Testimony of Dr. Annie De Groot before the Blue Ribbon Study Panel on Biodefense

April 1, 2015 – Washington DC

Governor Ridge, Senator Lieberman and members of the panel:

At your last meeting, my friend Senator Sheldon Whitehouse, spoke to you about regulatory systems that are in place to protect existing stakeholders instead of encouraging innovative methods for solving existing and new biothreats that we face. As Senator Whitehouse said, "protecting incumbents stifles innovation."

I am here to put a face on that issue, at least as it applies to vaccine development, having experienced it first-hand. I *know* that there are *far better ways to respond to and recover from a biological threat* than what we are doing today. I trust that by *the end of my presentation you will know it also.*

My name is Annie De Groot. I am the Founder, CEO and Chief Scientific Officer of EpiVax. Over the past 17 years, my company has engaged in developing and designing vaccines that are more *effective, safer, faster, and cheaper to produce than vaccines made with existing methodologies*.

In that sense, we are like many small biotech companies that have one solution or another for dealing with biothreats. But our company may be a bit different from others. We have become successful by challenging the scientific status quo. It has been a struggle, but we think it is worth the effort, because innovation can bring about new solutions to important problems. *That is why I am here today*.

What's unique about our small company is that we have special computer driven tools for vaccine and biologics design. We also put forward innovative vaccine design concepts, many of which have eventually percolated into the industry and have been adopted by "bigger firms".

I know that "percolation" is what sometimes it takes for new ideas to be adopted. However, what I have learned about biothreats over the years since 9/11, is that waiting for ideas to percolate 'to the top' means that these ideas *arrive too late to make any real impact*.

What's the important idea that we'd like to move forward for biodefense? Our company has developed methods for making more effective, safer, and potentially less costly vaccines *on*

demand. The *time to consider these novel ideas is now*. I recognize *that these ideas may not sit well with incumbents in the vaccine industry*, including some of the folks who are present in this room. Then again, isn't that always the case when new ideas drive change?

How do we do this? We use our extensive knowledge of immunology, our scientific acumen and our proprietary computational tools *to rapidly discover the components of pathogens that trigger immunity – as well as those that enable pathogens to escape from immune response.* As a result, our advanced computational tools allow us to *design a vaccine almost immediately – within 24 hours*. We do this from the sequence or DNA of the pathogen that is made available to our scientists through the Internet. *And not only can we design vaccines on the fly, but we can also predict which vaccines will work and which will not.*

The difference in approach is significant. Traditional vaccines are made using what I call the 'shake and bake' method – take the virus or a part of the bacteria and cook it up, then bake it until it's dead and inject it. That's a method of making vaccines that *hasn't really advanced since the time of Louis Pasteur*.

"Vaccines on demand" are a powerful solution to biothreats, and the approach has broad implications for vaccines in general. But to implement these new ideas, the way vaccines are *designed, developed, deployed and approved* must change. That's the message that is upsetting the incumbents and the regulators, but I am here to tell you that it's critical to change in order to address the biothreats we face today and to prepare for those we will see in the future.

Let me give you two important examples.

One example: H1N1 pandemic influenza. When H1N1 pandemic flu emerged in Mexico, the virus was shipped to the CDC, and the sequence was made available immediately to the scientific community. The bad news? *CDC found that antibodies from the existing seasonal flu vaccine were not effective against the new pandemic strain and then went no further in the analysis*. The good news? Using our computational tools, we determined that the same seasonal flu (vaccine) could be effective against the new pandemic flu strain because identical 'triggers' for another arm of immune defense were common to the pandemic flu and the seasonal flu (T cell epitopes).

The CDC never looked at that possibility even though the literature was replete with evidence that these T Cell triggers could and would make a difference. What did we do? We made that information available to the public and even emailed this information to all of the people we could think of, or reach, or who could be reached through our larger network, so that the information could be taken into consideration when efforts to respond to 'pandemic flu' got underway.

Essentially our message was – *hold your horses, it is possible that there are elements in the existing vaccine – and that vaccination or exposure to the flu strain of last winter will protect against the new flu strain, and while it will be easily transmitted, it will not cause significant mortality and will not fill hospitals to capacity as some were claiming. Our findings told us that rushing to spending millions on making a new pandemic flu vaccine – using existing methods – that – as it turns out – would not even be ready in time – was unnecessary.*

Were we right? Absolutely. Did these ideas get any traction? Absolutely not. Could we have

eased the panic with some rapid, well-focused clinical studies, had funding been available for "innovative ideas"? Absolutely! But bigger companies – the incumbents, the 'go to' group for the US Government, *were already in discussions about contracts to produce a new flu vaccine* using existing methods. Nothing we said, as loudly as we could say it, could interfere with the process since… the connections were in place and the established approach was viewed as *non-controversial.*

Example number two: H7N9. We put the same algorithms to work on the new bird flu strain, H7N9 that emerged in China in 2013. This particular strain causes death in more than 40% of individuals and is still causing a great deal of worry among pandemic flu experts.

What did we find out about that flu stain? Within 24 hours of having access to the published sequence, we were stunned to see that the virus was somehow missing those key triggers of immune response I spoke about a moment ago. It was a "stealth virus".

Again, we sounded the alarm, and predicted that vaccines our government was funding would be *poorly effective*. Were we right? Absolutely. Did it make any difference? No.

So you ask yourself, why should we care? To me, there is a serious problem when the H7N9 vaccine produced with funds from our government is one of the least effective flu vaccines ever tested. Especially when, *using tools available right now, it was possible to predict that outcome.*

There is a better way. At EpiVax, working with collaborators in Japan and Florida, we developed an H7N9 vaccine that is 20 fold better, simply by making 3 pinpoint changes to the original vaccine.

What is the chance of getting this more effective vaccine to the clinic? I'll let you know next week when I talk to the NIH program officers about funding production of the vaccine and a clinical trial. *I'm hoping this time will be different, but I'm not holding my breath*.

So what's my message? My message is that – using innovative new tools, we can design and produce the recipe for a new vaccine within 24 hours of receiving the DNA sequence of any biothreat, and we can distribute that information electronically to vaccine manufacturers anywhere in the world.

Our vision of the future is that we will be able to create vaccines-on-demand in decentralized production facilities. If the regulations were updated, these labs could splice the new sequence into an existing FDA-approved vaccine vehicle. Depending on the vehicle, enough vaccine could be produced in a few weeks, so that it could be packaged and mailed to every pharmacy, grocery store or even sent out to individual homes through the post office. Wouldn't it have been great to have that in place to respond to Ebola.

I believe that making "vaccines on demand" could save millions of lives and tens of billions of dollars. Instead, those dollars are currently being used to create *standard vaccines* that are stored in warehouses until their efficacy expires, only to be replaced by another set of standard vaccines that *may or may not work – just because someone can produce them doesn't mean that the vaccines should be made*! Stockpiling is a costly and potentially ineffective solution to creating a national biodefense system.

If you think making vaccines on demand is still science fiction, it is not. At EpiVax, we have done

everything I just described, except package the vaccine and distribute it to the public. We did this for Lassa fever in a live-fire test coordinated by DARPA, and we're about to start a DTRA-funded live-fire test for a Q fever vaccine. Agility like this is what our country needs today – because no one knows what we'll face when it comes to biothreats – no one.

In fact, the next engineered pathogen might contain parts of *one or more* bioterror agents, and will be *designed to be antibiotic resistant*, due to advances in cloning techniques. What then? Making a vaccine on demand is the only response that makes sense.

Instead of pushing these innovative, potentially life-saving advances to the fore, current funding and regulatory mechanisms are rooted in 19th century thinking. Plus, innovative approaches like these so seriously challenge entrenched incumbents and would so fundamentally change the way the FDA approves new vaccines, that the disruption is too great, in spite of the potential benefits to the public.

The very nature of disruptive innovation is that it disrupts the status quo.

Just as smart phones and tablets have almost completely replaced pay telephones and bookstores, so must new methods for vaccine design, development, deployment and approval replace the current 19th century approach.

Why, if we are so convinced, don't we move these techniques ahead ourselves? The current barriers are so high that it is all but impossible for anyone other than the entrenched incumbents to participate. It costs tens of millions of dollars today for animal trials, Phase I and Phase II tests and require hundreds of thousands of pages of supporting documents before regulators will even take a look at a new vaccine. *We no longer have the luxury of time when it comes to dealing with biothreats*, especially those that may be bio-terrorism.

What's the reality today? My company, and other disruptive innovators like us, have to work within the system. We have no choice.

But YOU have a choice. You can push for the alignment of regulatory and policy structures with new technologies that are now available or will be available as technology improves.

Your recommendations will carry a lot of weight, depending on the time and effort you devote to carrying the message forward. Please don't create a report that will sit on a shelf and gather dust while new ways of solving problems atrophy along with it.

I have put several recommendations in my written testimony and will be happy to discuss them with you during the question and answer period.

Thank you for allowing me to share my views and I hope that you will be bold – dare I say, "innovative" – in recommending solutions to the issues your panel will address.

I would like to see your list of recommendations include, at a minimum:

1. Requiring BARDA to devote no less than 10% of its annual budget to funding new, innovative technologies that will lead to faster response and recovery than current vaccines achieve. Requiring that any projects funded with those BARDA funds have a "resiliency

improvement" score with a higher priority being given to those projects that allow for faster, more effective and lower cost response (design, production and distribution) for bio-defense counter-measures to be given a higher priority.

That means that the "TLR" level for BARDA funding of these initiatives might have to change, and BARDA will have to reach across the invisible line that divides it from the NIH to fund the development of innovative approaches that have reached proof of principle in animal studies. One way to do this is to require the NIH and BARDA to regularly review and consider joint funding of any projects that represent potential solutions to current and future biothreats.

Take our tularemia vaccine for example! Over the past 8 years, we have tried to fund it 12 different ways through the NIH and the DoD. Recently, it received an excellent and rarely seen low score of *24* but we were told by our grant officer that it had to reach *22* to be funded. This was in the sequester year, when in previous years, a *32* would have been sufficient. We know that there are few viable alternative tularemia vaccines. We appealed to our officer and her supervisors, to no avail.

2. Fix the broken SBIR (Small Business Innovative Research) program. The "I" in SBIR no longer stands for innovative – instead it stands for "incremental" research. Create an office of Innovative Research within HHS, similar to that of DARPA within DOD and ARPA-E at the Energy Department, to provide funding and program support for disruptive and innovative health response technologies and approaches – make this office responsible for identifying projects within any agency that represent viable, rapid solutions to biothreats.

   I should add - we have deep experience with the SBIR system. I would be happy to provide more details, even testimony how *important this system is to medical innovation* and how *underfunding this program* combined with *lack of leadership at the NIH* has contributed to the deterioration of this important engine for innovation.

3. Work with the FDA to develop a strategy for making 'vaccines on demand'. This could be derived from the current approach to influenza vaccines, allowing vaccine developers to apply for approval of 'reusable delivery methods" such as DNA plasmids or carrier vehicles that can be approved for one use, and then re-used for another, so that vaccines no longer need to be stockpiled. Benefits from these changes will extend far beyond biodefense, as we need means of developing rapid vaccine responses to multi-drug resistant bacteria and emerging infectious diseases such as Ebola.

I would like to thank you very much for the opportunity to participate in this important process. It is my fervent hope that this great nation will benefit from the innovations that we are developing at EpiVax, in my lifetime. That's why I went into science, and that's why I get up and go to work with enthusiasm and hope, every day.