Testimony
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CDC's Policies and Procedures Governing the Collection and Study of Specimens

Statement of
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Good morning, Chairman Miller, Mr. Sensenbrenner, and other distinguished Members of the Subcommittee. I am Dr. Janet Nicholson, and it is my pleasure to be here today in my capacity as Senior Advisor for Laboratory Science for the Coordinating Center for Infectious Diseases (CCID) at the Centers for Disease Control and Prevention (CDC), an agency of the Department of Health and Human Services (HHS). In addition to advising the Director of CCID on all laboratory-related science issues, I also serve as the designated federal official for the CCID Board of Scientific Counselors, and the Co-Chair for the steering committee for the design and construction of four CDC Laboratory Buildings. I have co-authored 95 research/review papers and have made 80 presentations in the fields of emerging infectious diseases, laboratory response to bioterror threats, and immune responses to HIV infection. I also currently serve as the U.S. representative for the Global Health Action Group Laboratory Network, as a member of the Trans Federal Task Force for Optimizing Oversight of Biosafety, and as the President-Elect on the Board of Directors for the Clinical and Laboratory Standards Institute.

I am pleased to appear before you this morning representing the CDC, the nation's leading public health protection agency, to address the CDC's Laboratory Specimen Collections.

CDC Policies and Procedures Governing the Collection and Study of Specimens:

Each year, CDC laboratories receive hundreds of thousands of human and environmental specimens from its various partners in public health throughout the United States and abroad. Many of these specimens contain organisms or products that other

laboratories could not identify, and virtually all of these specimens are automatically archived because of their potential importance to public health and safety. These specimens are collected for the purpose of detecting, controlling, and preventing morbidity and mortality from diseases. Specimens are used for a variety of purposes, including research, pathogen discovery, diagnostics, reference diagnostics, vaccine development, and supporting external scientific research activities within multiple National Centers across CDC.

Upon receipt, CDC logs, tracks, and examines these specimens and provides reports of any laboratory tests to the submitter of the specimen or other appropriate authorities. Specimen logging, tracking, and reporting is managed by our automated Specimen Tracking and Retrieval Laboratory Information Management Systems (STARLiMs). Any given specimens or samples we receive may be entirely consumed by the testing process, or portions may be stored for safekeeping or retained for future use. In extremely rare circumstances, some of our archived specimens may be destroyed because of space limitations, lack of current relevance, loss of viability during storage, lack of appropriate documentation, or when required by an Institutional Review Board (IRB).

Maintaining CDC's world renowned culture collections of specimens is essential to carrying out the agency's core public health functions to detect, control, and prevent morbidity and mortality from infectious diseases. CDC manages its specimens in a manner commensurate with the scientific integrity required by HHS guidelines and policies. These policies and guidelines include, but are not limited to, the HHS Public

Health Service Policies on Research Misconduct (42 CFR Part 93)[1] and the HHS Protection of Human Subjects regulations (45 CFR Part 46). Laboratories also have guidelines specific to the types of specimens collected, as most collections must be handled in very specific and often unique ways, for example, CDC's "West Nile Virus: Guide for Clinicians", and CDC's "Instructions for Testing by the Division of Vector-Borne Infectious Diseases Bacterial Zoonoses Diagnostic Laboratory."[2] Each collection has a curator, whose responsibility is to create, maintain, and oversee the use of these special collections. These specimen collections are unique and unmatched anywhere in the world. They are critical to CDC's mission and to our commitment to the global community as a reference diagnostic center, as well as supporting the work accomplished in our nearly 30 World Health Organization (WHO) Collaborating Centers for Reference and Research on viruses, bacteria, parasites, and fungi.

Rare and irreplaceable collections of specimens stored at CDC are subject to the limitations of research resources that could block our ability to uncover the benefits to health and medicine that are contained in these specimens, some representing historical collections pre-1945 (pre-antibiotic era). For example, CDC routinely performs reference and research activities on rare, unusual, and novel bacterial pathogens. This work requires comparison of the new, unknown organism to isolates of archived strains with similar characteristics. New pathogens are discovered when novel isolates are shown to

[1] Some of the areas covered in this policy include: "Protection of the confidentiality of respondents, complainants, and research subjects identifiable from research records or evidence, consistent with" 42 CFR 93.108; and, "A thorough, competent, objective, and fair response to allegations of research misconduct consistent with, and within the time limits of the final rule, including precautions to ensure that individuals responsible for carrying out any part of the research misconduct proceeding do not have unresolved personal, professional, or financial conflicts of interest with the complainant, respondent, or witnesses," as explained at http://ori.hhs.gov/policies/Requirements-Reg-6-05.shtml.

[2] http://www.cdc.gov/ncidod/dvbid/misc/bacterial_zoonotic_shipping.htm

be unrelated to any archived organism or DNA sequence on record. We would be unable to conduct our comprehensive work on pathogen discovery without these valuable strain collections.

The CDC's diagnostic laboratories save and store the significant organisms they identify; the laboratories are certified under the standards of the Clinical Laboratory Improvement Amendments (CLIA) of 1988 and currently have policy statements and guidelines regarding archival and storage of laboratory specimens. Under CDC's Laboratory Quality Management System (QMS) approach to carrying out our laboratory science, all laboratories are required to document their policies and processes for specimen collection, disposal, and storage. The QMS is part of CDC's ongoing work to achieve even higher quality standards and is aimed at standardization of policies to the extent that is possible, given the distinct nature of each laboratory. CDC also is a participating member of the National Science and Technology Council's Interagency Working Group on Scientific Collections. CDC's specimen archival storage facilities and containers consist of -70°C freezers and liquid nitrogen containers that are monitored twenty-four hours a day, seven days a week, with up to three contacts available and listed on each storage container, should an alarm indicate a problem with temperature control that could threaten the contents. To further protect our collections, CDC and the American Type Culture Collection (ATCC) have an oral agreement that new and reclassified strains of enteric bacterial pathogens are placed into the ATCC collection so that the organisms are available from the ATCC to all scientists for purchase to use in their research.

Specimens at CDC that were collected for the purposes of human subjects research must comply with the HHS Protection of Human Subjects regulations (45 CFR Part 46). This includes specimens collected for research conducted by CDC employees or supported by CDC through funding or provision of other tangible support whether conducted inside or outside the United States. CDC investigators who collect and use these specimens are trained in compliance with the regulations that apply to investigators who engage in research using human subjects. Unless exempt, under the HHS regulations for the protection of human subjects, all research involving human subjects must be approved by an IRB prior to the start of the research and specimen collection. CDC IRBs are composed of members from various scientific disciplines including health fields, social sciences, methodology, laboratory sciences and toxicology; and non-scientific disciplines, including ethics, education, administration and youth advocacy. Most IRB panels have members with specialized knowledge of the interests of pregnant women, children, prisoners, and other categories of vulnerable groups and individuals, to protect them from inappropriate or unethical treatment. Each of CDC's seven IRBs is composed of 12 to 16 members, and at least one to three of these members are not affiliated with CDC. The guidelines of the CDC IRBs require that protocols specify the disposition of remaining specimens after completion of the research, and the principal investigator must request permission from the participants via informed consent to store the remaining specimens for future use, unless that requirement is waived by the IRB or the samples have been stripped of identifiers. These are common industry best practices.

How CDC laboratories evaluate the continuing need for, and scientific value of, the collections of specimens in its laboratories:

CDC reference collections are a core component of our mission, unique in the world, and absolutely critical to research in medicine and public health. When assessing archival specimens, we take into consideration a number of factors, including the needs of special patient populations (such as HIV-positive individuals, intensive care unit patients, ethnic populations, and women); novel or emerging agents of disease compared to archival isolates; pathogen discovery; pre-antibiotic era isolates (pre-1945); epidemics or pandemics; confirmation or development of taxonomic additions or changes; and correlation of new isolates to disease. CDC evaluates the value of particular collections based on the uniqueness of the isolate, its potential value in future studies, and especially the quality of supporting data that accompanies the collection. Additionally, the number of external requests for archived samples is another indicator for the need of our collections. These materials are readily available to requestors through Material Transfer Agreements (MTAs) that outline roles and responsibilities of both the provider and recipient. Last year, for example, CDC executed approximately 200 MTAs for materials in our collections.

Collections are only as good as the clinical and epidemiological information available for the specimens. Clinical data can identify specimens from persons with well-defined diseases, or persons well-defined as "healthy" individuals. Some rare collections may represent historical importance documenting the first introduction of a disease caused by a particular strain. For example, our virus collections were critical when CDC responded to the world-wide outbreak of Severe Acute Respiratory Syndrome (SARS) in

2003. Other collections allowed CDC to recognize the agent of Legionnaires' disease in 1977 as a newly defined organism and to trace its origins. Diagnostic tests and laboratory identification procedures developed by CDC are validated using dozens of archived isolates as well as specimens from both normal donors and donors that are identified with specific diseases, such as influenza and respiratory syncytial virus.

Currently most of our laboratories have no uniform protocols in place regarding the destruction of specimen archives. When necessary, destruction occurs only after study and consultation and in a very controlled and documented manner. Indeed, we never want to purposely dispose of rare collections, and it is uncommon that any are destroyed.

The establishment of the CDC and Agency for Toxic Substances and Disease Registry (ATSDR) Specimen Packaging, Inventory and Repository (CASPIR) and its contribution to specimen resource management at the CDC.

In the early 1990's, CDC/ATSDR developed a specimen repository that provides for secure, long-term storage and management of our valuable collections of specimens. The CDC/ATSDR Specimen Packaging, Inventory and Repository (CASPIR) is a significant resource for the management of specimen collections at CDC because it provides archival space not available on the main CDC campus and utilizes a documented management system for these archives.

The roles of CASPIR are to: 1) ensure each collection has a scientific curator who is responsible for the information in the collection and who approves the use of the collection by persons or groups outside of the scientific program that collected the specimens; 2) ensure the quality of the specimens in storage by monitoring freezer

temperatures and responding to alarms caused by temperature changes; 3) provide a single electronic database for the inventory; 4) provide a secure location for the specimens; 5) ensure that when investigators leave CDC, the collection is assigned to another CDC investigator; and 6) facilitate sharing of specimens, associated clinical and epidemiological data, and test results. CASPIR places critical record keeping in the hands of archivists, not busy laboratorians, and thus ensures availability of unique isolates to national and international research

Policies and procedures were developed through a CASPIR Policy Board. These policies include: apportionment of available storage space; admitting specimen collections; cataloging collections; ensuring confidentiality; ensuring data quality; documenting data and specimen sharing; ensuring data security; specimen and data withdrawal and use; additional testing of specimens; human subjects review issues; review of specimen usage and disposal of unwanted specimens; physical security of specimens; and contingency and disaster management. Storage space is allocated to a CDC program based on requests from each program, and space is reapportioned when necessary.

Collections for research are admitted to CASPIR when they meet basic criteria and have the appropriate approvals from CDC's National Center directors or their designees. The mandatory criteria for acceptance include submission of the following information: study design; study sites; duration of the study; study population; and a copy of the informed consent form for the overall study. Additional information needed includes whether epidemiological or clinical data were collected; types and number of specimens collected; types of tests performed directly on the study participants or the

specimens; and contact information for the custodians of the collection. Lastly, each collection must be unique and not redundant of other collection already stored. Individual isolates will be stored in CASPIR only if they are deemed to be unique and cannot be easily recreated.

In addition to this information about the study, there are additional explicit mandatory criteria about the samples themselves for specimens to be deposited to CASPIR. The specimens must be sera, plasma lymphocytes, other body fluids, separated white blood cells, nucleic acids, cultures of microorganisms, or other miscellaneous biologicals. They must be of a certain volume, age, and condition, to ensure that meaningful testing can be performed on the specimen if retrieved at a later date. There also must be sufficient volume of remaining specimen to be of value for testing. When appropriate, the method of specimen collection that was used is included. An important example of this information would be the type of anticoagulant in which the specimen was collected. Sterility and viability must be documented. Finally, the specimens must be in storage vessels appropriate for the proposed storage condition. For example, the use of glass vials is not appropriate unless storage is in a refrigerator.

Detailed information about the collection is necessary for the specimens to be meaningful. This information includes: the name and contact information of the custodian and designated organizational contact if there is a recommendation to discard the collection; a brief description of the project and study design and why the activity led to the collection; information about the source of the specimens; the age and time period of the collection; the geographical location or locations where the specimens were obtained; the study population (e.g., uranium workers in New Mexico); demographic data such as

age, gender, race, and ethnicity; whether the collection was the result of a research project and the consent form used, if available; types of tests performed directly on the study participants or the specimens; and, types, number, and volume of specimens in the collection.

Acceptance of collections requires completing a form with all the information noted above and with written approvals from the appropriate CDC officials. Externally-obtained collections are not accepted into CASPIR unless a National Center shares ownership of the collection and can assist in technical and scientific decisions regarding the use of the collection.

Distribution of specimens from the collection takes into consideration that though the investigators are custodians of the collection, CDC is the ultimate owner. This policy helps to assure that the investment made by CDC to conduct critical studies and analyze valuable specimens will be securely maintained. When collections are accepted into the CASPIR facility, a determination is made as to the availability of the collection for use by those outside of the scientific program that is the custodian. Each National Center must then establish a review process for requests of materials, including a process for assuring that IRB approval is obtained before human specimens will be provided for non-exempt human subjects research. Release of specimens and associated data must be approved by the National Center. There are provisions for appeals of denials of approvals.

All specimen and data bank information is treated in a confidential manner and safeguarded in accordance with the Privacy Act and any other applicable laws, regulations, and policies.

National Centers are required to review the usage of their collections annually to ensure the periodic disposal or transfer of materials that they determine are no longer used or needed. Before disposal or transfer, the appropriate CDC program officials must provide descriptions of the excess specimen collections to other National Centers, institutions, or organizations affiliated with the collection through the Associate Director for Science at CDC. Any disposal or transfer of specimens that can be directly linked back to the study subject must be consistent with what was stated in the consent form. When appropriate approvals are given, the recipient organization becomes the custodian of the collection and assumes responsibility for it. Any destruction of specimens must follow current biosafety guidelines established by CDC and the National Institutes of Health.

Conclusion

In closing, CDC reference collections are a core component of our mission, unique in the world, and absolutely critical to research in medicine and public health. CDC takes its use of and subsequent storage and disposal of specimens seriously. These specimens provide the agency with the ability to not only detect, respond to, and control diseases today but are vital to unraveling tomorrow's unexpected disease crises.

Thank you for the invitation to appear before the Subcommittee to share this information with you about our invaluable specimen archives. I would be happy to answer any questions.