Testimony – August 2 – Berkelman

It is an honor to testify today and I am pleased that Secretary Sebelius requested that this Commission address this important issue. I am also gratified that this body of distinguished individuals is tackling it so vigorously and thoughtfully.

This Commission has been asked to consider whether there are ethical grounds to proceed with safety and immunogenicity trials of medical countermeasures in children. We face the tension engendered when potential public health and societal benefits of research are juxtaposed with potential harm to clinical participants who would be expected to receive little or no direct benefit from the research. To make matters more complex, the clinical participants would be children.

Perhaps it would be helpful to see the issue at hand today within a broader context. The ethical framework guiding scientific research is aimed primarily at studies involving individual participants and assessing the potential benefits and risks to these individuals. If we rigidly adhere to guidelines developed for such studies without consideration of the societal benefit and risk, then the best decisions may not be made.

The issue facing this Commission today highlights the need for greater consideration of an ethical framework to guide research that may pose a risk or a benefit to the population and society, and may or may not involve human participants.

There are an increasing number of scenarios in which the current ethical framework may be inadequate. For example, there has been relatively less attention to the ethical review of life science research that is conducted in the laboratory, research that may result in a risk of harm to a population, such as research that makes a pathogen more deadly or more transmissible. Controversy over potential risks to a population recently erupted over the conduct of research on H5N1 influenza virus, a virus known to be highly lethal in humans but easily transmissible only in birds. The research sought to make the virus more transmissible among mammals, and did not include human participants. This research would have benefited from a review that considered societal risks and benefits before it was initiated.

In another case, individual participants in research may have a potential benefit that greatly outweighs potential risks to them as individuals, and the greater risk may be to the population. Today, we are faced with the opposite issue in which society is most likely to benefit and individual participants have most at risk. All of these scenarios share a need for consideration of societal risks and/or benefits.

Some organizations have made significant inroads into considering these societal issues in research. Yet training of researchers in the ethical conduct of research has generally not prepared scientists to consider societal risk and benefit as is done

with individual participants in studies, and there are few requirements to do so. The Commission may want to consider the need for a broader ethical framework in research that explicitly considers societal risks and benefits in addition to the risks and benefits to individual participants.

I will now confine my remarks to the issue of research that would involve testing medical countermeasures in children. It is recognized that the children participating in such research would be faced with some potential harm with little expectation of benefit. So why should such research even be considered?

Lets start with what is public health and what is public health's responsibility. The Institute of Medicine report defined public health as "what we, as a society, do collectively to assure the conditions in which people can be healthy." In the event of a catastrophic event, the government is responsible for assuring that society continues to function and that the government remains stable. Protecting the public's health and welfare is an essential component of its responsibility; and public health officials will strive to protect its citizens. Public health officials may rely heavily on non-pharmaceutical measures to protect the public's health in many crises. In some circumstances, such as a widespread anthrax release, utilization of medical countermeasures may be urgently needed.

Due to its responsibility to protect health and with its best assessment of threats, the government has put numerous resources into developing medical countermeasures.

Yet development and stockpiling of these countermeasures does not translate into an ability to utilize them during an emergency. The information and infrastructure needed to be able to utilize medical countermeasures during a catastrophic event is frequently underestimated.

So a vital question is what is the minimum information needed for the government to distribute a medical countermeasure for use in children and to receive needed support and public trust for their use?

It is important to recognize that public health is used to dealing with scant data in its decision-making during catastrophic events. The public accepts greater risk during catastrophic events than during routine circumstances. Public health however, is not likely to be able to deliver a countermeasure without knowledge of relative safety or potential effectiveness. There is a huge difference between limited data and no data.

The government does not need the extensive testing that would be done for acceptance of a routine vaccination in healthy babies. The sample size should be only enough that there is some assurance that the vaccine may be beneficial at a certain dose, and that severe outcomes are not common. Study design will also be important. Trials conducted pre-event may be best if initiated with older children

who can assent, the study results of which can inform any subsequent testing in younger children.

In the absence of data, the response to a major event would likely be quite confused and ill-informed, and may undermine not only the public's health but also societal functioning. Data that are quite limited may still provide a practical basis for moving forward expeditiously. There is a pragmatic streak in public health practitioners that is particularly required when faced with the need to make sound decisions with limited data.

An important point is that medical countermeasures are all different. Whether consideration should be given to testing a particular countermeasure in children pre-event depends on many things, including whether, in the absence of the countermeasure, an event would be likely to result in death or long-term disability. If death or long-term disability is not common, the argument for testing a medical countermeasure pre-event in children is especially weakened.

A green light for testing one countermeasure in children is not a green light for testing other countermeasures in children. The societal benefits and individual risks of testing medical countermeasures need to be considered on a case-by-case basis. The threat, the potential benefit of the testing to public health decision-making, the potential consequences of not doing so, and the risk to the children who participate all need consideration.

Other avenues of acquiring the minimum data should be explored before proceeding. If the testing can be done in less vulnerable populations and extrapolated to the pediatric population, that may provide a better avenue to get helpful data than testing in children.

If no testing were done for a countermeasure pre-event, could necessary data be rapidly acquired during an event through proposals that are pre-approved and ready-to-go? The effect of a delay in the distribution of potentially helpful countermeasures to children and the significant increase in difficulty of conducting research during an event would need consideration.

If the decision is made to proceed with a trial on a countermeasure pre-event, we should openly acknowledge that the well-being of individual children enrolled in such a study is being put at some risk and we should share the reasons and ethical grounding for doing so. Both the societal and individual risk must be considered. The challenges are daunting and the careful deliberation you seek today is part of meeting that challenge.

Thank you for the opportunity to share these remarks with you.