Statement of Dr. Jeffrey Trent
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Before the
U.S. Senate Committee on the Judiciary
Subcommittee on Terrorism, Technology and Homeland Security
Concerning
Rapid Bio-Terrorism Detection and Response

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Good morning, Chairman Kyl, and Members of this Subcommittee. My name is Dr. Jeffrey Trent, and I am the President and Scientific Director of the Translational Genomics Research Institute in Phoenix, Arizona. Prior to my move to Arizona 18 months ago, I served for nearly a decade as the Scientific Director of the Division of Intramural Research of the National Human Genome Research Institute of the National Institutes of Health in Bethesda, Maryland. I wish to thank the members of the Subcommittee and particularly Chairman Jon Kyl for inviting me to testify at this hearing today.

Today's panel of speakers has clearly outlined the dangers posed by a biological outbreak and the ability of modern technology to work toward addressing shortcomings of our early detection and treatment capabilities. In my brief comments I will discuss how one can examine the "injury response" to radiation in much the same way that one examines a response generated by an infectious agent. I commend the Subcommittee for your willingness to hear from representatives of the medical and scientific community about this serious and important issue. All of us at the table, as well as research scientists across the country, stand ready to work toward addressing solutions of our early detection and treatment capabilities.

I would like to address two additional key points for your consideration. The first is the critical need for supporting approaches to implement a comprehensive and effective end-to-end solution. Second, I will provide a brief description of work [a collaborative partnership between my laboratory and the National Cancer Institute (headed by Dr. Albert Fornace) and his former assistant, Dr. Sally Admundson (now of Columbia University] that when joined to other work from scientists in the US and elsewhere, is beginning to suggest that the activity of the genes of an individual may serve as biomarkers for radiation exposure. Our cooperative studies indicate that genomics-based measurement of injury responses to specific toxic agents, like ionizing radiation, can be used to develop signatures for exposure.

History tells us that for the case of a biothreat agent, pre-exposure detection is not likely to be feasible in every instance. As described by Dr. Meislin, we will

likely be presented at the time of a bio-threat crisis with sick and dying people or animals. For this situation the answer will lie in how quickly we can detect and identify these early cases.

Also, as you have also heard today from both Dr. Keim and Dr. Relman, the answer will also lie in new approaches to develop cost-effective diagnostic tests that can reliably separate bio-threats from the background of “noise,” thus distinguishing “genetic signatures” of the common cold/flu that may cause similar initial clinical symptoms to those of a weaponized bio-agent.

While our focus must appropriately be on biologic attacks that threaten our safety, fears of a possible “dirty bomb” detonation or similar situation have spurred interest in the search for biomarkers that could be used to rapidly assess radiation exposure status in large, potentially exposed, populations. With the September 11 terrorist attack and subsequent anthrax attacks, it seems more than a topic popularized for science fiction that a radiation-threat could result in a chilling scenario for the US or other nations who may be targeted.

Mr. Chairman, for nearly 20 years, I have worked to create and utilize tools and techniques to identify the genetic signature of killers. I have worked on reading the fingerprints of such killers as breast cancer, leukemia and malignant melanoma. While at the NIH, I also worked on identifying the genetic signatures, or what is known as the molecular fingerprint, of killer viruses such as HIV, human T-lymphotropic virus type 1 (HTLV-1), human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus) and, in collaboration with investigators at Ft. Dietrich, the dreaded Ebola virus. Also outlined by this panel today is the progress in surveying the response of the individual infected (the host) to provide a recognizable “molecular fingerprint” separating a naturally infecting virus, as an example, from bioweaponized strain of anthrax.

It is also important for this Subcommittee to be aware of similar progress, albeit preliminary in nature, of emerging work that is beginning to recognize that a “radiation-associated” gene response signature could be incorporated into a biomonitoring approach similar in design to that just described for biothreat-agents. Picturing the near-future, one can see the identification of sets of genes which once proven informative, could be incorporated into rapid assays (utilizing such techniques as nanotechnology and protein and gene expression analysis) performed on an easily biopsied tissue such as blood, and which could become part of a gene induction profile that could serve as an indicator of both an individuals’ rate of exposure as well as their absolute dose of radiation (part of the collaboration between my laboratory at the NIH and the National Cancer Institute).

Recently my laboratory at TGen also joined forces with investigators at the DOD funded “National Functional Genomics Center” at the H. Lee Moffitt Cancer Center in Tampa, Florida to investigate protein markers of radiation response as

well. By performing molecular signatures of patients undergoing cancer treatments with radiation therapy, we can establish a diagnostic profile using both genomics and proteomics that will be characteristic of someone exposed to radiation.

While there is hope that we may be able to utilize diagnostic testing to identify a biothreat or radiation-associated genetic signature, I remain convinced that the most important thing I can emphasize today is the need for an end-to-end solution that pushes forward early detection, focusing on the reality that early detection is the key to faster diagnosis.

This faster diagnosis will:

•Save lives;

•Optimize treatment selection; and,

•Enable the rapid triage of at risk populations which will provide the vital goal of reassurance to the (potentially exposed) "worried well" (thereby reducing the risk of public panic).

To achieve this goal of early detection, several critical elements must be in place, and a "systems-based" approach is essential to addressing the problem. The failure to develop any one of the four will not address the critical needs in biodefense or result in improved public health and safety. These elements include:

- **Molecular Signatures:** Gene and protein sequencing of selected pathogens; detection of genomic, proteomic, and phenotypic signatures of the host immune response; and the creation of unique markers radiologic as well as a broad range of biothreat agents.

- **Diagnostic Platform:** Incorporating the signatures into a low-cost diagnostic platform suitable for routine patient testing in a variety of clinical settings.

- **National Information Architecture:** An integrated collection of data, syndromic surveillance, reliable anomaly detection, and real-time alerting of local and national decision-makers that a bioincident has occurred and permit real-time assessment of incident progression and the effectiveness of containment actions. And,

- **Decision Support Systems:** – An infrastructure linking key decision-makers with relevant medical and public health authorities to ensure rapid launch of optimum treatment protocols, rational allocation of drugs and vaccines, and comprehensive incident containment actions.

Chairman Kyl and Members of the Subcommittee, as stated today by this panel of scientists and physicians, currently health providers do not have all of the necessary tools to distinguish between an infection caused by a bio attack and that caused by the average cold. They must rely on a series of sequential and intuitive actions that in some cases could delay mobilization of prompt responses**.**

Further, in the case of a "dirty bomb," to aid in the triage of patients, biologic tests could help provide information on an individuals' radiation dosage. The requirement that I personally believe could be of great benefit would be the pursuit of a purposeful end-to-end solution of the aforementioned system elements, something that will require an obligate demand for public/private partnerships.

These factors and more have compelled me to join my colleagues, including Dr. George Poste, Director of the Arizona BioDesign Institute at Arizona State University, and Dr. Paul Keim, in a consortium involving Arizona State University and Northern Arizona University, linked with Dr. Michael Tracy and his team at the Stanford Research Institute, International in Menlo Park, California, in the development of a project called the "Project Zebra," which can be part of the solution for this complex problem, allowing faster mobilization of all relevant incident management actions as the key piece in early detection.

In closing, I would like to thank Chairman Kyl for convening this hearing on an extremely critical subject matter and offering me the opportunity to testify before your distinguished Subcommittee. I would be pleased to answer any questions you may have. Thank you.