

## **Providing a Shot in the Arm: Boosting the Development and Distribution of Vaccines in the U.S. and Worldwide**

### **May 23, 2005**

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**ED HOWARD:** Hello, I'm Ed Howard with the Alliance for Health Reform. I want to welcome you to this session on the Role of Vaccines in Protecting the Health of America. I extend that welcome on behalf Senator Rockefeller our Chairman, Senator Frist, our Vice-Chairman and the rest of the board including, I should note Ray Gilmartin, who is the Chairman of Merck and Company and has a rooting interest in some of these things. We have I think an excellent jumping off point for our conversation today, that is to say the May/June issue of the Respected Journal Health Affairs, if you didn't get a copy of it on your way in make sure you get one on your way out. In fact, if you don't subscribe I heartily recommend that you subscribe. Where is John Iglehardt? He can give you that pitch. That issue's main theme is precisely that of the briefing that is to say how to improve our policies on vaccines both nationally and internationally. Health Affairs is also co-sponsoring today's briefing about, which we are doubly pleased. We do that from time to time. I did note that John Iglehardt is in the room. If we could coax him to say a few words either in phrase of subscriptions or otherwise he should take that opportunity now. or have you already left to go golfing [laughter]? Thank you John for your co-sponsorship. We tried to get your sign as high as we could next to the Alliance

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sign. Uh, I mentioned Ray Gilmartin, the former Chairman and CEO of Merck, I should also mention that Merck has provided support both for the Health Affairs Issue and for this briefing so we're grateful for that.

Let me just say a couple of logistical things for those of you who are regulars here have probably have heard me say them before but I see some new faces so I want to make sure the everybody knows the drill. In your packets you find a lot of material that will provide you with background in addition to the Health Affairs Issue, that includes our speaker's slides so you don't have to scribble every word you see on the screen, you have them in front of you. By the end of today you will be able to view the web cast of this session on Kaisernetwork.org along with most of the material in the packets and in a few days a transcript, which many people find useful. Everything but the video will also be on our website, that is to say Allhealth.org. Also in your packets you find green question card that you can use at the appropriate time to drill these folks on questions that arise in the course of the discussion. There are also microphones that you can use that are the only guarantee that your question will actually get asked because we usually have more cards than we can get to in the course of the discussion in the time that we have. There is also a blue evaluation form

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that I hope you will fill out and tell us how we can improve these briefings and make them even more useful to you.

You know there are so many policy handles on this vaccine issue that I'm fairly sure we won't be able to do justice to all of them today. I was talking with someone before the briefing and a lot of you know that perhaps the largest issue that the Alliance takes on according to our Board of Directors is the question of providing affordable quality healthcare to every American and the Institute of Medicine has determined statistically that perhaps 18,000 Americans die each year because they don't have insurance. We'll we're talking here about vaccines that the lack of probably cost 4 million in just a couple of instances every year. It puts into perspective the potential importance of the subject that we're talking about today. Vaccines need to be developed. They need to be manufactured. They need to be distributed and there are policy challenges in every one of those areas. Whether it's a shortage of flu vaccine in the United States or the threat of an Avian Flu pandemic that you might have read about over the weekend. Where those 4 million deaths from HIV and Malaria alone that a vaccine might avert, we are talking here about a high profile life and death issue at stake. And to help us grapple with these issues and some others we have three of the countries top vaccine experts with us today, not coincidentally all three

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are authors or co-authors in the issue of Health Affairs that you have. I'm not going to do justice to the speakers in their introductions. I commend to you the biographical information in the packets and so we will dispense with what they deserve in the way of an introduction and I will start by introducing Walter Ornstein who is the director of the Emory University Program for Vaccine Policy and Development and the Associate Director of the Emory Vaccine Center. Now until last year he was head of the National Immunization Program at the US Centers for Disease Control and Prevention. He is a physician, he Chairs the World Health Organizations Technical Consultative Group on Global Irratication of Poliomyelitis and he wrote the overview article in Health Affairs setting out the main issues in it so we're extremely fortunate to have you with today, Walter.

**WALTER ORENSTEIN, M.D.:** Thank you very much Ed and it's a pleasure to be here. When I consider the state of the vaccine system in the United States today I'm reminded about the beginning of the first sentence of Charles Dickens, A Tale of Two Cities. "It was the best of times, it was the worse of times". During the course of the next few minutes I hope to highlight some of the great successes the system that brought us those successes and the challenges that threaten to disrupt our achievements. This slide shows a number of the protrine vaccine preventable diseases of traulid when we

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no longer vaccinate against Small Pox. Representative 20<sup>th</sup> Century Annual number of cases reported generally in the few years prior to vaccine licensure provisional 2004 reports and percent decrease with the exception of pertussis or Whooping Cough all of them have been reduced by 98% or more and in fact for most of them we are at record or near record lows and even with pertussis or whooping cough we have had a 87% reduction compared as represented 20<sup>th</sup> Century numbers of cases. To just highlight some of the cases of the past half-century Small Pox has been eradicated worldwide. We have eliminated Polio in the United States and in much of the world where there have been some recent set backs in regards to global eradication Polio indematransmission is still confined to a very small number of countries in Asia and in Africa. Measles the most contagious of the vaccine preventable diseases and the greatest cause of vaccine preventable deaths in the world today has been eliminated from the United States, probably from Latin America as well and a number of other countries and we recently declared victory Rubella a cause of 20,000 children to be born with severe birth defects in the 1960s is no longer circulating within the United States. When we compare immunization to other preventive services it comes to the top of the list. Partnership for Prevention reviewed 30 of the most recommended and most accepted prevention services for wide

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spread use and the only one that received a perfect score on clinically preventable burden and cost effectiveness was childhood immunizations. We've also seen a major change in the number of diseases that are preventable by vaccination. In 1984 children were vaccinated routinely against seven diseases. In 2004, two decades later we're vaccinating against twelve diseases and we recently added a thirteenth. This shows you some selected vaccines in the pipeline or are actually here. Menococcal conjugate vaccine was licensed and recommended for adolescent. Menococcal conjugate disease causes severe meningitis and blood stream infections, can result into gangrene and amputation of limbs. This is now vaccine preventable. Recently licensed to be considered for recommendations is a booster dose for pertussis or Whooping Cough to try and get out the remaining reservoir of Whooping Cough, which is adolescent and young adults. A new vaccine against Rotaviruses, completed trials, this is the most cause of severe diarrhea, dehydration in young children and hopefully will be brought back into the schedule. While I don't see the results from the smiles I see on the investigators and the company there is a Shingles Vaccine that has completed clinical trials and we may soon have a vaccine against Shingles or Zoster available and another one that appears to be developing quite well is a Human Papilloma Virus vaccine. This is a virus that causes Cervical Cancer

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and the vaccine might be able to prevent as much as 70% of the Cervical Cancers in the US and around the world. Well all of this comes from a system that has at least twelve components and they are listed here. One is Health Burden Assessment, the need to disease surveillance and find out if this disease is worth preventing. Then there is basic vaccine research or vaccine discovery in which the pathogen the bacteria of the virus causing the illness is identified. The immune responses that are needed to induce immunity are identified so that you can begin to develop vaccine candidates that can induce better immune response, first in animals and then in humans. Vaccine development then proceeds with progressive testing among more people in humans until you get the pivotal what is caused Phase III trials, which can involve at times tens of thousands of individuals in that trial. Once a vaccine is licensed you must have assistance to assure its production on a routine bases and its distribution to the Alproriffery of the delivery assistance to assure all for whom vaccines is recommended can get it and you must have regulatory process in place to assure that vaccines are as safe and effective as they can be. Vaccine policy is critical in all of this and this is determined in large part by the CDC and its Advisory Committee on Immunization Practices as well as some of the major medical societies, particularly the American Academy of Pediatrics.

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Vaccine policy also determines what the market will be for a new product coming down the pipe. Vaccine financing is critical to assure that there are not financial barriers to immunization. For childhood we have a system that has about 50 to 60% government purchase the rest being private purchase and has worked quite well although it is under stress and I will cover that in a minute. You have to have an Administration or a delivery system that involves the physicians of this country. It involves nurses. It involves local and state Health Departments and it involves a whole variety of groups that for vaccines like food that might include grocery stores or pharmacies. You must monitor the use and determine when coverage is high and determine when it is low. You need to monitor whether vaccine is working as effectively as it should. What are the problems? Is it having the desired impact on disease? You need to monitor vaccine safety to assure that vaccines can continue to be safe and that there aren't new adverse advance not detected in trials that are detected and then it is important to have an injury compensation program because in contrast to other agents when a child is vaccinated in this country they are not only protecting themselves from most diseases but they are protecting their communities and society has an obligation and we do have a National Vaccine Injury Compensation Program which also protects manufacturers and

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physicians from liability if they comply with all the Federal Recommendations. Here are some of the major participants, the Federal Government and I listed some of the major agencies that are involved within the Department of Health and Human Services as well as other Federal Government agencies. Academe where most of the research is done, vaccine manufacturers who produce as well as do research and distributors, medical societies who are involved in promoting vaccines and working on policies. State and local governments and private physicians, third party payers and many, many more go into this system that allowed us to have these successes.

What are the challenges to the system? One is vaccine supply. We can't take it for granted. Since 2000 we have had shortages in vaccines against nine of the twelve vaccine preventable diseases of childhood. We have only four companies licensed to make vaccines for children under the age of four in this country and we have a single manufacturer for young children for vaccines against seven diseases. This is a vulnerability, which needs to be corrected. We also have challenges with vaccine financing. This has been a big problem as newer vaccines are going to cost more. Estimates are 800 million dollars or more for the development of some new vaccines. Cost is much more than the past and we need to assure if we are going to drive the benefits both to the

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individual in the community that we have financing systems in place to cover those vaccines. The Adult Immunization Program in essence is in its infancy. We do far worse with adult immunization than we do for childhood. For children we often get 90% or more for the individual vaccines. For adults, for influenza we generally get about 60 to 70% even when supply is good for the elderly. Vaccine research and development is an expensive undertaking. It is a risky undertaking and we need to assure that it continues. Vaccine safety concerns have the potential to derail the entire process if trust is lost in the system. We need to address both valid concerns and determine what are valid and what are not and to be able to provide information when the concerns are not supported by scientific data. And in bio-terrorism preparedness is also critical because of the need to get prepared for agents that generally won't be used in the overhaul population.

So in summary vaccines have been one of the most effective and cost effective prevention measures. Vaccine successes are the result of a complex pressure and process involving multiple public and private sector partners and the vaccine system is facing some major challenges that threaten to disrupt its successes. Thank you.

**ED HOWARD:** Thank you very much Walter, excellent introduction to a very multi-faceted topic.

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Next we will hear from Paul Offutt, a holder of a number of positions. You can see how many hats that he usually has there at the Children's Hospital there in Philadelphia he is Chief of Infectious Diseases, he is the Director of the Vaccine Education Center. He is the Henley Professor of Immunologic and Infectious Diseases there. He is a physician. He is also a Professor of Pediatrics at the University of Pennsylvania Med School. Winner of more awards than I have time to list and still leave him time to speak. Dr. Offutt has published a hundred and thirty or more papers in Professional Journals. He has co-authored several books, including Vaccines - What you should know. Hence, he is on our panel, Paul.

**PAUL OFFIT, M.D.:** Thank you Ed and thanks to the Alliance For Health Reform for putting this together. On April 17, 1957, Maurice Hillman [misspelled?] who was then at the Walter Reed Medical Research Institute read an article in the New York Times and that article talked about tens of thousands of children primarily in Hong Kong who were lining up with fever and glassy eyed stares. He reasoned that this could be Influenza Virus and called or telexed Zamaturpan to get people to send him throat washing so he could examine this virus and very quickly he realized that no adults in the United States or frankly anywhere in the world that he tested had antibodies to this virus. He predicated that his virus

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that ultimately caused 250,000 cases of disease and 10% of the population in Hong Kong was the beginning of the next pandemic in 1957. So what he did was he got the strains and he grew them up, he then coursed six pharmaceutical companies in the United States, all of whom were American Pharmaceutical companies to make a vaccine. Within three and half months he made 40 million doses of vaccine and distributed to US citizens. Although there were about 70,000 deaths of Influenza from what was the 1957 pandemic in the United States it is clear that Maurice Hillman saved tens of thousands of lives. Now at the time of the 1957 flu pandemic there were 26 companies that made vaccines and today as Walt said there are 4 International companies that make vaccines for young children. There are no American based companies that make Influenza vaccine and I think you are faced with the same circumstances today that Maurice Hillman couldn't do what he did today what was done almost fifty years ago. There is other evidence for vaccine, or crumbling of the vaccine infrastructure as Walt pointed out and of the twelve vaccines that are routinely that are recommended for young children, nine have suffered shortages over the last few years and seven of the vaccines are made by a single manufacturer.

Now I want to go through just briefly what I think are some reasons why pharmaceutical companies are gradually

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abandoning vaccines. The first is if pharmaceutical companies are businesses not public health agencies and vaccines are not a particularly lucrative business. I mean if you look at vaccines they are a product that are given once, most several times in a lifetime as compared to drugs like obesity drugs or cholesterol lowering agents or potency products etc, like heart products that are given often everyday. Therefore, vaccines are far less lucrative and these are pharmaceutical companies that make drugs and vaccines and vaccines often lose. If you look at the percentage of total revenue that are vaccines that are among these pharmaceutical companies and no cases that exceed six percent therefore vaccines are at risk. Vaccines can be eliminated without much impact on their bottom line.

The second I think problem is the willingness by the public and by the government to pay for treatment as compared to prevention. We are perfectly willing to spend a lot of money on bone marrow transplants or therapies for people including children who suffer. And certainly like the movie John Q is probably a dramatic example of that but the problem is we don't really know the names of the people that benefit from vaccines. This is a problem I think for prevention in general. Who are those 20,000 people this year in the United States who will not suffer meningitis or blood stream infections from the bacteria hemophilus influenza Type B? As

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Bruce Gillian is fond of saying, Bruce is the head of the National Vaccine Program Office, when you give a vaccine and it works nothing happens. It is not as if children throw away their crutches or suddenly stand up and say they can now see or hear but that is in effect exactly what has happened. Because of in the 1950s and early 1960s in this country Rubella or German Measles could cause as much as 20,000 cases of birth defects each year and those birth defects included blindness and deafness and because we have had five decades worth of giving the Polio Vaccine, children don't have to walk around with crutches so although those aren't the immediate effects those are in fact the real affect that those children don't have to suffer. The problem is that we don't know who they are and I think we're prevention sufferer the vaccines included is this kind of myth of invulnerability. We assume that it will never happen to our child. In Philadelphia my son has a friend on his baseball team who this year is a healthy eleven year old boy, no asthma, nothing else that would suggest he would be as risk of sever pneumonia had Influenza Pneumonia. He came into our hospital talking and making jokes and was hungry for air. He was initially put on oxygen by mask and eventually he was put on a ventilator and then an isolator and then he was put on a heart and lung machine and then he died. He died of Influenza, a vaccine preventable disease. The practice that

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he went to didn't have Influenza vaccine at the time because there was a massive shortage.

The third point I think is that Federal and State Governments are the principal buyers of vaccines and pharmaceutical companies have not received the strong message that they value the vaccines that they are buying. Both the Vaccine for Children's Program and the Three Seventeen State Programs pay for about 55 to 60% of all vaccines in the U.S. with insurance companies making up most of the rest. But if you look there have been inadequacies in that funding. For example as was pointed out in this journal that inadequacy was shown with a vaccine called the pneumococcal vaccine. The so called cognitive vaccine or Prevnair, which is a vaccine that is designed to prevent blood stream infections and meningitis and pneumonia caused by this bacteria pneumococcus but there are number of states, nineteen, that have had inadequate funding to allow for all children who benefit from this vaccine to get it. Assumably next year I think we will a crisis in some ways and see how it plays out but as Walt has said there are three vaccines which are likely to be licensed and should be routinely recommended for all children including the rotavirus vaccine to prevent common causes of dehydration and a virus that accounts for about 4% of all pediatric hospitalizations in the United States. A Papilloma vaccine, which can prevent a large cause of Cervical Cancer

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and the combination of Measles, Mumps, and Rubella varicella Vaccine. I think the crisis is officially here in force if one of two things happen, if either of those vaccines are recommended for routine use but Congress balks at funding them fully through the VFC or three-seventeen State Programs or worse and I think this would much worse, if the Advisory Committee for Immunization Practices or the American Academy of Pediatrics balks at making what is the best medical recommendation for fear of testing Congress's resolve to support these programs.

I think the fourth reason is liability. Vaccines were the first medical product almost eliminated by law suits in the early 1980s associated with that law suit against makers of Pertussis or Whooping Cough vaccine and as a consequence of those law suits we had the birth of the National Childhood Vaccine Injury Act which included the Vaccine Compensation Program, a wonderful program that protected I think vaccine makers from frivolous litigation and saved vaccines. There are three weaknesses in that program. The first is that one can frankly opt out of the program as witnessed by the Themersol litigation so we have to hope that the jury in Texas and in other places understand the science of Themersol well enough to know that the Themersol did not cause Autism. Also the unborn child is not covered by that program, for example about 20 years ago in

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the late 80s there was a vaccine that was made by Carol Baker to protect against a bacterial infection called Group B Strep. This is a bacterium, which classically infects children in the first week of life, too soon to give them an active vaccine, and when it infects them it cause meningitis and blood stream infection. Two thousand children every year in this country are hospitalized a hundred are killed by that bacteria every year. We have the technology to prevent it but no company is going to step forward to prevent that disease because it would mean giving a vaccine to a pregnant woman, which in this country can't happen because of fear of litigation. And the third thing is that the Vaccine Injury Compensation Program doesn't cover vaccines that are not routinely recommended. So for example Niche vaccines like the vaccine to prevent [inaudible] virus which is a common cause of disease and death you know in compromised patients certainly life limiting problem in our hospital I think it would not be detected in part because I think of fear of litigation. So we have technologies that are available that aren't being brought forward I think because of fear of litigation.

The last point that I want to make in terms of problems is the Zite guys. I mean it is just the culture of the times that we don't see vaccine preventable diseases. And as a consequence we're not as compelled to give vaccines and

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so to give them we have to have faith. Faith in three institutions, pharmaceutical companies, the Federal Government or Public Agencies that make those recommendations and physicians and I think there has been an erosion of faith that frankly isn't deserved. AS a consequence to that I think we've kind of focused on these false fears. If Congress hears from anybody they hear from parents who are concerned that vaccines have caused diabetes, or autism or multiple sclerosis when in fact there is abundant evidence that that is not true. What you don't hear from is you don't hear from those children who die of Influenza because there was a vaccine shortage or you don't hear from parent's of children who have died of pneumococcal disease or suffered pneumococcal disease or suffered pneumococcal disease because of shortages. You don't hear from them but that doesn't make their lives any less valuable. And I think to conclude then the solution to the problems I think are well outlined actually in this Journal specifically on page 703 by Alan Hinman. I think his series of a kind of eight-step program to strengthen the VFC and Three-seventeen State Programs and to strengthen I think the Administration of Vaccines and distribution of vaccines I think makes a lot of sense. So I think only Congress really can support the changes to maintain this vital infrastructure. I think it is hard for Congress to do something for which the public isn't really asking but I

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think we have to ask ourselves who is looking out for these children if this infrastructure continues to deteriorate. I don't think we have to look any further than places like the United Kingdom or Switzerland and the United Kingdom there was a decrease in Measles immunizations associated with this false fear that this combination Measles, Mumps, Rubella vaccine cause autism. Immunization rates dropped not surprisingly Measles disease increased including three deaths of children in Ireland. Children who died of a vaccine preventable disease. Something could have easily and safely been prevented which I think is unconscionable. Maurice Hillman who I talked about in the beginning was a vaccine researcher who in early April of this year passed away from Cancer. He died at age 85 and I got a chance to talk to him before he passed away and I asked him the question, isn't it possible to educate people about vaccines so that we can prevent the deaths I think one will occur isn't there a way to avoid this. I mean do we really have to have people die in order to get our attention and he thought about it for a second and he said no I think that is what has to happen. But I would just like to conclude by saying I hope he is wrong. Thanks.

**ED HOWARD:** Thank you Paul. Our last speaker is John Herberts who is not a physician he is a lawyer. As Paul noted litigation is a part of the vaccines issue here. John

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is at the firm of Covington & Burling no less where he co-Chairs Firms Life Sciences Industry Group and Chairs the Technology Transaction Practice there. He advises a range of clients on among other things vaccine related issues. He was named this year by Global Counsel's Life Sciences Industry report as one the three corporate partnering lawyers in the United States. He is Young Professor at the Georgetown University Law Center where he teaches Food & Drug Law. He has a special interest in the understanding of the problems in getting vaccines to developing nations and once again was co-author of one the important articles in the Health Affairs Issue that you have in your hands. John thanks you for joining us.

**JOHN HURVITZ, J.D.:** Thank you Ed. I guess we will shift gears now for a last talk and speak a little bit about vaccines and the impact in the developing world. We've heard a lot about the problems that are facing us here in the United States for getting vaccines for children and those issues are compounded when you are talking about vaccines in the developing worlds. And the impact is far greater. This slide I included just to give you some indication of what we are facing in terms of the pipeline for vaccines. What this shows chronologically moving from left to right is the introduction of vaccines. The size of the bubble indicates the number of lives that are taken by the absent of those

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vaccines or by the underlying diseases in even given year. As we can see on the lower left side major strides have been made with respect to certain existing vaccines but there are really significant challenges that lay ahead. The historic model for vaccine introduction in developing worlds have been that vaccines that were developed in the United States and other industrialized countries eventually make their way into the developing world. This typically occurs sometime decades and sometimes longer often when patents have expired and when not many manufacturing capacity and manufacturing expertise has been improved. We are talking about a significant lag in the introduction of these vaccines which first were developed for use in the United States and as I said before developed countries. Here we see just in terms again of another illustration of the lives that are taken by these diseases and if you look on the left side we're talking about 4.3 million deaths per year with respect to diseases where there are vaccines in use today in the developing world or there are vaccines very closely on the horizon. For vaccines that have yet to be developed and that are further in the distance for diseases like HIV, Malaria, and Tuberculosis we're talking about 5 million deaths per year. Now one of the reasons or the challenges that faces the existing paradigm is there are diverging causes of death in the developed world and the developing world. What these slides illustrate is

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that in industrialized nations communicable diseases represent just about 6% of deaths whereas in the least developed countries we're talking about 56% of death. So even to the extent that the infrastructure in the developed world is working well and we're producing vaccines to meet our needs those needs are increasingly becoming different than the needs of the developing world. So the traditional model no longer works.

A critical point in getting vaccines to market is the investment of industry of the pharmaceutical industry. The industry of first of all in terms of dollars and that's what in part these slides intended to illustrate. The top pie graph shows the investment in the developed world and the bottom shows the investment for the developing world. The total investment is about 7 to 8 billion dollars a year. It's a small or a fraction a tiny of fraction of what's invested for diseases for the developing world. And what we also see is that the amounts of private investment for these diseases are miniscule. Now it's not just dollars that we're talking about. The pharmaceutical industry has specialized expertise in conducting large-scale clinical trials. It has specialized expertise in manufacturing and one of the biggest thresholds when I talked about the decade or more lag is in developing adequate manufacturing capacities. Scaling these processes up so they can produce sufficient supplies of product at low

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enough prices to meet the demands of the developing countries. So the challenge that we face and what I'm going to speak about a little today is the potential solution to that challenge. And the challenge obviously or the goal is to develop vaccines faster and to speed the introduction of those vaccines into the developing world so to get new vaccines and to get existing vaccines there quicker, have adequate manufacturing capacities to provide those vaccine in a cost effective manner. The constraints that we face and the constraints that exist in the United States are just acerbated outside the United States and in the developing world. The developing country markets are very small. They are paying pennies for vaccines traditionally. The ability for them to purchase vaccines is unpredictable. They rely largely on donor funds, which cannot always be counted on. There's not long-term purchase contracts and, as I mentioned before, priorities are diverging. So there is a variety of solutions that are being explored today from the, on the one hand Gavey and the Vaccine Fund are focusing on buying vaccines that are available today and introducing them into developing countries. And that is going a long way to help improve the confidence of the pharmaceutical industry that if they produce these products that actually somebody will buy them and distribute them. They are also working to strengthen existing delivery systems in the countries so when

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purchased vaccines can be distributed and not wasted. There is preparation going on for future products in the form of the accelerated development and introduction plans as well as through UNICEF. Part of the problem in these countries is that because there is this lack of primary healthcare that people don't even know what the disease burden is. They don't know that their child is dying from Influenza or from or maybe they know now from AIDS but from other things like Malaria and in fact from Malaria they might know as well but for many diseases they are not aware of what the causes or death is. They just know that their children are dying and they are dying young. And then the additional area is the investment of public resources and R & D. The US is one of the leading investors in AIDS research for a vaccine but few companies are actually investing with the exception of I think Merck who is sponsoring this is investing their own money in developing AID vaccines for example. So what's missing in this picture is really the market for the products because we have a lot of what is traditionally is referred to as push funding. We have people putting money in the government and private donors putting money and making bets on specific technology and trying to invest in early research but we don't have the market there to really pull products through, getting the private company invest in development of these products through clinical trials and developing and

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investing in manufacturing capacity necessary to make these products available. So the solution or a proposed solution that was explored by a working group that was centered at the Center for Global Development was to develop an advanced market commitment. A mechanism by which we could simulate for the developing world the very types of markets that exist in the developing worlds and the theory is really very simple, up front the donors would get together and set a specification for the vaccine, they would make a legally binding contractual commitment to basically pay a price instead of just paying pennies for the product to pay dollars for the product, perhaps fifteen dollars or more when a qualifying vaccine is delivered. And there would be a guarantee of a specific number of treatments that that price would be available for. In return the suppliers would agree that once they receive three billion dollars in supplemented price support they would agree to continue to supply the product at a reduced price that would be affordable for the countries to purchase it on their own. So that is the basic proposal. How it would work in practice with the timeline here, well the first thing that would happen is that you would introduce the framework agreement, the donors would get together and say for example we're going to offer three billion dollars for two hundred courses of treatment of vaccine for Malaria or AIDS we will pay fifteen dollars for a

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course of treatment. At that point manufacturers could sign on to this framework agreement and that would put in place a guaranteed contract commitment. Companies would then do the development work there would be an independent adjudication committee that would be put into place that would allow the flexibility to deal with uncertainty over time. Remember to the extent that you are putting into place for things like Malaria or Aids. Today we don't really know what a vaccine would look like and so there would be an independent committee established that would decide if waivers could be granted. When a vaccine is approved then the guarantee agreement would kick in. That agreement would be attached to the original framework agreement and it would be an obligation of the donors. The donors could not get out of their obligations under the guarantee agreement but the individual companies could make an election, do they want to participate? Now the price of participating is that on the one hand they get the guaranteed commitment to price support on the other hand they have agree to supply over time at a sustainable price. They have to meet the requirements of the developing world for the given product and they have to continue to meet those requirements even when they are not getting the price support any longer. So that is the guarantee agreement. There is the possibility in the scheme that you could have a superior vaccine and that could be a

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later entrance. That too could be approved and the beauty of this system is that the donors are not making the determinations as to which products get used it is the market that is effectively doing that. The eligible countries will make their own decisions as to whether or not the product will be used and so we see that what we are talking about here is a market. We're not talking about a guaranteed three billion dollar award to the company that succeeds in developing the product because the countries have to make their own decisions as to whether to purchase the product and they have to what amounts to a co-payment just like we do in the United States when we have insurance and we go to the pharmacy and we pick up our drugs and maybe pay five dollars, ten dollars, fifteen dollars as a co-payment and somebody else pays the rest. In this case the countries would be responsible for paying say a dollar for the product. They could get through other donor support but somebody would have to be willing to pitch in a dollar to buy the product and then the donors would agree to top that up in the hypothetical I discussed before to fifteen dollars. So the donors would kick in the additional fourteen dollars to make it a reality. As I said before what this amounts to is a market, the manufacturers are still bearing some demand risk. There is not a guarantee that they will get any sale at all because if the countries aren't interested and don't want to

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purchase it the product will never be sold so the donors from the donors perspective whether that is the United States or whether it's the Bill and Melinda Gates Foundation, the donors only pay for success.

Again just one last point what you are paying for as I said is you're paying for a qualifying product and you're also paying for ongoing continuity of supply. So in the scenario where I talked about three billion dollars, that three billion dollars is not simply going as reward to a pharmaceutical company it is going to purchase product. It is going to purchase two hundred million courses of treatment and then it's going to purchase ongoing supply perhaps at a dollar or slightly above the marginal cost of production going forward. So I just want to say in closing this is an idea that started off in theory and has really gained some traction recently. This year the U.K. is chairing the G7, has the presidency of the G7. They have expressed a lot of interest in development issues and some of them are health issues. This is one of the proposals that are on the table and the U.S. Government has also expressed some preliminary interest in this. Not clear where it will go or if it will be something adopted or not but it is a real opportunity to put into place the types of incentives that we have here in the United States to help stimulate pharmaceutical companies to make the private investment in development of both drugs and

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manufacturing capacity to accelerate the introduction of much needed vaccines into the developing world. Thank you.

**ED HOWARD:** Thank you John that's quite a well thought out proposal. Now we would like to get you into this conversation both domestically and internationally. Fill out the green cards and hold them up and somebody will take them from you to bring them forward. And/or come to our microphone here or we have microphones in the back and let's get the discussion going. Let me try a question for our panelist to get us started. A couple of mentions to the Vaccine for Children Program, can somebody give us a sense of how that program works, what the order of magnitude is, how much does it cost? Walter?

**WALTER ORENSTEIN, M.D.:** All right. Vaccines for Children Program is about ten years old. At the moment it covers about 40% of the birth cohort in terms of the vaccines that are universally recommended and purchased. The Vaccine for Children Program is an entitlement. It covers the following groups of children; children who are on Medicaid, children with no insurance whatsoever, an Alaskan native and American Indians. In addition, if a child has insurance but whose insurance did not cover immunizations this is called the so-called underinsured they can get VFC vaccines if they go to a federally qualified health center. The VFC allows an advisory committee of experts, the Advisory

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Committee on Immunization Practices to vote vaccines into the programs. The Federal Government then attempts to negotiate a contract, OMB portions funds and children can begin receiving vaccines. It is quite different than the other public funding sources, one of which is the Section 317 Discretionary Grant Program which requires an annual appropriation from the Congress and then state funds but of the roughly of the 57% of vaccines that were purchased with public funds for children in 2002 40% of that 57% which were about 2/3s was from VFC.

**ED HOWARD:** Thank you. Yes, Martha. Want to identify yourself.

**JILL WEXLER:** I'm Jill Wexler. I'm the Washington Editorial of Pharmaceutical Executive Magazine and some other magazines. I'm been wondering for a while why there are so few manufacturers serving the U.S. market compared to the European markets, which traditional don't pay as much as pharmaceutical products as we do. For the flu vaccine situation that we had last year there seemed to be more manufacturers serving those markets. Are they actually paying more for those vaccines? Do they provide some kind of guaranteed market or is it just the liability issue that makes those markets more attractive for manufacturers than the U.S.?

**ED HOWARD:** Walt do you want to take that one?

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**WALTER ORENSTEIN, M.D.:** Well I'm not sure I can answer that completely. What I know happened in the U.S. is we did have four Influenza manufacturers as recently as 2000. Two of those four were found to be in violation of current good manufacturing practices. One felt making the changes necessary was not worth it so they dropped out. A second paid a very hefty fine and did produce, produced late and was left with extra doses of vaccine, multiple times and after the 2002 and 2003 season just dropped out completely. It wasn't worth it but we did have four going into 2000 and compliance with regulatory issues and putting in the improvements of the plant were the major problems as to why we had two. We then had a third manufacturer enter into the U.S. market. Metamune with a live attenuated flu mist which is a different kind of vaccine that is administered into the nose however, it had very, very narrow indications so it really was I think an excellent vaccine it doesn't really get out to the populations that we cover most with Influenza. We set the moment. With regard to the European situation many of them don't use anywhere near the volumes of does that we do. The market size is actually smaller and so I don't know why there are many more manufacturers in those smaller markets but whatever reason they are able to do that.

**ED HOWARD:** Okay. This questioner would like all of you to address the pros and cons of the Bioshield II

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Legislation S975 according to the questioner in addressing the needs or solutions regarding the lack of vaccines or suppliers of vaccines. Maybe I should ask the questioner to explain what is in S975 so that our panelist can make sure they address the pros and cons that they think might be there or you can remain anomalous or maybe you have left. John?

**JOHN HURVITZ, J.D.:** I'm not familiar with all of what is in Bioshield but there is several pieces of legislation on Bioshield too but I mean there are several pieces of legislation that is out there now that are design the remedy some of the defects in Bioshield I. One of the problems, somewhat touches on what I speaking about that there is a lack of a guaranteed commitment in terms of purchase with respect with the actually price that would be charged. One of the fears that industry faces is that if they develop a counter measure that meets the requirements and we're faced with the unfortunate occurrence of bio-terror attack that the product could be commandeered and the pricing would be forced to very low levels that wouldn't allow them to re-coup their R & D. An added challenge is the fact that if we're lucky they will never need these drugs so we're asking the industry to develop products that will hopefully never have a market. In addition there is a series of liability concerns associated with the development of these products because for many of them there is not an opportunity to test them in

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humans and so they can only be tested in animal models. So the present Bioshield proposals include a variety of market-paced incentives to encourage pharmaceutical companies to develop counter measures and then there is also some liability protection as well and some of those very same issues are the things that we are talking about to respect to vaccines. I think also in some of the recent Bioshield proposals there is a recognition that by focusing on infectious diseases outside the United States we're leaving to security inside the United States and there is pandemic flu and things like that that could make their way back into the United States. In addition to the extent that countries are suffering under AIDS, Malaria or Tuberculosis that lowers the standard of living and when people are living in poverty and miserable they are more likely to end up as potential terrorist so from that perspective as well there is a recognition that we ought to be focusing besides the moral commitment there is a self interested component that ought to lead us to focus on these issues.

**PAUL OFFIT, M.D.:** I think it is interesting. It is kind of like the Tsunami thing. We are very much compelled by the disasters so 911 certainly alerted us to fears from being attacked from the outside including by bio-terroristic agents from the outside. That gets a lot of play and emotion but I mean if I told you that last year there was a biological

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agent, which killed 36,000 people in the U.S. I mean that would get your attention and its flu. And as it was just mentioned by John the notion of pandemic flu gets our attention but some how that kills us in inter-pandemic periods doesn't even though if you add up those inter-pandemic periods of flu that far out weighs actually the number of flu deaths of certainly pandemics since the 1920s so I mean I guess all I'm trying to say is that nature is our greatest bio-terrorist and I think we need to build up the infrastructure to counter act that also.

**WALTER ORENSTEIN, J.D.:** If I could just add to that? I'm intrigued that we have not had much in the way of new companies entering the U.S. market for new vaccines for many years now. Almost all of the manufacturers are the same ones that were around a decade or two decades ago, acquisitions, mergers, etc and name changes but still the same manufacturers. On the other hand some of the bio-defense vaccines we are seeing other companies really step up to the plate. I'm aware of at least three companies that don't manufacture routinely to my knowledge of vaccines in the United States for civilian use but are developing vaccines for bio-defense. Just to name the three, Canbas, Dinport and Vacsgen are all involved in developing vaccines for bio-defense and there maybe others as well whether there can be incentives to move them into some of the civilian non-defense

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areas would help very much. What those incentives are I don't know. We would have to ask those companies but it would sure be nice to try and improve our infrastructure but there are far more companies producing or developing vaccines than the one that we have for licensed manufacturer for our routine immunizations of most of vaccines in this country.

**ED HOWARD:** Walter can you speculate or maybe one of the other panelists why they were willing to get into the national defense aspects of vaccine developments? Are there protections in that area that aren't available in the civilian area?

**WALTER ORENSTEIN, M.D.:** John maybe the best one or Paul but I think or presume part of it is that there has been a lot of government funding into some of basic research that has helped them quite a bit and I would think Bioshield I and perhaps with the fixes in Bioshield II we'll be doing it. But I think there is far more company capacity than we then we traditionally think about when we think about the routine vaccines for children.

**JOHN HURVITZ, J.D.:** I don't know first hand but my guess is a lot of it is push funded, R & D investment, on the model of government contracting of a jet or building an aircraft.

**WALTER ORENSTEIN, M.D.:** The NIH is particular, it's been very, very helpful in terms of funneling funds to

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academe and to the companies in order to deal with the first stages of vaccine development.

**ED HOWARD:** Speaking of pandemics I've got a question here that picks up on some of what John was saying. I've heard in the news about the prospect of flu pandemic, a fear which has arisen lately in the wake of an Avian flu outbreak in China and Hong Kong several years ago. How can the U.S. prepare for the possibility of a flu pandemic and here are two suggestions. Is the strategy to increase regular annual flu vaccine productions so that there's increase capacity to respond to a pandemic or do we need to create a reserve parallel vaccine supply eg. Egg based cultures in addition to the regular flu vaccine production. How flexible is that or three, how are other countries responding to this flu pandemic scenario?

**PAUL OFFIT, M.D.:** I can at least try part of it. I think when you talk about a pandemic strain what you are talking about is a strain for the most part no one has prior immunity to so it has the capacity to infect all in cause and tens of thousands and millions of deaths so therefore you are talking about immunizing everybody. If for example suppose for argument sake although I actually don't think this will be true that the current bird flu that circulating in Southeast Asia so-called the H5in1 strain really does mutate to the extent that it is able to be officially transferred

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from one person to another. If that ever happened you have basically 280 million people in the United States that have never been exposed to this virus and if it really remains as lethal as it appears you know with the fatality rates in the 70% range then you would have to immunize everybody. So you're talking about immunizing 280 million people in this country alone. There is no way in god's earth that that is going to be done with the number of pharmaceutical companies that we currently have. I mean you really have to expand the base of pharmaceutical companies that are committed to making flu vaccine. Also, just as an irony because I think it sort of ties into the liability issues is that if you were going to try and immunize for this company, 280 million people there is no way you are going to be able to do that with single dose vials. You would have to have multi-dose vials and if you are going to have multi-dose vials then you would have to have a preservative and if you're going to have to have a preservative what preservative would you use. I mean I think the most sensible thing is to use what is to date arguably the best tested and safest preservative that we have the most data on which would be Themersol and I think this government, I wonder and really wonder whether they would be willing to step forward with a multi-dose vial that contains Themersol. I mean you could use other preservatives like [inaudible] etc. but that certainly less well tested so I

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thin you would have to build up the base of Influenza base manufactures. If you really talk about a pandemic which I think was point A that you have to get better at immunizing against yearly Influenza.

**WALTER ORENSTEIN, M.D.:** I, I would like to agree with that. There are several things in my opinion that need to be done for pandemic Influenza. One is improve global surveillance. The sooner we can detect it and understand it spreading in humans the more time we have. Flu vaccine today normally takes about six to eight months to produce. Many of the pandemics haven't given us that advanced notice. So the more advanced notice that we can get the better off we are. The second is I would like to agree completely with Paul about the importance of improving our routine vaccination and the extent right now is in a good year about 83 million doses have been distributed in the U.S. market. If we could get and in the meantime flu vaccine is recommended for almost 190 million Americans each year so if we can get the routine production up we would have that kind of capacity. How do we do that? In my opinion there are several ways of trying to improve our routine coverage. Number one is that flu vaccine is an extremely risky endeavor for the manufacturers. It is the only vaccine that is seasonal. You make it and if you don't use that season, generally October and November it gets tossed and that is one of the reasons we ran into the

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shortage this year is one of the companies that I spoke about who was in violation of Good Manufacturing Practices made lots of vaccines particularly in 2002 and 2003 was stuck with it and said they are not willing to do that anymore. So if we could cushion the risk of some sort of government buy back or government back-in guarantee for vaccine that goes unused I think that would be very important. The second issue is how do we increase the demand and I think that is a critical thing. If we're 83 million verses 190 million we need to have more demand and we could do that in several ways. One is I think there needs to be a substantial educational effort. And by that I don't mean a media campaign, I mean with people in different local and state health departments and otherwise sort of pressing the flesh, meeting with people, and convincing to get flu vaccine. Number two is I think we need an adult immunization program. We have a very successful childhood immunization program. As I said that routinely for most of the individual vaccines gets 90% or more and we have a very strong infrastructure in the state and local health departments that is absolutely critical to making this happen. They have established relationships with the pediatricians, with the family physicians and others to try and improve immunization coverage in their communities so I think for an investment in the Three-Seventeen Infrastructure Program I think we can gain that in terms of demand. I think

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the third thing that we need in my opinion is some sort of decreasing of the financial barriers to access for at least some of the population I think we need a vaccines for adults at least for what I would call uninsured adults. Those are the adults that have no insurance what so ever, many of whom would be in that 190 million figure I quoted for vaccination and this would do two things. It would decrease their financial barriers and it would also help establish a collaboration that exist for childhood that doesn't print out a collaboration between state and local health departments and private sector providers that in the childhood side has been used to really improve coverage. So I think those are some of the things, there are a whole variety of other aspects with regard to vaccine such as moving more to cell based production from egg based production to have more degree of assurance that we will have cells and other aspect to try and improve the speed and time for development.

**ED HOWARD:** Walter, actually someone had asked that very question whether or not we ought to create a Vaccine for Adults Program and don't we have in effect such a program at least for the flu vaccine for the Medicare eligibles.

**WALTER ORENSTEIN, M.D.:** What we currently have is a reimbursement based program and for the Medicare population they are covered with regard to vaccine cost and reimbursement and recently there has been a big increase in

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vaccine administration reimbursement which is a big help. One of the problems that we face in flu vaccine is bought at risk. When a doctor buys flu vaccine for his or her patients if they don't use it they don't get any reimbursements. Now they maybe willing to do that for their insured patients but for the uninsured patients this will be a problem. And so what I'm thinking of is trying a very narrow program to try and focus on uninsured adults and try and leave as much of the private sector market, which is very important to the vaccine companies in the private sector. So I would focus it with eligibility criteria much of we have with the Vaccines for Children Program but I would limit this for uninsured adults who don't have and it can be costly. I know I got my daughter vaccinated a few years ago at a neighbor Kroger's and it was twenty dollars. That was fine and I had no problem paying it but for some people twenty dollars at that time could be substantial cost.

**ED HOWARD:** Yes, Alan.

**Alan [Inaudible]:** Alan [Inaudible with Senator Biden [misspelled?]]. Dr. Ornstien I want to go back to your first example, which was the 57, Maurice Hillman attempt. A lot of people think we just had a very close call with [inaudible] virus recently and that was contained only with no vaccines but with traditional public health restrictions. What did we learn from that? Are we any better prepared now to deal with

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something like that again in terms of the three month gear up and vaccine if something like that happened again but it ended up in a couple of places in the U.S. and not in Toronto?

**WALTER ORENSTEIN, M.D.:** I've not been involved actual current planning but what I can say is certainly for a disease that was spreading very slowly and was not efficiently transmitted there is the potential to contain it and that was what was done with SARS is basically by quarantining and isolating cases they were able to contain it. My presumption would be is with Influenza one would attempt to do some of the same things. The problem where it would be most helpful for Influenza is where it's likely to originate and most of the flu strains tend to originate, I'm not sure I understand why in Asia. Should they come to the U.S. my presumption is that there would be attempts to isolate the cases and one of the other aspects is there are anti-viral medications for Influenza and it's important to stock pile and to be able to use them to try and curtail transmission. What I'm a little skeptical about is once if, the strains don't mutate and suddenly take on the characteristics of normally transmissible Influenza I think you have some chance but if they do mutate and they take on the same characteristics of wild virus transmission I think it is going to be very difficult. Influenza can be

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transmitted before the patient is sick then maybe people with mild illness who may come on spreading. While I think one has to try and contain it I have some concerns of how successful that would be compared to SARS.

**PAUL OFFIT, M.D.:** Yeah I completely agree with that. I'm not sure those situations are, I mean if you go back to the 1957 example that and 68 were really the last two really big pandemics. If you go back to that 57 example I mean Hillman came to know of those strains in mid May. He then took control and frankly bypassed the regulatory agency at the time which was the Division of Biologic Standards under the National Institutes of Health which I would think would have to be truly not bypassed but at least have some fluidity with the current regulatory standards whereas you have to do things quickly. I mean here is a virus that started in Southeast Asia which is often true and the reason it is often true is usually these pandemics have a hemogluten which is through the cell binding protein that comes from birds and you need to not only have birds in large numbers but you also need to have pigs actually in large numbers because they are the kind of mixing vessels that now enable the bird virus to become attached to the human virus because both bird viruses and human viruses can infect pigs, so when you have large numbers of chickens and pigs and humans in one spot which is certainly true in Southeast Asia you get this perfect mixing

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bowl for these creations of new strains but it happened very quickly. I mean if you look in 57 in May he made the observation that here is a virus that nobody had antibodies to. That virus hit the United States in full force by September so he didn't have much time and he did it in about three and half months. So you don't have much time and I think that is the hard part.

**ED HOWARD:** John, I'm going to challenge you both with a question and the fact that I think your microphone is not working, but focusing on the model of purchasing that you laid out where there would in effect a real demand by countries for vaccine at a much lower price say a dollar and a guaranteed price for those doses that were purchased say at fifteen dollars. Why would the country not set or why would the company rather not set that "market price" at a nickel instead of a dollar or a tenth of a cent in order to make sure that that three billion dollar bonus if you will that has been guaranteed ends up getting paid?

**JOHN HURVITZ, J.D.:** I think there is two issues, one the contract would require that the product be purchased at the dollar or whatever the threshold minimum is so if companies were under pricing that would not be entitled to receive the, somebody has to pay the dollar in order for the product sales to eligible for the fourteen dollar top off. The other reason is whatever the product is old for at outset

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it would in effect create an ongoing expectation for the continued supply after that price is exhausted. So if you were selling a product for five cents on the expectation that you get fourteen dollars and ninety five cents once the fourteen dollars and ninety five cents support was exhausted there would be at least an expectation in those countries that you would continue to supply and probably public pressure that you would continue to supply them for nickel so those two factors.

**ED HOWARD:** Let me turn once again to a card. The question is what states can do to increase their vaccine purchase and to prioritize prevention? Paul you talked about that in your remarks. Is there something other than simply spending more money on their vaccine purchase that they can do or is that the key?

**PAUL OFFIT, M.D.:** I think probably Walter is better served at that answering I guess the specifics of it. I guess if I can speak to it in general, I think you know we just have to get better at this local and state and national level at understanding that vaccines are an important thing to do and I think it is a matter of education and how that education happens has been the hard part. You know it's obviously pharmaceutical companies are motivated to educate because they make a product that serves the public good and they want people to know about that but I think when they

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step forward in front of Congressional hearings or Legislative hearings at the state level you know they are just seen as trying to line their own pockets. So I think it falls to those in academics or it falls to those in public health agencies to do that but traditionally they haven't been great at doing that, they sort of stand back from that. I think traditionally that's probably the bigger part of it trying to get us out of our house and in the public health world and in academics and beat the drum for the importance of this.

**JOHN HURVITZ, J.D.:** I think one of issues that is important as having been in government you feel somewhat up tight at times of advocating is the formation of collations and many of the states have developed them but I think that is one of the good thing about the Childhood Immunization Initiative of the decade ago is many states did form coalitions with other people who were not as rad to go out and advocate. And that is what I think is absolutely critical. I think the states need the resources to put into that coalition building and coalition nurturing and in terms of providing information to individual partners who can make the case for them particularly with their state legislatures.

**ED HOWARD:** I have two more questions on cards that I want to get to and then I want to give our panelist a chance to chew on the sort of over arching question of the role in

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government in private sector that Walter has been eluding to. One of the questions I want to relay from a card writer is the following: Would someone comment on the effective transferring funds from vaccination programs in developing countries to HIV/AIDS treatment? That is for example polio vaccines in India that the use of which is being thwarted by HIV/AIDS treatment. Is that a common phenomenon and if it is, is it a good phenomenon and if it isn't what can we do about it?

**JOHN HURVITZ, J.D.:** Not qualified to speak to the underlying assumption but the one thing that I would observe is the cost today for AIDS treatment we're talking about hundreds of dollars and life effectively lifetime use of drugs and were we able to make the investment to develop a vaccine then I think that's what everybody was talking today and that is a really dramatic example of where you could, I mean the burdens on these countries in terms of the health care cost of providing these drugs even at the significantly reduced rates that they are provided is staggering. So I don't know about the diversion of the funds but certainly by investing in vaccines it wouldn't obviously eliminate the need to continue to treat the existing infected populations but it would really down the road go a long way to easing the financial and social burdens that these countries are facing today.

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**ED HOWARD:** One last card question. What's being done to increase physician in antibiotic prescription to reduce microbial resistance? Sort of connected.

**PAUL OFFIT, M.D.:** Yeah sort of, I think that, I guess at the heart of the question is that with antibiotic or intro issues of antibiotics that one can create bacteria that is more resistance and therefore more difficult to treat and therefore problematic. Certainly the CDC has actually done a great job I think at stepping forward trying to educate the public and physicians about antibiotic over use and actually associated with that educational effort you've seen a somewhat decrease in inappropriate antibiotic use so I think CDC actually has done a very good job with that.

**WALTER ORENSTEIN, M.D.:** I think the other thing is that some of the vaccines actually decrease antibiotic resistance. Pneumococcal conjugatae vaccine in a sense has been a miracle vaccine. It's not only protecting children but it turns out that many of the adults who account for some of the most severe complications of pneumococcal disease were getting it from children and by vaccinating children particularly with types that have a high prevalence of antibiotic resistance many of the remaining pneumococci are more sensitive to antibiotics than they were before so vaccines can help reduce the problem in fact I saw Steve Laughton who was here, and I don't know if he is still here

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who is representing NAVI which is a company that is trying to develop a staphacoccal vaccine. This vaccine for staphacoccal disease has been emerging, multiple drug resistance staphacoccal disease has been emerging has become a very significant pathogen both for children and adults and so there is another example of vaccines potentially being around to help us reduce that problem but I think obviously use of antibiotics is critical.

**ED HOWARD:** Before I serve up this last opportunity for our panelist to question let me just point out that if you fill out the blue evaluation form before you leave it will protect you against harassment by Alliance Staff at the exit of the room so it's an excellent investment in a preventative procedure. And if I can I would like to get each of our panelist view on what I infer from a lot of the questioning and from the presentations is at some level the central question involved in so many aspects of the vaccine issue and that is what is the role of government in trying to fashion the most defecatiuous way to deal with this potentially deadly weapon if you will of vaccines. Not just in the question of litigation but in the question of spending, whether it's at the state and local health department level or in federal research at NIH, or production or purchase or guarantees of production in the case of the vaccine itself and use that as your opportunity to sum up

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your take on where we are on this issue if can. Do you want to start Paul and we will come this way?

**PAUL OFFIT, M.D.:** I think the fact is that vaccines are a relatively small market product and because they are only used a few times in ones lifetime and because they frankly always will be used a few times in ones lifetime they will always remain a fairly small market product. That is not going to change and so I think in order to encourage, if we believe that there are public health benefits, which Walt showed in one of his early slides they are clear are and if we want to keep them in place than I think we have to set up systems that encourage their manufacturer by companies who if you just add up the you know what they make money on and look at their bottom line would not, I think instinctively do that. So I think government has an important role and I see that I guess in several ways being helped. The first is that as was said I think by all of us and to me is best summarized in that Alan Hinman paper you know that you need to let the manufacturers know that the government cares very deeply about vaccines as reflected in their absolute commitment to the VFC and 317 State Programs and I don't think to date that has happened or at least it certainly can be made better. So that is one thing I think that the distribution of vaccines also physicians get stuck as Walt said before you know with often having to purchase vaccines with not being certain

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whether or not insurance companies are going to be covering vaccines or it may even be covering them for at price or even less than price. They tried to around that with the so-called Administration fee, which was called the Consultant's Fee because it makes it sound like all they do, is administer vaccines but they do far more than that. But I think you know that there needs to be in place programs that make it clear that doctors aren't going to suffer from giving vaccines which occasionally happens. The other thing and this is subtle but I think it is a little bit of crap shoot vaccines for these companies at the level of the ACIP and AAP although the Institute of Medicine or the CDC will say these are important and here are important diseases like rotavirus or Papilloma and I think they need to be prevented. It would be nice to see them take the next step, which is that if the vaccine has certain criteria of safety and effectiveness that we will recommend it for these groups. You never quite know how it's going to come out at the ACIP and I think that can be a little scary for these companies and just finally I would say I do think that litigation is part of this and I think just personally when you see diseases like Group B Strep or respiratory viruses, the virus of the very common cause of pneumonia. It causes tens of thousands hospitalizations and thousands of deaths every year. I mean we're not that far away from having technology in hand to do

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that. You know to eliminate that disease. It may mean a maternal immunization strategy, which is absolutely taboo for companies unless they are going to be covered by a Federal program so you know you will never hear from those parents. You will never hear from Groups of parents against RSV or parents mad about Group B Strep infections and that's too bad that we don't have those kinds of advocacy groups but then maybe they would get more attention but I think the government can be that advocacy group and help prevent diseases you know that is clearly preventable.

**JOHN HURVITZ, J.D.:** My simple perspective on this is that we're better off having more companies playing in this game and that leads to competition which leads to lower prices which leads to greater security of supply and so government can play a role in creating proper incentives for industry to participate in this area and also help address some of the liability issues that that industry is facing as was done in the past with the National Childhood Injury Act and perhaps needs to be done again today in certain respects. Not only are we faced with the issues around the vaccine preventable deaths in this country but we're also now facing the specter of potential of bio-terrorist threats and having a health and vibrant vaccine industry will make us in a better position to address those threats and challenges in the future. The advance market commitment that I talked about

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and I didn't have the opportunity to go into a lot detail but what we tried to do there was to immolate the markets. I think fundamentally markets work and the government shouldn't necessarily be intervening to take the place of markets or displace the markets because I don't think it would ever do efficiently as or wouldn't ever operate as efficiently as the markets do but there are opportunities and mechanisms that can exist and we've seen it with the National Childhood Vaccine Injury Act. We've seen it with the orphan drug legislation in this country and there is good track record of where government intervention to nurture and remedy specific defects in existing markets works and works effectively and I think there are opportunities to do that not only with respect to bio-terrorism and not only with respect to diseases that are unmet challenges facing the developing world but also with regards to challenges that are facing us here today and the serious risks that we face if we lose another vaccine manufacturer.

**ED HOWARD:** Thank you. Walter.

**WALTER ORENSTEIN, M.D.:** I think the most important thing is to support the current vaccine production system which is a private sector system and which has brought us the tremendous number of innovations we have today. Certainly I don't see the Federal Government getting involved in the vaccine production. We've had public sector production in the

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state of Michigan, which stopped producing, and in Massachusetts, which I now accounting for a very small portion of the market because they can't keep up with the investments needed to innovation. So I think it is very important to continue with that climate. I think it has a responsibility to assure supply and one of the most important things particularly given the few companies that are currently producing is to support stockpiles. I think it is unbelievable that we don't have them when we have the funding for them because of the revenue recognition issue. Seems to me if my naïve take as a non-lawyer is that ought to be very fixable with a law as quickly as possible just exempting vaccines because vaccines are a community resource they are not simple an individual resource. I think there needs to be incentives for research. I think the NIH plays a big role in helping some of the basic research. I think there needs to be continued support of that process. I think there needs to be reduction of industry risk. I mentioned for flu vaccine and there are others as well, so way of supporting the R & D process for vaccines that are considered a high priority. I think the government has an obligation given the public benefits of vaccination to help people get those vaccines and to minimize or eliminate financial barriers to immunization. That means vaccines purchased for certain groups of people. That means support of an infrastructure to deliver that

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vaccine but I think that is critical and I think it is most critical in the adult immunization right now where they are having problems. I think there is a need to fix as Paul was saying some of the problems in the Childhood system where particularly the discretionary appropriations have not kept up with these substantial increases in cost as new vaccines have come to market. And finally I think there is advocacy is trying the resources the federal government can do to educate people and explain what vaccines are, what the benefits are, what the risks are and to help set the climate for all of this could be substantial.

**ED HOWARD:** Thank you Walter and thank you panelist. I think we've had an intriguing discussion and I want to thank our friends at Health Affairs for providing us both grist for reading and such fine speakers this afternoon. I want to thank you for hanging in there on what is often a very tough subject for those of use who don't specialize in vaccines and I especially want to thank our panelist for I think illuminating an awful lot of issues that have been dim and can use a lot of illuminations of the course of the next few months. So if you would join me in thanking them I would appreciate it [applause].

[END RECORDING]

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