



Presidential Commission
for the Study of Bioethical Issues

TRANSCRIPT

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Meeting 9, Session 4
May 17, 2012
Washington, DC

DR. WAGNER: Will Professor Hodge and Doctors Taylor and Kaplowitz please come forward?

As they're grabbing their seats, this next section is one where we'll discuss special ethical considerations that arise in medical countermeasure research and use.

Speaking to us first is Dr. Lisa Kaplowitz. Welcome.

She is the Deputy Assistant Secretary for Policy in the Office of the Assistant Secretary for Preparedness and Response at the Department of Health and Human Services. In this position, Dr. Kaplowitz is responsible for directing and coordinating policy and strategic planning for all components of that office.

Previously, she was the Deputy Commissioner for Emergency Preparedness and Response in the Virginia Department of Health and served as Director of the Health Department for the City of Alexandria in Northern Virginia.

In addition to public health and emergency preparedness, she has a strong interest in health policy, health care financing, and in improved access to health care.

We're pleased to have you join us.

DR. KAPLOWITZ: Thank you very much.

Today I will be describing the requirement setting and risk evaluation for an anthrax bioterrorism event specifically, but in the broader context of how we plan for a range of high consequence but low frequency public health emergencies.

My office within ASPR is responsible for coordinating activities of the public health Emergency Medical Countermeasures Enterprise. We call it the FEMCE. It's a federal multi-agency, multi-department enterprise responsible for setting policy and determining requirements for medical countermeasures for treatment and prophylaxis of illness resulting from a broad range of emergency events impacting

public health.

The FEMCE addresses the continuum of medical countermeasures development and use from setting requirements to basic research, advanced research and development; purchase, stock piling, delivery, distribution and dispensing of medications and other treatment or prevention modalities to populations at risk at the time they're needed. We describe this as end-to-end medical countermeasure enterprise.

Chemical, biological, radiological, nuclear medical counter measure requirements for civilian populations are determined through an interagency decision-making process within the FEMCE framed in concert with, and as a result, of risk and threat assessment from the Department of Homeland Security.

The process has multiple components with determination of threat and likely event scenarios including the determination of requirements for specific treatment and prevention measures.

The end product yields answers on the type and approximate quantity of medical countermeasures needed as well as issues related to special or at risk populations within the general population needs.

Authorities come from the Project Bio Shield Act of 2004. The Homeland Security Secretary in consultation with the HHS Secretary and heads of other agencies shall assess current and emerging threats of chemical, biological, radiological and nuclear agents and determine which of such agents presents a material threat against the United States Government and United States population.

So the secretary of Homeland Security establishes a material threat to national security exists by making a material threat determination, or MTD, that is based on a material threat assessment that takes intelligence reporting, assessments of

technical plausibility and exposure modeling for various release scenarios into account and establishes the high consequence scenario that could result from a deliberate attack.

The risk of an event incorporates both threat and probability of an event, as you've discussed already, as well as the consequences for a population. There are inherent uncertainties in determining the risk. We really can't give a number to any specific risks of a bio terrorist event based on available intelligence, an unknown probability of any single event or scenario.

On a relative likelihood scaling, certain threats, such as anthrax, stand out in our planning and have material threat determinations. The FEMCE addresses a broad range of possible bio terror agents as well as chemical and radiologic events and outbreaks, such as pandemic influenza.

But as you've talked about already, the term "risk" means many different things outside of the traditional Homeland Security environment. I wanted to bring up several different kinds of risks when considering ethical considerations.

You've already heard about and discussed considerations related to clinical testing of countermeasures that may never be needed, since it is impossible to know with certainty the likelihood of a specific event actually occurring.

There's risks related to delay in recognizing exposure and delay in instituting treatment, which can certainly result in illness and death.

You've already talked about the risk of lack of appreciation of altered risk benefit ratio once an event has occurred. The risk benefit calculus of any prophylaxis or treatment is very different during an actual event when the likelihood of illness or death is high than during the planning period when the risk is perceived as very low or and largely theoretical.

As a former state and local public health official, I can tell you first hand that even under the best of circumstances providing treatment en masse with licensed products, whether medications or vaccines, is difficult and challenging. To the extent that the process is slowed or complicated by other factors, the risk of illness will increase. A more complicated process not only reduces the number of people who can receive countermeasures quickly, but creates additional fear and confusion in an environment where there may already be illness and death.

If children and adults are treated differently during an emergency, this will need to be addressed with optimal messaging to avoid the risk that the public will believe that we care less about children after an event.

I believe, as Dr. Parker mentioned, the importance for government to maintain the public's confidence cannot be overstated. We are seeking to avoid delays in treatment and complicated messaging, which in and of themselves pose real risks to the confidence of the public.

The safety and protection of children is paramount in any discussion of medical countermeasures and you've already heard that from Secretary Sebelius. We want to make sure that all issues are thoroughly addressed and all ethical considerations related to having adequate available safety immunogenicity data on our medical countermeasures to protect them before and during and after an event and to be sure all these issues have been adequately addressed when there was time to plan ahead.

I hope that I have conveyed to the Commission that the risks involved go well beyond the likelihood of an event, which is really unmeasurable and that you will consider all the broad range of risks in your deliberations.

Thank you.

DR. WAGNER: Thank you.

Next is Dr. Holly Taylor. Currently Associate Professor in the Department of Health Policy and Management at the Johns Hopkins University Bloomberg School of Public Health, and a core faculty member of the Johns Hopkins Berman Institute for Bioethics.

Before pursuing her doctoral degree, Dr. Taylor was a presidential management intern in the Department of Health and Human Services and spent two years as a Special Assist to the Director of the National Institute of Allergy and Infectious Diseases.

She has served on the institutional review boards of Johns Hopkins Bloomberg School of Public Health and the Johns Hopkins Medical Institutions as well as IRBs in private, non-profit and federal settings.

Her primary interests are research ethics, local implementation of federal policy relevant to human subjects research, civil bio defense, HIV-AIDS policy and qualitative research methods.

Welcome, to you.

DR. TAYLOR: Thank you for that introduction and thank you for inviting me to present today.

So I want to thank in advance all of the folks that came before me, because many of the issues have been discussed and it means I can sort of cut to what I think is the chase of my presentation.

So I wanted to start, though, with given my own background and given the way I approach research ethics questions, Dr. Gutmann mentioned this article by Emanuel that is now on your website. It's a way to sort of articulate the things that I

would review in my own assessment if someone came to me with this question.

I've highlighted the three things that I think are most important as we move forward, not to diminish the others, but I think those three are the ones that I'd like to focus on.

The way I would sort of articulate this is to first start with a question or the first decision point is, does the project have social value. I think that's a really important one for you all to decide and I think, you know, whether you can come to consensus on that is an important one. If the answer to that is, no, the study can't go forward.

In thinking about social value, a component of that is under what circumstances would testing a countermeasure in a pediatric setting be ethically acceptable. A number of these have come up already. Can we do it when there's a potential threat, reliable information about that threat, exposure in a nearby community during an event or after an event. I think there's different ways to articulate the pros and cons of doing each of those.

The next question is, is the study design valid. We've talked a little about that. I think what we've been speaking about most is the phase one trial, or a variation on that, to determine safety.

But the related question, or the first question, is there uncertainty about the potential benefit of the proposed intervention, and I think we've already sort of talked about can we extrapolate from the adult population and make a decision about that benefit or what value will such a trial add to our assessment of that benefit.

The next question would be, do the risks to which the subjects will be exposed constitute a more than minor increase over minimal. We've talked quite a bit about this, and I'd just like to highlight the last note, in which I think is sort of the most

problematic is, what's the risk of not conducting the study. I think that, in particular, is the component of the analysis that those of us who think about research ethics proper, that is, you know, whether to test a therapeutic in a child, we often don't necessarily think of this in the larger social context or don't need to.

We then have to think about the risks and benefits and whether those are balanced, and only if they are can we go forward.

What I'd like to do is just sort of graphically display this. This is how we generally think about balancing those risks and benefits. There are risks to identifiable children, future benefit to not identifiable children, though those who are sort of in close proximity to use in the life course.

We also think about in conducting pediatric research there's sometimes a potential benefit to pediatric subjects. I don't believe there's a potential direct benefit to pediatric subjects in this context and so we're really talking about the balancing of the potential risks on one side and the future benefit.

As I said before, I think the real issue to consider is the potential risk to future children if we don't do the trial. And this doesn't quite show up as well as I thought it would on my slide, but I'm sort of putting this in the context of national security.

Just, again, if you start to think about where to place those, this potential risk to future children doesn't actually fit, I don't think, in our current ethical analysis of the way in which we think about this.

I want to just flip through some of these and get to where I think the sort of most important issues are in terms of the consequences of non-action.

We've talked about what we would do if there is an intentional release and

that there would be some post exposure prophylaxis, the known risks that were just presented by our colleague from the Children's Hospital, and then the post exposure vaccination under an IND and I guess under an EUA.

Just to add a little data, and you've talked about this already as well, that in the history of whether or not adult vaccinations are applicable in the child setting, there's a number of cases. I've listed a couple here. One, for lack of safety and a couple for lack of efficacy. So when we've determined that it's not efficacious in children, we don't expose them to that, not because it's unsafe but because it won't work.

Then thinking ahead, and I think it follows on Dr. Kaplowitz's presentation about what are the consequences if we move forward. Do we need to do additional trials? Do we then add that to the stock pile? Then, how would any of the information we gather make our response any different to the one that we would implement if we don't take any action in trying to value those risks and benefits across the board.

DR. WAGNER: Thank you for that.

Finally, for this session, we turn to Professor James Hodge. Professor Hodge is the Lincoln Professor of Health, Law and Ethics at the Sandra Day O'Connor College of Law at Arizona State University; Director of Public Health Law Network, Western Region; one of five centers nationally funded by the Robert Wood Johnson Foundation and Director of the Arizona State University's Public Health Law and Policy Program.

His scholarship teaching and projects extend into multiple areas of health law, public health law, global health law, ethics and human rights, with particular expertise in public health emergency legal and ethical preparedness and public health

information privacy law and policy.

He's a current and former member of several expert committees of the IOM Institute of Medicine and is current member of the CDC's Directors Advisory Committee and Policy. Mr. Hodge, thank you for being here.

DR. HODGE: Dr. Wagner, thank you for that very kind introduction; Dr. Gutmann for your invitation to address the members of this Commission. It's a real pleasure to be able to join you here this afternoon.

Let me tell you what I'd like to try to do in the brief time that I've got. That clock is already ticking on me.

DR. GUTMANN: That's what clocks do.

DR. HODGE: Lawyers are so familiar with that, Doctor, I can assure you.

So listen, I've got a brief outline of material that I believe some of you may have received. It's called the Ethics of Allocation Preparedness in Public Health Emergencies. This is a brief, two-page outline. It is dispensing and trying to go through a mountain of material that I'm going to share with you here in these very brief comments. We can go into any depth that you want to in regards to this.

Here's the real central points that I just want to try to make. Let's talk about, just so we know, the critical difference between a public health crisis and a public health emergency. These are very different terms legally and ethically. Why? Because when we get to a public health emergency, the legal environment will change. I'll give you a brief snapshot of that. But most importantly, so do the ethics in regards to what and how we may allocate a medical counter-measure assuming it is even available for our purposes and use.

I will distill from a very divergent series of observations across this

country at the federal, state, tribal and local levels what I call my top ten core principles for how we are prepared to ethically allocate limited resources in actual public health emergencies. So with that in mind, let's jump right into it.

So basically a public health crisis is something we're all experiencing as we speak. The obesity epidemic is a crisis. HIV-AIDS remains a crisis. Gun control in our urban environments. These are public health crises. Contrast these immediately with public health emergencies defined and capable of being distinguished by several common elements.

First of all, public health emergencies, like the H1-N1 pandemic, have a sudden onset. They have a relatively short duration and potentially catastrophic consequences. They have intense impacts on the physical and mental health of this nation or any nation. They have a need for immediate global, national or regional responses. Public health emergencies will severely potentially have economic consequences. They will change the legal environment instantaneously, and then most importantly, perhaps the most critical definitional capacity of a public health emergency, there will be scarce resources and our ability to allocate those will be tested significantly.

This is exactly what was at the center of the IOM's recent Crisis Standard of Care Committee. When we defined a public health crisis pursuant to setting a standard it started with, first we have extremely limited resources.

So with that in mind, the legal response to a public health emergency will be significant. It will happen instantaneously and the environment will change drastically to reflect and respond to those particular issues. So we are prepared through emergency declarations, both in emergency sort of all hazards approaches as well as in

public health emergent declarations, as the Secretary of HHS as she was just here, has the power to issue in several states.

We will change the legal environment. We will provide new legal reforms for how we can address these critical concerns, but there's not a thing we can do in regards to those legal changes that will dispense with that critical facet. And that is how will we make those critical decisions when it's time to allocate those scarce resources?

The law provides a menu of options. It provides tools we can use, but it does not provide that answer. That's why we need ethics to step in and to help us do that to be sure. The type of ethics we're going to discuss here, this is not bioethics, in my mind. It's not research ethics. It's not even public health ethics. While your Executive Director Lisa Lee has written very eloquently on the key role of public health ethics, public health emergency ethics is something altogether different as well.

So what you're going to see across this country when you look at these critical issues there is simply no national consensus on what the major important core principles of public health emergency ethics are.

You see approaches at every level of government from CDC to HHS down to local governments, all attempting to provide some ethical guidance on how they will allocate scarce resources. Let me, if I may distill from that these ten core principles.

These are the ones that I think you're seeing over and over again. While they can be divergent and at times conflicting, as many principles in ethics are, these are the ones I think you can take to the bank as what and how this nation's trying to work through how we would allocate scarce resources in an emergency.

First of all, prevention. Let's talk about this not from the public health prevention perspective in that capacity, but as an ethical principle. Above all else,

protect the public's health from preventable causes, morbidity and mortality. The ability to accomplish this, to maintain this, is a core ethics principle driven by that public health emergency recognition.

Then there's the principle of soundness, matching responses to what we know works as a best practice in public health. There is no time for guess work. There is time for using known convention, best practices, that really will result in allocating resources in the way possible to further the prevention goal which is, again, limiting morbidity and mortality.

The principle of equity is consistent throughout many of these approaches providing similar treatment for similarly situated individuals. You might compare it to an equal protection type of norm from the legal perspective, except here we're talking about a broader base. We're talking about eliminating discrimination based on everything that might be relatable in the human condition, so it's not just about eliminating discrimination on race or ethnicity, but about ability to pay and other factors related to socio-economic status. They simply aren't legitimate criteria to allocate resources; don't let them be used from a principle of equity.

Tied to that is the principle of what you might see called vulnerability. At times we will dispense a central services and care based on the medical vulnerability of a particular party or group that is most in need of a particular issue. This is exactly what you may have seen violated in regards to the Cipro distribution following 911, the anthrax particularly, when we saw Cipro going to certain members of society that had, you know, the most possible access when others may have been left on the sidelines, at least in the initial distribution.

Transparency, the idea that we're going to make these decisions in some

closeted-fashion outside of what the public may have an opportunity to provide input, unsustainable according to most people looking at these issues. There's a need for openness in decision-making. There is a need for public input whether that comes before the event or during the event. Many protocols that you're seeing in place for how to respond ethically built in a transparent factor, something that we can at least have an opportunity for something like due process or input along the way of making these decisions.

Reciprocity is a very important principle to mention here, because it's one that really builds on the vulnerability facet but it's really about supporting those who face a disproportionate burden and emergencies because they're on the front lines. They're your health care workers, your emergency responders, your firemen or other persons involved, who have through their own duty to provide care given up or put themselves in sort of vulnerable positions. How do we respect that? We put them potentially first in line. See many states, for example, in relation to how we might allocate a particular medical countermeasure.

Proportionality, using the least restrictive alternative where possible. Reserving coercive measures only when necessary. So this particular type of issue in relation to vaccines is really compelling. Would you coercively force individuals to be vaccinated even with the no medical countermeasure that could work for kids. Legally, you couldn't get away with it. I don't think there's any question about that. From an ethics perspective, you have to ask whether that would be ethically sound especially in regards to historic qualities of some interventions from the public health perspective going that route, then, just serving the population.

Solidarity, you've talked about and heard about. I like to define it briefly

as coordination over competition. We need to share openly. We've got to respond similarly across communities, states and localities. This particular norm of an ethics perspective is one that is often looked upon.

This fair innings approach is one that you may have heard about. I tend to disfavor it, but let's define it so we have some sense of it. It's about when and where we may prioritize, let's say, for example, the young over the old or person's with experience or person's who lack a certain experience over those with experience. This idea that those individuals under the particular circumstances are entitled to some sort of fair inning. They drive some allocation decisions. It's particularly rife with controversy because it's so difficult to apply and to determine why somebody who lacked a fair inning approach in life would be more or less at risk from all the other bases in regards to that distribution.

The final principle I just wanted to suggest for us today in regards to the sort of top ten core principles of public health emergency ethics and allocation will be accountability. Honestly, let's recognize the decision-makers in every level of government and in the private sector that are going to be responsible for these decisions must be accountable for these decisions as well. Some failure to provide an accountability factor in relation to these critical facets may allow for unethical decisions to be made that would never reach back to the actual party involved.

These ten principles are not meant to provide the type of guidance that this Commission may find instantly applicable. What I will say is, these are the ones you're seeing over and over again in relation to how government and the private sector are attempting to make these difficult decisions. Developing a national consensus on this would be fantastic.

But at the moment, that's the snapshot that I think that you can take to the bank as accurate for how we're looking through these allocation concerns.

Thank you.

DR. WAGNER: Professor Hodge, thank you. Thanks, all three of you.

We will open the floor, and I believe Amy has a question.

DR. GUTMANN: I have a question for Holly.

We heard from David DeGrazia earlier and he presented a different -- something -- a framework that would actually not agree with your scales of justice picture. I wonder whether it's just that you left something out or that you fundamentally disagree? Let me just explain just for a moment.

You say if the risks outweigh the benefits, then you don't go forward, and then if the benefits outweigh the risks, then you do. But what Dr. DeGrazia suggested, which is part of most frameworks for doing testing, is that there are side constraints that you don't go forward. So, for example, the benefits of giving out organs from dead people far outweighs the risk to dead people, which are zero, right, and yet we don't just harvest organs.

I'm not saying that flippantly --

DR. TAYLOR: I know.

DR. GUTMANN: -- because there's a strong argument on a certain framework that, why don't we.

DR. TAYLOR: Yeah.

DR. GUTMANN: But we don't. I wonder if you're arguing that not only we should but we must because the benefits outweigh the risks?

DR. TAYLOR: No. Thank you for the opportunity to clarify.

I would never advocate that as long as the benefits outweigh the risks that, you know --

DR. GUTMANN: That's why those -- you ought to be careful with those scales because --

DR. TAYLOR: Right. So what I was trying to --

DR. GUTMANN: -- the scales are very simple.

DR. TAYLOR: Well, what I was trying to argue --

DR. GUTMANN: It's the calculations aren't.

DR. TAYLOR: Absolutely. What I was trying to articulate with the balance was that as we traditionally think about research ethics we always want to in our assessment have at very least risks and benefits and balance. The point I was trying to make that in our traditional way that we do it, we often look for that balance. As long as that balance is in sync, we're allowed to go forward.

My point here was that when we're talking about intervention where there's clearly no direct benefit, if there is benefit to children it's benefit to children that is of uncertain measure because there's no immediate risk or harm and/or the threat is uncertain. So there's no place to put our assessment of the risks of not going forward into the traditional way that we assess risks and benefits.

DR. GUTMANN: So let me make the point that I think you were -- now you've made but more strikingly and you made it at one point but only at one point.

You made a very strong point, I think, that we have to consider, which is, if you only consider the costs of going forward, you're forgetting about the costs of no action.

DR. TAYLOR: Yes.

DR. GUTMANN: The costs of no action are why we're deliberating about this.

DR. TAYLOR: Yes.

DR. GUTMANN: We have to take that very seriously. I think that I just wanted to underline that.

DR. TAYLOR: Yes.

DR. GUTMANN: At the same time, take very seriously the importance of side constraints.

DR. TAYLOR: Right. I guess I assumed that we were talking in a setting where we were talking about where there'd be an evaluation of whether or not those risks and benefits were in balance or not.

That this sort of utilitarian proposal that you made in terms of, you know, harvesting Dr. Kaplowitz' organs would benefit many but we, of course, wouldn't sacrifice her.

(Laughter)

DR. GUTMANN: Well, it was dead people. Not live people. I wasn't going there, Holly.

DR. WAGNER: I'd like to get back to countermeasures.

(Laughter)

DR. WAGNER: Dr. Atkinson, Barbara.

DR. ATKINSON: Those were all excellent. The whole morning has fit together extremely well. I was sitting here thinking before hearing about the complications of the antibiotics, for instance, for 60 days, and then thinking about the risks of not conducting the trials. I want to push it to the far extreme. When would we

decide that we would prophylactically treat everybody in the United States with a vaccine? What will we need to have to make that decision?

We'd want to know, maybe, that it didn't have any more complications than a polio vaccine, for instance. We might want to know some other things. But once we had come to that conclusion, then it would, backing it up, be very clear that we would want to right now do dosing studies. We would want to then do efficacy studies, even in children, and then we would want to find out what the complication rate was so that we could make that decision.

So it would back us up to the first decision that we were asked to make here if we were ultimately going to make that end point decision.

DR. TAYLOR: Yeah. And I guess what I was encouraging was to anticipate the consequences in thinking about, are we willing to start the ball rolling in this case and under what circumstances and how would it then be applied to other MCM settings?

DR. WAGNER: Either of the other two? You want to?

DR. HODGE: Sometimes I think it's fair to say that you're concerned about when government may have to make a decision to go ahead and vaccinate the population. The population will make that decision for you sometimes. They see the risk is very real, and they're considered about the potential threat, they'll line up for that vaccination and be banging on government's door to get it.

DR. ATKINSON: They'll want to know that the vaccine is okay first.

DR. HODGE: Sure. Exactly. But even they -- I mean, even reasonable persons will take more risks with a potential unknown vaccine as far as its implications when they see the opposite side of that to be significantly more severe.

DR. KAPLOWITZ: There's the factor of perception of the risk as well because we're actually struggling with the whole issue of pre-event vaccination. There are certain populations who really would like access to pre-event vaccination and we're working closely with DHS to set some criteria, at least for a pilot, of how to do this.

But, again, to expand on what James said, we're also talking about a limited resource. We don't have the resources in terms of anthrax vaccine, per se. That's going to be a challenge for us. Post event as well as with our discussions. A pre-event working with first responder populations, for example. But, again, with my experience with H1-N1 as well, the perception of risk makes a big difference in terms of how acceptable, especially vaccines or any treatment to a population.

DR. WAGNER: Let me follow up on that, because I think the theme, Dr. Kaplowitz, of your presentation was that there is, in your judgment, and correct me if I'm wrong, in your judgment there is ample motivation to go forward in addition to, or maybe even in spite of, the specific threat level at this point. Is that what I heard?

DR. KAPLOWITZ: What I was trying to do was actually a bit of what Holly was trying to do was to point out risks of not moving forward and putting it in that context. I really want this to be put in the context of considering everything in a pre-event fashion. You know, my position and many of us, including Alex, is to look at what we can plan for in advance so that when something happens, we at least have the ability to respond in a reasonable way. It will never be perfect, because we'll never have perfect plans.

But this is an anticipation. And factoring in -- this is part of what we've been struggling with, with, you know, Dr. Lori's charge through the NBSB.

DR. GUTMANN: So I thought you -- if Holly's main point was, we have

to think about the costs of inaction, which I understand you made other points. But that's an important point that we hadn't really focused on.

I thought your important point was that if we in our deliberations recommend under certain circumstances going forward with testing safety of a vaccine, we also ought to recommend that it better be available. I mean, the funding -- if we're going to go forward and test this, then it darn well better be available in the context of an emergency because we've taken the risk part. The government better guarantee the benefit part, to put it dramatically. I thought that's what you were -- you may not want to have said it that strikingly, but I thought you were saying all of the need for having, you know, actually being able to deliver the goods when the time came.

Now, I say that because we have had experiences with our government where the means are available but they're not delivered.

DR. KAPLOWITZ: I think part of what I was trying to get at with the delivery piece is that decisions that are made now are going to impact the ability to deliver. You know, as a better way --

DR. GUTMANN: That's going a step further.

DR. KAPLOWITZ: As a better way to put it. If we have a medical countermeasure that is distributed under different circumstances to children and adults, let's have our message clear why we have done this and have we considered the consequences ahead of time. Had we thought about that, which really gets to the core of what Dr. Lori requested of the NBSB. Let's make sure we really have considered ahead of time the implications of decisions being made.

DR. GUTMANN: That's the converse of what I was saying, so if we decide not to go ahead with the testing, we should indicate, tell the public why, and

what the consequences of that would be in the case of an emergency.

DR. KAPLOWITZ: Or at least ourselves be aware of the consequences.

DR. GUTMANN: No, that's not enough for ourselves to be aware --

DR. KAPLOWITZ: And explain --

DR. GUTMANN: -- right?

DR. KAPLOWITZ: I guess I wasn't thinking in terms of explaining to the public ahead of time. At the time, at least, but that's another factor that I hadn't actually gone that far.

DR. HODGE: Absolutely. And it really is an issue.

DR. WAGNER: We've got to be accountable to the public.

DR. HODGE: Exactly, Dr. Wagner. It's really an issue where you must recognize. Developing the measure's great, proving the work is great. If you can't get it in the hands of people that really need it under any ethical norms that sustain that allocation decision, you've got an even bigger concern on your hands.

DR. WAGNER: Accountable either way.

DR. GUTMANN: Could I just make sure, Lisa, that I don't know if we -- I don't think accountability would be satisfied with waiting until emergency happened to explain to the American public why it wouldn't be. At least we shouldn't be -- if we're deliberating ahead of time so we can provide some accountability, whichever way we recommend, and that requires at least informing, if not educating, the American public about what we are and are not prepared for.

DR. KAPLOWITZ: Actually, you know, you're right. I agree. At heart I wish we were having more of these discussions in a broader sense, because really engaging in that discussion is key to making these important decisions.

DR. HAUSER: Thanks. Perhaps for Dr. Kaplowitz. If there was a decision to go forward, what level of knowledge do you think is needed in order to be able to consider deploying with reasonable confidence, an AVA vaccine in children? Obviously, if one looks at immunogenicity and just very common side effect, it's a different scale project than if one is interested in rare side effects, some of which have been the signals that have been in children with other vaccines.

DR. KAPLOWITZ: Well, for that, I would sit down with Skip Nelson.

(Laughter)

DR. KAPLOWITZ: Seriously. I can't emphasize enough how essential it is that all of us work together on this from DHS all the way through FDA and CDC because it's the FDA that is going to be key to making the decision about whether something qualifies for emergency use authorization, for example. Is it enough to have safety data, you know? I have my own understanding but I would go to them and say, do we need just safety data; what about safety and immunogenicity? What is it that's going to be adequate so that we can then distribute a vaccine or any medical countermeasure under similar conditions to both adults and children?

We have an emergency use authorization for use of this vaccine after an event in adults. What would it take in order to be able to do that in children while putting children at minimal risk?

You know, I've worked with Skip. I've heard him speak numerous times. We turn to them all the time.

So that's the first thing that I would do, because they're going to be the ones making those key decisions.

DR. WAGNER: Skip, your name is being invoked. Do you care

to comment on this?

DR. NELSON: Just very briefly to say what the plan would be in the absence of a pre-event study.

So there's two levels of data you need to consider. There's the IND to the EUA transition. In other words, what data do we need to be able to release something under an emergency use authorization? And then there's the data you would need to actually label it, which would mean it would be out there for general use.

So for adults, anthrax vaccine would be released under an EUA because we have sufficient data based on the post -- the pre-exposure prophylaxis experience in the military and so forth to say that it's reasonably possibly effective and safe. We don't have any data in pediatrics.

The current plan would be to release it from the stockpile under what would best be considered a treatment IND so that the children could get the anthrax vaccine and the data collection that would occur in association with that IND would be a vaccine adverse event reporting system similar to what was effective in the pandemic.

So a similar type of post vaccine distribution passive reporting system. That would be the treatment IND. That generates some safety data around some of these rare adverse events.

Coupled with that would be -- in the NBSB report you would hear that referred to as a non-research IND, treatment IND. Coupled with that would be a research IND, which would be a more intensive IND to get immunogenicity data and active surveillance safety data in a smaller number of children. I've heard, I'm not with the Center for Biologics, I've heard numbers between 100 and 200, something in that range, that would allow you to have some confidence that you get immunogenicity and

then some active surveillance data.

That data would allow you, then, to say that you could administer it under an EUA. Why the difference? You don't need an IRB for an EUA. The informed consent process is different. We could debate how different. Personally, I don't think it's that much different other than getting a signature because it's now a one-page form for the informed consent.

So that's basically how it would be distributed. When Lisa's talking about how do you explain the difference? Currently, if you had a pod, the parent would come in with their child and the parent would have the EUA with a form that they might look at similar to an influenza form that we call get when we get our yearly, and then the child would have an IND form.

Those would look very similar but the one would need a signature of the parent. So part of the messaging is, why is that different, what do we do know, what do we not know? I think that's what she's alluding to. So I hope that is helpful to provide some context.

DR. WAGNER: Great clarification. Thank you, Skip. Christine?

DR. GRADY: Actually, can I start with a question to you, Skip?

(Laughter)

DR. GRADY: If the pediatric vaccine was covered under the EUA, wouldn't the parent still need to sign?

DR. NELSON: There it would be treated much like a treatment decision and so whether -- I mean, I guess we all sign our influenza thing, but you wouldn't need an IRB. There would be some simplification, but it just wouldn't be different.

DR. GRADY: Okay.

DR. NELSON: I don't know if we would sign. I mean, you don't need a signature. There's no legal requirement, but I guess we all sign our little influenza form to say that we got it when we get our influenza vaccine.

DR. KAPLOWITZ: Or maybe you wouldn't. In this case I'll put on my, you know, former local public health hat. What I was referring to was the kind of situation we'd be faced with in dispensing, whether it's antibiotics or a vaccine, to a large number of people in a short period of time. Our goal in planning is to limit the chaos that's likely to occur.

We've had many, many discussions of what it would mean to take that extra time to not only sign the form but to really have parents understand why they're signing a form for their child versus not for themselves. We have concerns about vaccines in general it's going to take more time than just handing out packets of pills.

What maybe didn't become clear with all of this, is that we really are concerned about anthrax remaining in the environment and so much discussion on vaccine.

So it's an unknown, but it clearly has the potential to increase confusion and time when you're trying very hard to get measures out as quickly as possible.

DR. GRADY: So that was going to be the basis of my question.

I think the question about what would happen if we don't do this study I think is a very important one, but in my mind, that has to be asked study by study. You know, what happens if we don't do it?

I was wondering -- and this is why I asked the question about the signature -- at a moment of an emergency of that nature there's going to be chaos no matter what we do. And it sounded to me, from what you said, Dr. Kaplowitz, that the

two different systems for distribution plus the messaging are both issues that possibly could be dealt with independently of whether or not we do this study. I guess that's what I was trying to figure out.

You know, the messaging could be done way in advance, right? And the question about what's the actual difference on the ground between giving a vaccine to an adult and giving a vaccine to a child with or without the data is really the question. If that could be fixed, then that's not something that would drive the decision about doing the study, I guess, is what I'm trying to say.

DR. KAPLOWITZ: Again, my point was to really consider it as a factor. Believe me, we've put a lot of work into pre-event messaging, especially for those agents that have a material threat determination.

So it will be challenging any way you look at it, but it is something that we've had to factor in when doing our planning, especially at the grass roots level with the points of distribution.

DR. WAGNER: Well, it has been a remarkable morning with stimulating testimony. To you three, in particular, we thank you for being at this latter session. And to all of our other guests we hope you'll be part of the roundtable which convenes --

DR. GUTMANN: We come back at 1:30.

DR. WAGNER: Oh, we come back at 1:30. I'm sorry. We have a -- isn't the roundtable at 1:30

DR. GUTMANN: Yes.

DR. WAGNER: So it is 1:30. We're both saying the same thing, actually. So anyway, thanks to all of you and thanks to our guests. We'll see you

back here at 1:30.