

CDC immunogenicity data were discussed at FDA's vaccine advisory committee meeting (2010)[20] but safety findings were conspicuously not discussed at the open public meeting. FDA scientists, the advisory committee and the manufacturer (Emergent BioSolutions) then met **behind closed doors for over two hours.**

Why are US public health agencies hiding the full safety findings of this "pivotal" trial? The DHHS Secretary can authorize the release of the safety data at any time, but she has not done so.

Being informed about vital safety information from CDC's "pivotal trial" should be of paramount importance for you, if you are to credibly evaluate the ethics of exposing children to this vaccine without a medical justification.

Will you seek to obtain and review the findings or will your Commission render its recommendation without knowledge of the vital facts?

Failure to disclose negative scientific medical research findings has corrupted the scientific literature and American medicine. This subject is the focus of vigorous debate and criticism, mostly directed at pharmaceutical companies that spin and "cherry pick" data for publication—in order to increase their products' sales. In the case of vaccines, in which the government has a substantial stake, CDC's failure to disclose the full data, while claiming positive findings based on only partial data—does not inspire public trust. **Will the findings from the proposed children's anthrax trial likewise be buried, if the results are not to the liking of DHHS officials?**

Is this Commission prepared to risk its reputation by endorsing scientifically dubious experiments that test unproven medical countermeasures with known significant hazards in children?

7. What is the legal and historical framework governing pediatric research in the US?

The ***Nuremberg Code***[32] (1947) is the most important document in the history of medical research ethics, serving as the cornerstone for all subsequent national and international codes of medical ethics. Principle #1 ensures that "*The voluntary consent of the human subject is absolutely essential."* But children are legally incapable of exercising that fundamental human right, and cannot protect themselves from risks in painful biomedical experiments not designed to benefit them. As a result, children have suffered harm in experiments that were not of their choosing.[33]

All other ethical principles of the Nuremberg Code apply for research involving children. Principle #2 mandates that for research involving human subjects to be permissible*, "the experiment should be such as to yield fruitful results for the good of society,* ***unprocurable by other methods*** *or means of study, and not random and unnecessary in nature."* Your Commission strongly concurred with this principle in its report last year about the US Public Health Service research in Guatemala.[34]

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was established in 1974 under Public Law 93-348**.** The Commission's reports and recommendations laid the ethical and legal foundation for human subject research in the US. The

Commission's ***Report and Recommendations: Research Involving Children***,[35] (1977) provides the most authoritative ethical framework for evaluating the permissibility of research involving children. And it provides the framework for determining whether "*exceptional circumstances*" do in fact exist to justify *"exposing children to research attended by more than minimal risk:"*

> *"The Commission acknowledged that* ***exceptional circumstances may arise*** *in which considerable dangers to children or to the community at large might be avoided or prevented by exposing children to research attended by more than minimal risk…* ***the ethical argument should be made, not over a hypothetical case, but over an actual situation, in which the real issues and the likely costs of any solution can be more clearly discerned****…Thus, Recommendation 6 urges that should such a situation occur, it be* ***defined in the most stringent*** *way and determined by those at high levels of public accountability."* (pages 140-141).

There are currently no *"exceptional circumstances… in which considerable dangers to children… might be avoided"*: children are not at risk of anthrax. The bare minimum ethical principles summarized in the National Commission's ***Belmont Report*** (1979):[36] 1. ***Respect for Person (autonomy) 2. Beneficence ("do no harm") 3. Justice (fairness),*** are the guiding principles of the **Code of Federal Regulations**[37] governing research with human subjects. [45 CFR 46]

For human research to be approvable, Federal statute requires evidence of: *"the importance of the knowledge gained or to be gained."* [45 CFR 46.120] Federal regulations set limits on approvable research involving human subjects: **speculative future risks or benefits may not be considered.**

> *"In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research…the IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy)."* [45 CFR 46.111]

Whether or not the current Administration chooses to be guided by a simulated exercise ("*Dark Zephyr*") to set public policy, federal law prohibits justifying approval of research involving risks to human subjects on the basis of speculations about future benefits or future risks.

Because children are legally incapable of exercising their human right to say NO to research, children have been targeted for medical experiments that were not in their best interests—experiments that were more likely to harm them than to provide a benefit. Over the past 35 years specific regulations have been enacted to protect children from exploitation in clinical research involving risks, with no

direct benefit to justify the risks. Federal regulations prohibit exposing children to research involving risks—that are greater than *"minimal risk"* or a *"minor increase over minimal risk"*—in the absence of a potential direct benefit to the participating child.

FACT: The proposed anthrax vaccine experiment indisputably poses greater than minimal risks with no direct benefit for the specific children involved. This government-initiated experiment fails to meet the statutory standard in Federal regulations for exposing children to greater than a *"minor increase over minimal risk"* in research:

> *"The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is **of vital importance** for the understanding or amelioration of the subjects' disorder or condition"* [Sec. 46.406]
>
> *"…the research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children."* [Sec. 46.407]

The child subjects in the proposed experiment will have no "disorder or condition;" the risk of anthrax exposure is speculative, not *"a serious problem affecting children's health or welfare;"* and inasmuch as none of the adult *BioThrax* trials have provided reliable efficacy and dosing information, the pediatric trial results will be of no clinical or scientific value, much less *"of vital importance."*

Judged by the ethical standards of science, medicine, and law, the vaccine trial proposed by DHHS is unapprovable and should not be performed.

As your Commission put it in its Guatemala Report:
"Whether the threat to public health posed by a particular disease outbreak is severe enough to justify aggressive tactics that temporarily suspend our usual ethical norms is itself an important question of ethics and policy."

In the absence of an imminent anthrax threat to public health, how can you and the Commission even consider endorsing a proposal to subject American children to significant risks from a toxic, controversial vaccine, in an experiment that offers no benefit for the children?

The performance of such an illegitimate experiment would suspend foundational ethical, legal and scientific norms protecting children—who are not volunteers, who are legally precluded from giving

informed consent to research. How can you justify such an abrogation of the human rights of children?

In the ONLY two **judicial reviews** about the legitimacy of conducting nontherapeutic medical experiments on children who would be exposed to greater than "minimal risk" without a direct benefit for them, **the courts roundly condemned such experiments as unethical.** In each of the judicial rulings **the judges compared such experiments to the medical atrocities committed by the Nazi doctors, and cited the *Nuremberg Code,*** and warned against *"embarking on the slippery slope."*

And in each of the judgments the Court rejected parental consent as justification for exposing children to greater than minimal risk. In a NYS Supreme Court ruling[38] (1995) the Court stated:

> *"Parents may be free to make martyrs of themselves, but it does not follow that they may make martyrs of their children."* T.D. v NYS Office of Mental Health

We recommend that the Commission read the landmark decision of the **Court of Appeals of Maryland**,[39] (2000) the state's highest court:

> ***"It is not in the best interest of a specific child, in a nontherapeutic research project, to be placed in a research environment, which might possibly be, or which proves to be, hazardous to the health of the child."***
>
> *"We have long stressed that the 'best interests of the child' is the overriding concern of this Court in matters relating to children. Whatever the interests of a parent, and whatever the interests of the general public in fostering research that might, according to a researcher's hypothesis, be for the good of all children, this Court's concern for the particular child and particular case, over-arches all other interests."*
>
> *"**It is, simply, and we hope, succinctly put, not in the best interest of any healthy child to be intentionally put in a nontherapeutic situation where his or her health may be impaired, in order to test methods that may ultimately benefit all children.**"* [emphasis added]
>
> *"To think otherwise, to turn over human and legal ethical concerns solely to the scientific community, is to risk embarking on slippery slopes, that all too often in the past, here and elsewhere, have resulted in practices we, or any community, should be ever unwilling to accept. As a result of the atrocities performed in the name of science during the Holocaust, and other happenings in the World War II era, what is now known as The Nuremberg Code evolved. Of special interest to this Court, **the Nuremberg Code, at least in significant part, was the result of legal thought and legal principles, as opposed to medical or scientific principles, and thus***

should be the preferred standard for assessing the legality of scientific research on human subjects. *Under it, duties to research subjects arise."*[39] Higgins/Grimes v Kennedy Krieger 2000.

- If ever children were exposed to anthrax spores, the proven safe and effective treatment of choice is antibiotics, such as Ciprofloxacin or Doxycycline, which have been FDA-approved for pediatric use against anthrax—and recommended by CDC.[40]
- From its inception, the proposed anthrax vaccine experiment violates bedrock medical ethics principles, the Hippocratic Oath—"*Primum Non Nocere," "First, do no harm,*" the Nuremberg Code, and the Federal statutory protections.

Dr. Gutmann, you and the Commission have been asked to provide a veneer of legitimacy for federal officials to trample foundational principles of medical ethics, and law. Your Guatemala report warned against this very thing:

"one lesson of the Guatemala experiments, never to take ethics for granted, let alone confuse ethical principles with burdensome obstacles to be overcome or evaded, is a sobering one for our own and all subsequent generations. We should be ever vigilant to ensure that such reprehensible exploitation of our fellow human beings is never repeated."[34]

- **Will your Commission sanction countermeasures research in American children that fails to comply with medical ethics and statutory legal standards?**

8. <u>Exactly what medical or scientific question is the proposed pediatric trial intended to resolve?</u>

At your Commission's May 2012 meeting, **Robert (Skip) Nelson, MD, PhD, Senior Pediatric Ethicist at the FDA** explained the lack of scientific rationale for conducting the pediatric trial. He pointed out that evidence to enable bridging survival data from animals to humans has never been obtained, even for adults, and there is no justification for a pre-event pediatric trial. And he cautioned you to *"make sure you are working with good facts."*

"***I don't believe we have data on adult dose sparing and different dosing strategies to where you could do a pediatric pre-event study that could show you whether or not doing some dose sparing or different approaches would actually lead to sufficient immunogenicity to allow bridging in adults.***"

"*If the argument for doing the pre-event is to be able to do something different than you do in the post-event, then get the adult studies to show that, in fact, you could do something different in pediatrics. In other words, the science would drive the ethics.* ***I would find it more***

> ***compelling if there was a scientific reason why a pre-event study.*** *I don't find the logistical arguments compelling."*
>
> *"**anthrax is treatable by Ciprofloxacin, Doxycycline**. **In other words, there's no urgent need to vaccinate**, provided people take their antibiotics… And the other would be if we want to look, for example, at immune bridging and want to do testing of different doses and that sort of thing, we would need first that data in adults to know that we would have a knowledge of what dose sparing would happen with adults… make sure you're working with good facts. "*

From the information on the Commission's website it does not appear that your invited "experts" had expertise about the "known and unknown facts"—scientific, legal or contextual—facts that should have informed your deliberations prior to rendering recommendations.

FACT: A pediatric *BioThrax* trial cannot possibly generate scientific evidence that would establish efficacy or optimal dosing—just as adult trials have failed to do so. This is due to the inability to bridge immunogenicity data to extrapolate protection from infection or death.

FACT: The antibody data to be gained from a pediatric trial will thus be clinically and scientifically uninformative. The proposed experiment will be scientifically useless and unnecessary—thereby violating ethical principles of the Nuremberg Code and Federal regulations.

The Commission's suggestion, at your January 2013 meeting, that DHHS could "immediately" start a trial with 18 to 20 year olds and gradually enroll younger and younger children is likely to be viewed as **a disingenuous attempt to shift the focus** to young adults—who are legally capable of making an informed choice whether or not to volunteer. The issue before you is not young adults. The issue is whether an experiment that is unapprovable under Federal statutes that were enacted to protect children up to the age of 18—protect them from nontherapeutic experiments involving greater than minimal risk with no potential direct benefit to the children involved—whether such an experiment can go forward.

Furthermore, your proposal to test *BioThrax* on 18 to 20 year olds makes an underlying false assumption that we have no knowledge about whether or not the vaccine poses more than minimal risk, and therefore a trial is needed to establish a risk.

FACT: A large body of evidence (mostly) from trials in young adults, documents serious adverse events linked to this vaccine. This evidence from previous trials should have been brought to the attention of the Commission.

It is well to remember: *"Facts do not cease to exist because they are ignored."* – Aldous Huxley, *Proper Studies*, 1927.

The speculative nature of an anthrax attack, the level of risk for children from the vaccine, and the lack of clinical, scientific, or circumstantial justification for this proposed experiment constitutes a radical deviation from Federal regulations that surpasses those encountered by any federal panel convened under 46.407**.**

9. Does Anyone Really Know Why Children Are Being Targeted for a *BioThrax* Vaccine Experiment?

- No federal official has provided a valid justification for conducting an anthrax vaccine trial in children. When experiments have no scientific merit, they are ethically and legally prohibited. No amount of sophistry can change that.

In 2004, the National Institute of Child and Adolescent Development approved a protocol to test the AVA vaccine (renamed *BioThrax*) in 350 adult volunteers (aged 18 to 30) and 100 first and second grade children. Senator Bingaman expressed *"grave concern about any intent to proceed with clinical trials with children at this point"*[41] in a letter to Secretary Leavitt—and the experiment was cancelled.

Why then, is DHHS Secretary, Kathleen Sebelius, seeking endorsement for an experiment testing anthrax vaccine in children now? What scientific facts or circumstances have changed? Is there any credible evidence of an imminent anthrax risk for children? Lacking any credible rationale for conducting such an experiment on children, DHHS officials have evaded the inconvenient scientific facts and resorted to misleading propaganda.

In 2011 DHHS Dr. Nicole Lurie, Assistant Secretary for Preparedness and Response asked the National Biodefense Science Board (NBSB) to render a recommendation on performing an anthrax vaccine trial in children. The Board concurred, but only if a federal ethics panel agreed.

Both advisory panels—the NBSB and your Commission—were misled to believe that the proposed study would provide the "safety, immunogenicity and efficacy data" that is currently "lacking in pediatric populations."[42]

An invited "expert" presenter at the May 2012 meeting of this Presidential Commission was **Major General John Parker, MD**, retired, co-chair of the Anthrax Vaccine Working group, of the NBSB.[43]He stated that he and the NBSB ***"strongly support having safety trials for a children's vaccine…"***

The NBSB had endorsed the proposed children's experiment in 2011, making two specious claims:

> *"it would be in the best interests of children, their parents, and the United States Government to attempt to gather the safety and immunogenicity data about AVA PEP [post exposure prophylaxis] in children prior to an anthrax event."*
>
> *"Antibiotics would offer prompt (but temporary) protection, and vaccination would offer delayed (but extended) protection against infection."*

- **Did the NBSB scientists and experts not understand that a vaccine safety trial—which seeks to assess whether the vaccine causes no rare, but serious, potentially disabling, even fatal, adverse effects—requires many thousands of child subjects?** It appears they did not.

- Did the NBSB scientists and experts fail to understand that for valid data to be obtained for vaccine efficacy, one either needs to expose humans to the disease (anthrax) or be able to bridge animal data to reliably predict human protection?

It soon became apparent at your Commission's May 2012 meeting that, like the NBSB, your Commission lacked clarity about the basic objective of the experiment. No one seemed to know whether it was supposed to test safety or efficacy? How many children would be recruited as subjects, of what ages? Vague numbers were thrown around—300 children at first, then 1,000…

Dr. Nelson of the FDA, and ex-officio of NBSB, tried to clarify the difference between trials testing for safety and trials testing for efficacy, and he tried to correct Dr. Parker's misrepresentation:

> *"I think the NBSB was just talking about their small immunogenicity study. I don't think they had a 70,000 large-scale safety study in mind. No one's putting on the table the safety study*

prior to an event. Seventy thousand was what we did for Rotarix. No one's talking about that. So I would hope we don't put that on the table."

At this Commission's January 2013 meeting Col. **Nelson Michael MD** confirmed that a reliable animal model was still lacking, and that serologic "benchmarks" could still not establish efficacy:

"the animal models had not been validated for human bridging...that said, there are markers in the blood, "benchmarks" that can be looked at that we think predict efficacy...BUT there are no strict correlates of protection that tell us that for sure we are using the right benchmarks."[44]

FACT: Decades of immunogenicity trials in adults have not produced data acceptable to the FDA as demonstrative of efficacy, due to the absence of a valid bridging model. Neither DHHS' proposed trial, nor any other that might be proposed, can surmount this hurdle. Nor can the proposed experiment answer dosing questions.

FACT: The proposed trial cannot answer meaningful safety questions—which would require using thousands of children. The inescapable conclusion, therefore, is that data to be obtained from the proposed pediatric experiment will have no scientific or clinical value. Undertaking such trials is, therefore, unethical and unapprovable under US statute.

Indeed**, Dr. Christine Grady**, a member of this Commission, who is Chief of the Department of Bioethics at the National Institutes of Health Clinical Center, and also serves as Head of the Department's Section on Human Subjects Research, pointed out that knowing the specifics about the purpose of the experiment was essential before a decision on the ethics could be made. She also recognized that **nothing useful about safety** would be learned from a small trial in children. She understood that the trial would not change the plan of action if an anthrax exposure event occurred: Antibiotics would remain the government's treatment of choice for anthrax, followed by the vaccine.

"I think the details of the study as proposed matter in terms of whether there's a go or a no-go. And so I was very curious, General, Dr. Parker said, we are prepared to give antibiotics and the vaccine to children in a post-event right now. ***So what would a study change about that?****"*

"I can't imagine we're going to get real safety data that—enough children in a pre-event study that we would find something safety-wise that would then change the plan about giving vaccines post-event. ***So what do you think -- a study would tell us, could tell us that would change the current plan?"***

In his response **Dr. Parker let the cat out of the bag**:

> *"We debated that question. And—it boiled down to a very human type thing that, if we're talking to a parent about giving a child a vaccine, it would be a much better situation to be able to say that we know the vaccine is safe."*
>
> *"[We need to] sustain the credibility of the United States Government through the Department of Health and Human Services. This credibility is sustained by the United States Government being able to say we tested the vaccine in pediatric populations."*

Dr. Parker thus acknowledged that NBSB's rationale for supporting a scientifically bankrupt and ethically and legally unapprovable anthrax vaccine trial in children was to provide credibility to the government's promotional vaccine campaign. In other words, the trial's purpose is for public relations: *"to be able to say that we know the vaccine is safe"* or "*to be able to say we tested the vaccine in pediatric populations."*

- **This level of cynicism, the misrepresentation of a promotional trial as science, and especially the lack of respect for children's rights and human dignity is truly shocking.**

The NBSB endorsed DHHS' proposal to conduct the experiment as an Investigational New Drug (IND) trial**,** which **could expand the vaccine's license to include children**. **The Alliance for Human Research Protection (AHRP)** finds it curious that federal officials have assumed the role of the vaccine manufacturer, who would normally submit an IND and conduct its own clinical trial to expand the indications for its product, to increase its sales. **This is especially remarkable, in that the US government is virtually the sole purchaser of this vaccine.**

DHHS Secretary Sebelius' letter to you as Commission chairperson, requesting this study, is disingenuous and intentionally misleading when she states:

> *"The safety of our children is paramount, and it is vital that we thoroughly address any and all ethical considerations relative to having adequate and available safety and immunogenicity data on our medical countermeasures to protect them before, during and after an event."* [45]

She insinuates that the proposed trial will provide *"adequate and available safety and immunogenicity data"* and that will "protect" children. Curiously, she refers to "our children"-- does that indicate her intent to volunteer her own child or grandchild?

Most troubling, however, is her use of the phrase *'before, during and after an event.'*

This is a clue to the real purpose of the proposed *BioThrax* experiment: it foreshadows an intention

to use anthrax vaccine in children before an anthrax emergency, possibly even to mandate such *pre-event* anthrax vaccinations. Your Commission's endorsement of a scientifically meaningless, morally unconscionable pediatric trial may have been sought as a necessary step in that direction.

Secretary Sebelius also asked you *"to address… the broader question of how best to obtain clinical data on medical countermeasures in children…"*

Note that you were not being asked *whether* there was a legal and ethical way to get clinical data from children who did not have a clinical condition and might be subjected to considerably more than minimal risk. You were instead asked "*how*" to obtain the data—even though federal laws prohibit just such experiments with children.

You and your Commission have been asked to render broadly applicable recommendations for hypothetical scenarios for testing medical countermeasures, including but not limited to anthrax vaccine, in children. Rendering such recommendations could eviscerate Federal protections for children.

The Secretary's request to you collides with the ethical and legal foundation laid by the National Commission, which requires that ethical considerations about exposing children to research risks, *"should be made, not over a hypothetical case, but over an actual situation, in which the real issues and the likely costs of any solution can be more clearly discerned…"*[35]

It is almost inconceivable that a Presidential Commission appointed by President Barack Obama, would even consider formulating a research framework that would deviate from the hard won, federal research regulations protecting children—absent any validated risk of an imminent anthrax attack, and absent evidence that this highly controversial vaccine is even necessary, given the proven efficacy and availability of antibiotics—the treatment of choice.

Dr. Gutmann, your Commission is being asked to sanctify a scientifically bankrupt experiment that would sacrifice children—like so much collateral damage—for marketing purposes. Is it the role of your Commission to assist government officials to violate federal ethics statutes—thereby setting a dangerous precedent that history has demonstrated, leads to the descent along the slippery slope?

10. <u>Approval of DHHS' proposed experiment would be a throwback to the ignoble history of US government- sponsored, non-therapeutic medical experiments that have brought shame to our nation</u>:[33,38,39,46,47,48,49,50]

- Tuskegee syphilis experiments on African-American males,
- Willowbrook State School induced hepatitis experiments on retarded children,[46]
- Fernald State School radiation-laced Post cereal experiments, [47]
- Iowa Soldiers' Orphan Home induced-stuttering--"The Monster Experiment,"[48]
- NIMH-Columbia University racist "fenfluramine violence-prediction" experiment conducted on 6 to 10-year-old Black and Hispanic NYC children,[49]
- EPA-Johns Hopkins-Kennedy-Krieger lead poison exposure experiments on toddlers,[39]
- National Institute of Health-Columbia University, Johns Hopkins, Children's Memorial Hospital, Chicago, AIDS drug tests on foster children,[50]
- Guatemala syphilis transmission experiments…[51]

Experiments such as these encapsulate the Utilitarian culture of opportunism in which the ends justify the means—whereby children's welfare is sacrificed for the ends of others.

None of the children in egregious past government experiments were recruited from middle or upper class households. None came from the educated academic class—those who sponsored, designed, conducted, and benefited from the experiments. The child subjects in nontherapeutic experiments offering no direct benefit to justify even minimal risk, were recruited from uneducated, disadvantaged, mostly minority households—just as the intended subjects of the anthrax vaccine experiment are likely to be. Then and now, the researchers defended the experiments as being of "vital importance" for obtaining knowledge for "the greater good." In some cases, they defended the experiments by arguing that they were conducted with parental consent. Those specious arguments have been emphatically rejected by the judiciary.[38,39]

This Commission is being asked to assist the Secretary of DHHS—a political appointee—to help circumvent hard-won Federal statutory protections that were established over the last 35 years to protect children from just such unapprovable experiments as she asks you to endorse.
The vaccine's safety hazards for children are real—the anthrax emergency is not.

Is this Commission prepared to justify radical government experiments prompted by a speculative scenario in a virtual reality exercise ("Dark Zephyr"), and thereby endorse the sacrifice of children's human rights?

11. <u>How did the anthrax letters breathe new life into the vaccine?</u>

Prior to the letter attacks, government oversight investigations confirmed a multitude of problems associated with the military's anthrax vaccine program, including unreliable quality control in the manufacturing process. The vaccine manufacturing plant failed a major FDA inspection in 1997. The plant was then entirely rebuilt, and sold to a private company by the state of Michigan in 1998—but FDA inspectors kept finding faults, and the new plant failed to regain a license to begin producing anthrax vaccine.

> On February 17, 2000, after a year-long investigation by the House Committee on Government Reform, Congressman Shays stated: *"Plagued by unstable supplies, **uncertain safety and unproven efficacy** against the anthrax threat, the mandatory, force-wide immunization program should be suspended until DoD gets approval to use an improved vaccine."*[52]

> In September, 2000, Candidate George W. Bush stated:
> *"The Defense Department's Anthrax Immunization Program has raised numerous health concerns and caused fear among the individuals whose lives it touches. I don't feel the [Clinton] administration's anthrax immunization program has taken into account the effect of this program on the soldiers in our military and their families. Under my administration, soldiers and their families will be taken into consideration."*[53]

By August 2001, memos reveal that the Pentagon was leaning toward scrapping the whole anthrax vaccine program.

Ironically, the letter attacks served to reinvigorate the troubled anthrax vaccine program, which was on the verge of collapse and had run out of vaccine.[53]

After the 2001 anthrax letter attacks, DHHS Secretary Tommy Thompson insisted the vaccine should be relicensed—only then did FDA approve new production of vaccine and the new plant, in January 2002. However, when the vaccine's licensing history was investigated, it was discovered that the vaccine had never completed all required FDA tests, including a test for human efficacy requested by the licensing authority in 1970.[54]

In December, 2001, Anthony Fauci, MD,[14] Director, NIAID, expressed serious concerns about the vaccine's toxic effects and the absence of proof of its efficacy. He therefore stressed the importance of giving people *"free and open choice"*:

> *"this is important -- that people are given the free and open choice to make a decision based on what they feel is the level of risk that they are willing to take -- one risk of the vaccine itself, as well as the perceived hypothetical and theoretical consideration that maybe the vaccine might help you out, and since there are toxicities associated with the vaccine, and importantly the vaccine has never been used in a context like this, that's the reason why you need informed consent and you need a decision on the part of the individual themselves….The number one potential risk is the risk associated with taking any vaccine -- namely toxic side effects."*

In 2003, federal district judge Emmett Sullivan strongly criticized government policy denying members of the military, the right to informed consent:

> *"The women and men of our armed forces put their lives on the line every day to preserve and safeguard the freedoms that all Americans cherish and enjoy. Absent an informed consent or presidential waiver, the United States cannot demand that members of the armed forces also serve as guinea pigs for experimental drugs."*[55]

And in 2004 Judge Sullivan ruled, *"the vaccine is either a drug unapproved for its intended use or an investigational new drug…"*[56] rescinding the license.

DHHS Secretary Thompson responded by issuing an Emergency Use Authorization [EUA] for the vaccine,[57] allowing its use under voluntary conditions, even in the absence of a license. This was the first time an unsubstantiated anthrax emergency was declared by an HHS Secretary, and the first-ever use of the EUA provision of the BioShield Act.

In 2005 FDA accepted the original 1970 evidence and issued the vaccine a new license, stating that additional data were not needed. But fundamental doubts about this vaccine's efficacy and safety have never been put to rest.

12. What is the Public Readiness and Emergency Preparedness Act (PREPA) and how does it impact on "countermeasures research"?

"Countermeasures research" is covered under the Public Readiness and Emergency Preparedness Act (PREP Act, 2005), a controversial statute that was tagged on to the 2005 DoD appropriations bill in the "dead of night" and signed into law on December 30, 2005, "**for the purpose of providing immunity from legal liability** to manufacturers of any vaccine or drug"[58] that the Secretary of HHS designates to be a "medical countermeasure." *BioThrax* was so designated by then HHS Secretary Leavitt on October 1, 2008 to be in effect through December 31, 2015.[7]

"Immunity from tort liability means there is no legal tort claim that can be pursued in court […] under Federal or State law for any type of loss including death; … with any causal relationship to any stage of development, distribution, administration or use of the covered countermeasure recommended in the declaration."[58]

Victims who are harmed—even if caused by negligence—by countermeasure products or by poorly planned or poorly administered programs or policies that are covered by the PREP Act,—are precluded from seeking compensation through the US legal system.[59]

The PREP Act does not specify any criteria for declaring a public health emergency. "Medical countermeasures research," therefore, poses serious additional risks that you, the Commissioners, have not discussed. But these are major risks, which you must consider when assessing the scope of risks that a child in a "medical countermeasures research" protocol would incur, and that any child or adult who used a countermeasure such as anthrax vaccine, outside a trial, would also face.

The anthrax vaccine continues to pose serious risks of harm—including fetal harm (it is designated Pregnancy Category D by FDA)—and its efficacy post-exposure to inhaled anthrax remains in doubt. Indeed, the unilateral suspension of legal responsibility for vaccine injury is a tacit acknowledgment of the inherent risks**. Why else would HHS Secretary Leavitt have immunized the manufacturer, Emergent BioSolutions, and all public and private officials involved with the vaccine from legal liability?**

By declaring a public health emergency DHHS Secretary Leavitt did not protect the public health: he protected biodefense stakeholders: corporate, government, and healthcare personnel, by sacrificing civil and human rights. Countermeasures research poses real hazards for children—hypothetical anthrax emergencies do not.

13. Would You Submit Your Child to "Countermeasures Research"?

Most Americans are unaware of the sweeping power granted to the Secretary of DHHS under the PREP Act. Simply by declaring a health emergency, manufacturers and public health officials are granted extraordinary waivers from liability that surpass even the military's immunity from liability. While soldiers are prohibited from seeking damages for injuries from the government or the

manufacturer, at least they are entitled to lifetime care from the VA system. **Civilians—including children—who may be seriously harmed from "medical countermeasures" will not have the benefit of that safety net.**

Nor are most Americans aware that under the PREP Act the Secretary—a political appointee—has the unilateral authority to suspend citizens' constitutional right to seek judicial review and just compensation for injury caused by a "medical countermeasures" product.

FACT: In June 2009, Secretary Sebelius issued a PREP Act declaration[60] to shield the H1N1 Swine flu vaccine manufacturer from liability. Most Americans were unaware of this declaration when they received swine flu vaccinations in 2009. Most Americans had no knowledge that this declaration would prevent them from using the US legal system to seek compensation if they or their children had suffered an injury or death due to the vaccine.

Now the Secretary has mounted a campaign to circumvent federal statutory prohibitions shielding children from unwanted medical experiments, in order to test "medical countermeasures" in children.

- Will prospective parents be informed that the anthrax vaccine manufacturer is shielded from liability by law?
- Will prospective parents be informed that in CDC's "pivotal *BioThrax* trial" 12% of adults suffered serious adverse events which are defined by FDA as death, a life-threatening event, or one causing hospitalization, disability, birth defect, or other serious medical event?[3]
- Will prospective parents be informed that manufacturers of all "covered medical countermeasures"—whether used in clinical research or clinical practice—are shielded from legal liability, unless the DHHS Secretary allows a suit to go forward?
- Will they be informed that anyone—including children—who may suffer injuries from use of these "countermeasures" are barred from seeking compensation in either in Federal or state courts?
- If they were fully informed about the potential hazards, what parent would volunteer their child?

What if a child is disabled or dies? Since everyone involved in the planning, execution, and providing the apologia has been indemnified, who bears responsibility for the plight of the children?

- **Whose children will be the sacrificial lambs in a corporate-government collusion scheme to expand the *BioThrax* stockpile and expand civilian vaccinations?**

14. <u>To gain insight about the motives behind DHHS' anthrax policies one needs to examine the hidden web of financial conflicts of interest, and the corruption of revolving doors.</u>

The entire history of the anthrax vaccine enterprise has been rife with profiteering at taxpayer expense. The years immediately after 9/11 were boom years for many biodefense contractors. They were able to cash in on public concern over future terror attacks, and the apparent willingness of government to ignore procurement safeguards and circumvent requirements for competitive bids, accepting high profit margins for industry. Since 1998, throughout the Bush administration, and continuing under the Obama administration, Emergent BioSolutions has garnered unprecedented profit margins from its single product, *BioThrax*, sold almost exclusively to the US government.

Emergent is headed by Fuad El-Hibri (a German-born Lebanese businessman) and (until 2005) by retired Admiral William Crowe, Jr., a former Chairman of the Joint Chiefs of Staff (appointed by President Reagan) and the U.S. ambassador to Britain (1994-1997, appointed by President Clinton, whose election he supported).[61]

After a year-long investigation of the vaccine, Congressman, Chris Shays, Chair of the Subcommittee on National Security, Veterans Affairs and International Relations, Committee on Government Reform stated: *"As the program heads toward almost certain collapse, we have even more reason to be critical of DoD and FDA for coddling the vaccine maker. We've known for some time that DoD was propping up a company and a vaccine that would otherwise never survive scrutiny by the FDA or the commercial marketplace."*[52]

In 2007, David Willman,[62] a Pulitzer Prize winner, reported how Emergent succeeded in eliminating a competitor, VaxGen, thus remaining the sole producer:

> *"Emergent responded by mobilizing more than 50 lobbyists, including former aides to Vice President Dick Cheney, to make the case that relying on the new vaccine was a gamble and that the nation's safety depended on buying more of Emergent's product."*
>
> "*The company and its allies in Congress ridiculed VaxGen and impugned the competence or motives of officials who supported the new vaccine. The lobbying effort damaged VaxGen's credibility with members of Congress and the Bush administration."*

In 2007, the GAO reported[23] that beginning in 2008, more than $100 million of the stockpiled *BioThrax* would expire each year, requiring repurchasing. The GAO report led Sen. Susan Collins (R-Maine) and ranking member of the Homeland Security Committee to issue a statement:

> ***"This GAO report makes clear that the federal attempt to procure an improved anthrax vaccine has yielded not a new vaccine, but instead a textbook example of prodigious waste.*** *HHS must learn the lessons from past failures so that we can improve our preparedness for a possible terrorist attack using biological weapons."*[63]

Another investigation in 2007, by *RawStory*[64] found:

> *"According to company documents filed by Emergent BioSolutions with the Security and Exchange Commission, two former officials with the Department of Health and Human Services -- Jerome Hauer, who was Acting Assistant Secretary of the Office of Public Health and Emergency Preparedness in 2002-03, and Dr. Louis Sullivan, who served as HHS Secretary under former President George H.W. Bush -- worked as paid lobbyists in an aggressive and well-connected lobbying effort to secure the Biothrax contracts.*
>
> *In their administration posts, both Hauer and Sullivan had helped oversee the National Strategic Stockpile and aided in policy development and drug procurement related to countering bioterrorism. After working as lobbyists for Emergent, the two men were invited to sit on the company's board of directors."*[64]

The major beneficiary of the emergency declaration is the anthrax vaccine manufacturer:
"In testimony to congressional committees, BioPort CEO Fuad El-Hibri has indicated BioPort's viability depends on being able to sell anthrax vaccine to a much larger market than to just the Defense Department..."[65]

This inadvertent acknowledgment by Emergent's CEO suggests the extraordinary lobbying efforts the company exerted on government officials to increase Federal procurement of its anthrax vaccine. Those lobbying efforts and others, the company's employee campaign contributions, and additional relationships between Emergent and US government officials were brought to light by several investigative reports.

Suddenly, the country "needed" a large civilian stockpile of vaccine, in addition to its military supply. Following Secretary Leavitt's declaration of an anthrax emergency, Daniel J. Abdun-Nabi, president of Emergent, stated:

> *"This PREP Act declaration is further evidence of the U.S. Government's commitment to our efforts to develop a portfolio of medical countermeasures to address the threat to public health posed by the use of anthrax as a weapon of biological warfare."*[66]

Indeed, the same day that DHHS Secretary Leavitt declared an anthrax public health emergency, DHHS contracted to buy an additional 400 million dollars' worth of anthrax vaccine for the civilian stockpile from Emergent. One week earlier, a contract had been announced between DHHS and Emergent for development of a next generation anthrax vaccine.[67]

Within a month after the declared emergency, the CDC Advisory Committee on Immunization Practices (ACIP) revised its eight-year-old recommendation **against anthrax vaccination for first responders** prior to an event—a recommendation which ACIP had subsequently reaffirmed after the anthrax letter attacks in late 2001.

Inasmuch as no threat of an anthrax attack has emerged since then and no new improved vaccine has been developed, what led ACIP in 2008 to reconsider its earlier recommendation? According to the Center for Infectious Disease Research and Policy (CIDRAP)[68] at the University of Minnesota, ACIP was persuaded by CDC officials who:

1. claimed that although the risk of anthrax exposure is low, it "may not be zero"
2. presented selective safety data to assure ACIP that the vaccine was "safe and effective"
3. assured ACIP of a growing supply of *BioThrax*…

None of those rationales passes the smell test:

1. Crossing a street poses greater than "zero risk"
2. Unless CDC fully discloses the safety data from its pivotal 43 month trial, its claims about the vaccine's safety are untrustworthy
3. A growing supply of an admittedly inferior vaccine for civilian use is not a benefit: increased government purchases of a vaccine whose value is questionable compared to the proven efficacy of antibiotics wastes public resources. It does, however, enrich Emergent.

A member of your Commission, Dr. Alexander Garza[69] of the Department of Homeland Security, is actively involved with expanding the use of *BioThrax* in first responders. One is led to suspect that the push by DHHS to conduct a *BioThrax* trial in children is to prepare the ground for the vaccine's expanded use in ever wider civilian populations—independent of any risk of exposure to anthrax.

An article published in the *Proceedings of the National Academy of Sciences*[70] (2010) by a group of scientists representing the FDA, the Washington DC Veterans Affairs Medical Center, the National Cancer Institute, and other organizations, expressed strong reservations about *BioThrax* because of its inadequacies in response to a bioterrorism incident. The scientists expressed concerns about its adverse effects, its undefined composition, lot-to-lot variation, and multiple dose requirement over a protracted period to achieve (questionably) adequate levels of protective immunity.

Why is the US government procuring so much of a product with so little to recommend it?
DHHS has been committing vast amounts of taxpayer money to procure large amounts of *BioThrax* for the civilian stockpile—even as the vaccine's shortcomings as an effective preventive treatment following exposure to inhalation anthrax are obvious to scientists and specialists in bioweapons. *BioThrax'* significant safety problems are a serious matter of concern for those affected and those who care about safety, and the vaccine's short shelf-life results in discarding expired vaccine lots—representing over $100 million of annual wasted taxpayer funds.

Despite the vaccine's known deficiencies, on April 27, 2011, Dr. Nicole Lurie, Assistant Secretary for Preparedness and Response wrote to the NBSB requesting its recommendation "*on the best course of action to prepare for a potential use of AVA vaccine in a pediatric population."*

On Oct 3, 2011, the government awarded Emergent *"a five-year contract worth up to $1.25 billion to provide millions of doses of an anthrax vaccine for government stockpiles…"*[71] Three months later, on January 6, 2012, Secretary Sebelius wrote to ask you and your Commission how best to obtain *"safety and immunogenicity data about AVA PEP in children prior to an anthrax event,"* and to consider "*how best to obtain clinical data on medical countermeasures in children."*[45] On June 18, 2012 Secretary Sibelius announced a public-private partnership between the US government and 3 private entities for future pandemic influenza vaccines and other unspecified countermeasures, stating:

> *"The Centers we're announcing today... are critical. Emergent [BioSolutions], Novartis, and the Texas A&M, the three organizations chosen to lead these centers, all have experience in developing or manufacturing medical countermeasures. And with each contract able to be renewed for up to 25*

years, our partnership represents a long-term commitment to national health and security." [72]

"*Getting Rich on Uncle Sucker,*"[73] is an investigative report *by* Scott Lilly, published by The Center for American Progress (2010). Mr. Lilly, a 31-year Congressional staff veteran, and former staff director with the House Appropriations Committee, describes the massive scope of lobbying which Emergent used to overcome the unproven efficacy of its vaccine after exposure to anthrax,[5] and the lack of justification for the government's purchase of $1-2 Billion of *BioThrax* for a stockpile that expires every 3-4 years:

> *"To put Emergent's lobbying in perspective one might compare it with Merck, one of the most heavily represented companies in Washington, which has close to 40 registered lobbyists … To have the same ratio of lobbyists to revenues as Emergent, Merck would have to hire more than 4,000 additional lobbyists."*[73]
>
> *"It was the taxpayer who developed the vaccine, paid for its testing and licensure, set up the manufacturing facilities, and refurbished and reequipped those facilities once they were taken over by a private for-profit enterprise. The taxpayer, how- ever, was not only not rewarded for that risk but was bilked a second time by having to pay excessive prices for the product from a company that had taken almost no risk. The taxpayer was bilked a third time when the profits from this excess pricing were used to discourage the development of better and safer drugs."*
>
> *"Even if you allow a generous amount for administration and overhead above the $46 million "cost of product sales," the $217 million in revenue from those [2009] sales would indicate a markup in the neighborhood of 300 percent... a markup of even half the size suggested by this annual report seemed mind boggling... The fact that profit margins of the magnitude negotiated by Emergent were not only agreed to but were not a point of major controversy within the agencies that agreed to them raises broader questions about the integrity of the procurement system..."*

See also, Emergent Employees Campaign contributions, 2012[74] and 2010 [75]

Four recent Secretaries of the Department of Health and Human Services—political appointees—have turned DHHS' mission on its head: rather than protecting or improving public health, two have declared specious public health emergencies for anthrax. A declaration of a public health emergency by the Secretary of DHHS protects manufacturers of vaccines deemed "medical countermeasures,"[58] from any and all financial liability for harm. And the declared emergency facilitates the transfer of substantial taxpayer funds to biodefense industry contractors—Emergent BioSolutions has been especially favored by DHHS Secretaries. One Secretary lobbied for Emergent after leaving government and later joined its board, and the fourth, Secretary Sebelius, is financing expanded production, procurement and use of "medical countermeasures," most prominently, Emergent's *BioThrax*.

Now your Commission of bioethicists is being asked by Secretary Sebelius to turn its mission upside down as well: you are being asked to undermine Federal child protective regulations, and bless the sacrifice of children at the behest of DHHS, the Commission's parent agency. You would do better by paying heed to the Maryland Court of Appeals: [39]

> *"Whatever the interests of a parent, and whatever the interests of the general public in fostering research that might [ ] be for the good of all children, this Court's concern for the particular child and particular case, over-arches all other interests. It is [ ] not in the best interest of any healthy child to be intentionally put in a nontherapeutic situation where his or her health may be impaired, in order to test methods that may ultimately benefit all children."*

As a Presidential Commission for the Study of Bioethical Issues, **your decision will draw a moral line in the sand**—either you uphold children's statutory protected human rights—or you provide the Administration with a disingenuous rationale for circumventing statutory safeguards enacted to protect children from exploitation as human guinea pigs.

Which legacy do you wish to leave?

The Alliance for Human Research Protection (AHRP) is a national network of lay people and health professionals dedicated to advancing responsible and ethical medical research practices, to minimizing the risks associated with such endeavors and to ensuring that the human rights, dignity and welfare of human subjects are protected.

Yours sincerely,

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