

Testimony of

Dr Paul Keim

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STATEMENT OF PAUL S. KEIM
REGENTS PROFESSOR OF BIOLOGY,
THE COWDEN ENDOWED CHAIR IN MICROBIOLOGY,
NORTHERN ARIZONA UNIVERSITY
FLAGSTAFF, ARIZONA

AND,

THE DIRECTOR OF PATHOGEN GENOMICS,
TRANSLATIONAL GENOMICS RESEARCH INSTITUTE
PHOENIX ARIZONA

BEFORE THE

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SUBCOMMITTEE ON TERRORISM, TECHNOLOGY & HOMELAND SECURITY
UNITED STATES SENATE

CONCERNING

THE USE OF PATHOGEN GENOMIC ANALYSIS FOR DETECTING AND EVALUATING ACTS OF
BIOTERRORISM

PRESENTED ON

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My experience in biothreat analysis. In early October 2001, a photo editor for a Florida, USA, tabloid newspaper contracted anthrax and died. In the initial days of his infection, we weren't sure that this was indeed a bioterrorism event. An anthrax case in the southeastern United States was unusual, but perhaps it was a natural case? The inhalational diagnosis was doubted by at least one national expert, who questioned the ability of the naïve medical team to make the correct diagnosis. A primary "anthrax" culture from the victim's cerebral spinal fluid was jetted by courier to our relatively remote Northern Arizona University laboratory on Thursday October 7th, while the Centers of Disease Control experts did parallel studies. Early on Friday morning, a conference call between the Keim Genetics Lab and Drs. Alex Hoffmaster and Tanja Popovic at the CDC concluded that the initial anthrax-letter victim had been infected with the Ames strain. Our work has shown that this strain is very rare in nature. But we also knew that it was a highly virulent and commonly used in laboratory experiments and vaccine challenge trials. The first anthrax-letter victim died later that day turning this from just an epidemiological investigation, into a forensic investigation of murder. My testimony on the anthrax-letter attack will be limited today because of our involvement in this ongoing criminal investigation. Though, I can provide this one insight into the investigation: one of our most valuable services to the FBI and this country has been our ability to exclude natural cases of anthrax from the criminal investigation. For example, in November 2001 a herd of cattle died of anthrax near San Jose California. Our rapid analysis quickly identified the strain as a naturally occurring one and diffused a potential regional crisis. Like in human forensic

analysis, conclusions about "exclusion" are very powerful and important.

The well known "anthrax letter attacks were preceded by several other anthrax investigations that pushed our DNA-based technology along and the status necessary to identify the Ames strain in 2001.

Anthrax's use as a biological weapon by many countries' weapons programs (e.g., USSR, Britain and the USA) doubtlessly contributed to the wide spread knowledge of its weapon potential. The technology to produce large amounts of "anthrax" spores, weaponize them, and deliver the agent was well developed by several different countries. In 1979, there was an accident at an anthrax spore production facility in Sverdlosck (Yekaterinburg) USSR. A spore plume stretched downwind across the city, infecting individuals and, ultimately, killing at least 64 individuals from anthrax.

Along with my colleague Dr. Paul Jackson at Los Alamos National Laboratory, we have investigated the 1979 Sverdlosck military accident where a spore cloud was released across this eastern Russian community killing at least 65 people. Strain analysis of victims' necropsy tissues suggested that the plume was a composite of multiple genotypes. The multiple types of "anthrax" suggested that the Soviet bioweaponers were mixing types during their weaponization program. Alternatively, they may have just accidentally released multiple types.

How or why an industrial accident of this scale would have spores from multiple strains is not known and details from the accident were never officially revealed by the Soviets. Thus, the strain identity work is still one of the few publicly known insights into what happened in this tragedy.

A second example our pre 2001 efforts involved the Aum Shinrikyo dooms day cult in Japan. Indeed it was in early 2001 that we had completed strain analysis on "anthrax" culture isolated at the site of an attempted bioterrorism event in the Tokyo, Japan, suburb of Kameido. The Aum Shinrikyo cult was striving for social chaos, in order to overturn established political institutions for their own benefit. In late June 1993, cult members sprayed liquid B. anthracis cultures over this densely populated suburb for several days. The spray resulted in a stench and caused the local population discomfort, but no one contracted anthrax. After the cult's deadly sarin gas attack on the Tokyo subway, interest was renewed in the earlier Kameido incident. We analyzed the single remaining environmental sample from 1993 and discovered B. anthracis spores that were still viable. Strain analysis identified these spores as Sterne, a common veterinary vaccine strain. The cult would have had easy access to this strain, as 100,000's doses of the Sterne vaccine are produced, distributed and utilized every year in Japan. This easily explains the cult's failure to kill, as the Sterne vaccine is highly attenuated and cannot cause anthrax in humans. This investigation had an eerie parallel to the anthrax letter attacks, in that our technology identified the type of "anthrax" and led to a reasonable explanation for what had happened.

Genomic based diagnostic analysis. The key to strain identification is the genomic technology developed in my Arizona laboratory. Even before the first victim died in the anthrax-letter attacks, the U.S. government knew that this threat started in a laboratory setting and was not a natural infection. As it turned out, as a country we were better prepared for a forensic investigation of anthrax than just about any other bioweapons. (Because this is an ongoing criminal investigation, I will go into no further details on this particular case.) We had

Lessons learned. From a decade of experience in bioweapons research and from my investigative role in these bioweapons incidents, I have learned several things.

First, you have to be broadly prepared for crises involving bioweapons. While the threat is extremely real, it represents a very diffuse target. It is hard to anticipate what the next biothreat agent will be and harder yet to predict what scenario will play out. While specific preparation for a particular scenario and a particular agent, for example anthrax in letters, may or may not help in the next bioweapons event. Highly skilled personnel can adapt to just about any crisis situation. Building a broad infrastructure in infectious disease and public health will be valuable in any biothreat scenario. Maintaining stocks of suitable reagents, diagnostic devices and capabilities to respond are crucial once a crisis occurs. Point-of-care diagnostic devices are badly needed and not yet developed sufficiently.

Secondly, I have found that it is impossible to prepare everything. We were surprisingly well prepared in the forensic arena for an anthrax attack. My lab had tools, we had databases and we even had recent experience in tackling a bioterrorist event. But, when I got the call from the FBI that a clinical sample was in route from an anthrax victim - I shuttered and thought "Oh God, give me another six months to prepare!" I got six hours. So, again I would urge for building infrastructure that is adaptable. This needs to include both well equipped laboratories and a trained work force that can fill in the gaps and expand our knowledge as needed. It is impossible to exactly predict the next event arguing for broad healthcare based efforts.

Thirdly, we need to have established communication mechanisms. In a crisis you gravitate towards what you know. In our case, we had long-established personal contacts at the FBI and the CDC. These were far from the upper echelon folks, but rather with the skilled technical personnel in each agency. Years of scientific interaction with these folks had established our area and specific expertise with them. They knew and trusted our work. Following September 11th,

our country's communication and transportation infrastructure was greatly impacted. We need to have established networks of experts and communication channels in order to react effectively in a crisis situation.

Fourthly, flexible contracting and mechanisms for moving funds need to be available. Even in crisis situations payrolls have to be met and supplies have to be purchased. In days following September 11th, basic economics still applied. In our cases, we temporarily stopped all other government contracts and moved these people and resources on the investigation. The government needs contracting mechanisms to quickly respond to a crisis. This sounds easy to the folks high in the chain of command, but it has to be implemented at the level of accounts and contract officers who try really hard to obey the government rules. While this topic lacks all the pizzazz of hazmat suits and genetic engineered germs, but it was a real problem and distraction in the investigation of this case, which began in a crisis situation.

Finally, our nation has such great scientific and technical expertise and this gives us a distinct advantage in the fight against terrorism. In the future, we will be able to monitor infectious disease pre symptomatically and this will minimize the impact of future bioterrorism events. It is important that the US government is forward thinking and moving in this direction. Clearly, this is not a solution for what happens next weeks or even next year, but it will not happen at all if we are not planning for 5 to 10 years now.

The great potential of genomic research. Forensic investigations are driving diagnostic analysis to the absolute limit of specificity. In the area of bioterrorism defense, you will hear a lot of talk about specificity levels. Can we tell one bacterium from another? In forensics we are required to "precisely" identify the biological agent involved in an event. Now that forensics has become so important, we are benefiting the whole field by providing exquisitely precise and specific identification. This specificity will greatly benefit both environmental and medical diagnostics assays.

One of the sad realities associated with forensic work is that our technical capacity is only realized when crimes have been committed and as they are investigated. Thus, forensics is focused on post event characterization in order to prevent and deter future terrorist efforts. However, our work and technological advancements can be important in environmental detectors and healthcare that are important before and during a terrorist event.

We don't know what the next bioterrorism event will be, let alone the next terrorism event will be. However, it is easy to predict that terrorists will be striving to hurt American citizens. While there are many non exclusive strategies for protecting our citizens, ultimately the point-of-care is where all of the different terrorist scenarios coalesce. A terrorist attacks have and will create confusion and chaos. It is easy to envision the potential for a panicked population to overcome our healthcare's capacity to effectively treat and manage the influx of "worried well" and truly sick citizens. Comprehensive, sophisticated and highly specific diagnostic resources are needed to avoid or mitigate this scenario. Thank you, Mr. Chairman for holding this hearing on this important topic. Our efforts today and those that will follow in the future weeks will have pronounced affect upon biodefense and healthcare in general. I will gladly answer any questions you may have.