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Harnessing Medical Surveillance Assets to Improve Force Health Protection

The Role of the DoD Serum Repository and the Defense Medical Surveillance System

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PREFACE

For the past twenty years, the Department of Defense has maintained a serum repository and associated database. These have expanded in size and in recent years have been assigned additional mandates and requirements that extend beyond their original purpose related to HIV testing, to serve a broader set of purposes related to deployment health and military force health protection. The Army's Center for Health Promotion and Preventive Medicine (CHPPM) serves as executive agent in managing the DoD Serum Repository (DoDSR) and Defense Medical Surveillance System (DMSS) on behalf of the entire department. As the mandate and value of these resources have grown, there has not been a commensurate systematic assessment of capabilities and untapped opportunities to better fulfill their missions, nor to consider how these might be better positioned to meet the needs of the military of the future. With these considerations in mind, CHPPM commissioned this study, conducted from July 2006 to February 2008, to examine current requirements and capabilities, identify gaps, and suggest strategies to improve the capabilities of these resources to meet current and potential future needs in the areas of surveillance, outbreak investigation, research and clinical support, particularly as these relate to influenza and other infectious disease threats.

This report should be of particular interest to health personnel in DoD, especially military health leaders and planners, those responsible for health surveillance across the services, medical providers, and health researchers. It should also be of interest to the Veterans Health Administration within the Department of Veterans Affairs, the U.S. Congress, which has chartered within statute many of the functions of DoDSR and DMSS, and potentially to civilian health researchers.

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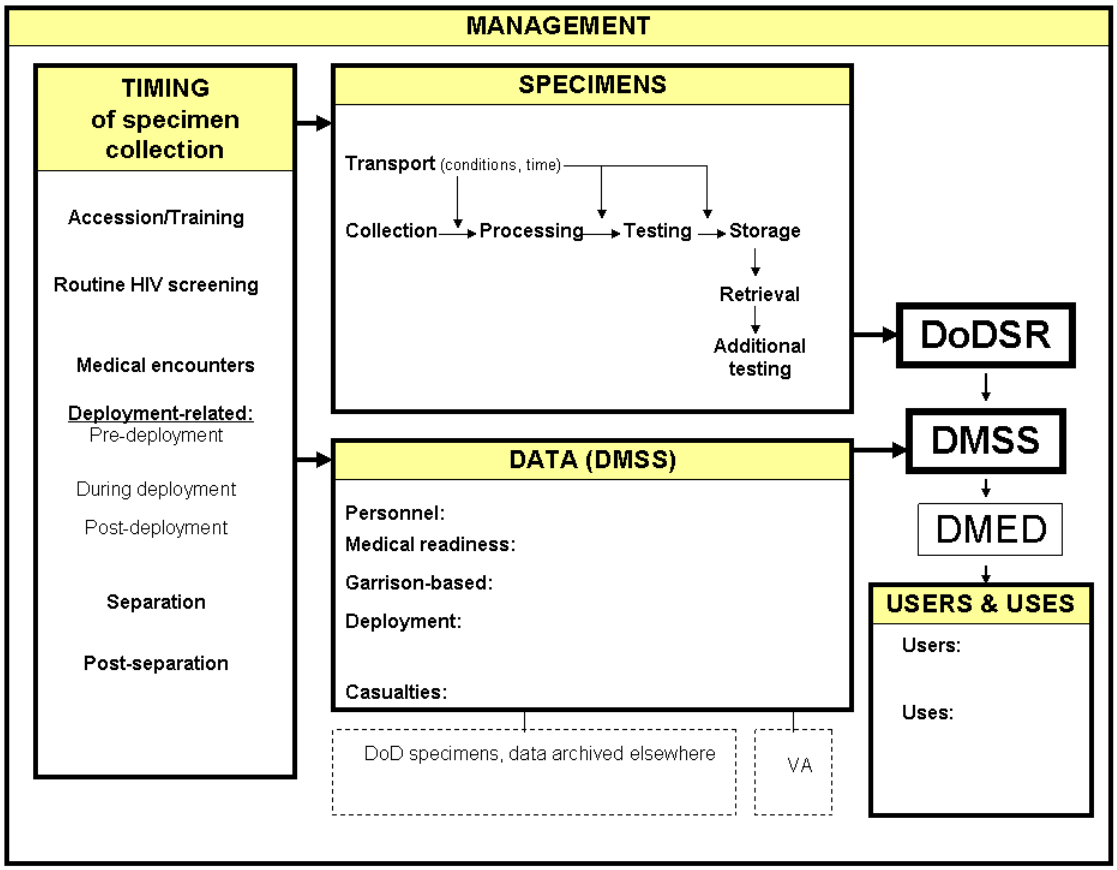
The Department of Defense Serum Repository (DoDSR) and Defense Medical Surveillance System (DMSS) are longstanding and vital assets to U.S. Armed Forces medical surveillance. The repository contains over 43 million serial blood-derived serum specimens from over 10 million military applicants and active duty and reserve service members over the course of their service careers; the DMSS database contains serial health data that can be linked to these specimens. The Army Medical Surveillance Activity (AMSA) manages both of these systems. AMSA recognized that the DoDSR and DMSS have grown in response to evolving military health needs, but their current and full potential use have not been systematically examined. Mindful of this, AMSA asked RAND to assess the DoDSR and DMSS to help identify ways that AMSA management can make them available to meet the health needs of the current and future military as fully as possible.

The DoDSR and the associated DMSS database were originally designed for routine HIV screening purposes, but in recent years they have been assigned additional requirements related to deployment health and the prevention and control of diseases relevant to the military more broadly - Force Health Protection. Over these years, the specimen of convenience to fulfill new requirements has remained serum (the liquid component of blood), with specimens collected for all purposes archived in the DoDSR. With over 43 million serum specimens, the DoDSR is by far the largest serum repository in the country, perhaps the world. The associated DMSS database allows for analyses at a given period of time or over time, and the ability to link such data with serum specimens creates a valuable resource for military health and even the broader civilian community.

This report focuses on the current and potential role of the DoDSR and associated DMSS database to support comprehensive health surveillance - referring to surveillance over the career lifetime of a service member, across all locations, epidemiological investigation, research, and clinical management. It describes current requirements and

capabilities of both systems, identifies issues and gaps, and assesses specific strategies to increase the capabilities of these vital surveillance resources to serve the needs of the U.S. Armed Forces today and into the future. We reviewed DoD policy, doctrine and other published documents as well as published scientific literature, and we interviewed health experts inside and outside DoD to help identify and assess issues and their potential solutions. We also examined a number of other biological specimen repositories to glean insights potentially relevant to the DoDSR. We constructed a conceptual framework to help identify potential improvements to system elements and to organize the collection, analysis and presentation of our data related to these potential improvements (figure S.1).

Figure S.1.
Conceptual Framework to Help Identify Potential Improvements to System Elements



Chapters 1-5 frame the study (Chapter 1), trace the evolution in requirements for the DoDSR and DMSS (Chapter 2), describe DoD's medical surveillance (Chapter 3), describe the current capabilities of AMSA, DoDSR and DMSS (Chapter 4), and then examine other biological specimen repositories to glean insights potentially relevant to DoDSR (Chapter 5). Chapter 6 then draws upon the findings related to current requirements and capabilities and our interviews to present issues and 26 potential improvement strategies organized according to our conceptual framework. We identified potential issues in the following areas:

Management

- Mission (AMSA, DoDSR, DMSS)
- Organizational position
- Consideration of promising new biotechnologies
- Staffing
- Access to specimens
- Protection of human subjects
- Available repository storage space
- DMSS physical infrastructure and back-up
- HIV and other screening

Timing of specimen collection

- Frequency and timing of specimen collection
- Extending specimen collection beyond separation

Specimens

- Variation in specimen processing and transport conditions
- Finite nature of serum specimens
- Freeze-thaw cycles
- Utility of serum and archiving of other blood fractions
- Storage conditions
- Screening beyond HIV

Data

- Data quality and connection issues
- Deployment-related health data
- DMSS links to classified data
- Connection to other military biological specimen collections
- Behavioral risk factor data
- Access to DMSS

Use

- Level of demand for serum specimens
- Perceived reasons for under-utilization of DoDSR
- Access to specimens

Chapter 7 presents our recommendations, which reflect thematic packages of the strategies developed to address these issues:

1. CLARIFY AND COMMUNICATE THE MISSIONS OF DoDSR, DMSS AND AMSA BOTH WITHIN AND BEYOND DoD

There is a mismatch between Congressional direction for the use of the DoDSR and the DMSS data system as articulated in several enactments of the National Defense Authorization Act and the articulation of the mission and use of the DoDSR and DMSS by AMSA. Clear articulation by military policy makers and a common understanding by AMSA managers and DoDSR and DMSS users of the full range of uses for these resources – including surveillance, epidemiologic investigation, clinical management, and research related to both infectious and non-communicable diseases - should lead to their more efficient use within DoD. Further, the mission of DoDSR and DMSS to collect specimens and data could also extend beyond DoD active and reserve populations to include continuation of data and specimen collection on a voluntary basis from separated service members followed in Military Treatment Facilities and/or the Veterans Administration health system. To harness the full potential of the DoDSR and DMSS resources, the full range of mission areas for these resources and their organizational oversight must be made explicit and communicated widely across DoD and into related research and epidemiologic communities.

2. EMPOWER, STRUCTURE, AND RESOURCE THE ORGANIZATIONAL OVERSIGHT OF DoDSR AND DMSS SO THAT THEY CAN FULFILL THE FULL RANGE OF MISSIONS

DoD officially established the Armed Forces Health Surveillance Center (AFHSC) within CHPPM in late February 2008. This organization is intended to encompass and integrate DoD-wide health surveillance. We recommend that the AFHSC be organizationally situated, empowered, and resourced to connect the various experts, contracts, and systems that are required not only for its primary surveillance mission but also for the full range of uses (primarily within the military but also extending to the civilian community) for the DoDSR and DMSS resources it manages

through its Executive Agency function, including surveillance, epidemiologic investigation, clinical management and research. The chain of command and oversight for this organization should be such that it can receive guidance and resources from policy makers responsible for all of these functions, e.g., the ASD(HA), Surgeons General and Army Medical Research and Materiel Command, in order to ensure proper alignment with current Military Health System strategy and resources and medical research and service health priorities. The AFHSC should be configured and staffed to provide the support needed by all users, and especially those within the DoD, supporting execution of its various missions.

3. CREATE AN INTEGRATIVE DATA PLAN FOR COMPREHENSIVE HEALTH SURVEILLANCE

Ideally, AFHSC should create an overarching and comprehensive data plan prescribing integration of all relevant heath surveillance data. Such a plan should address issues such as connectivity to occupational and environmental health surveillance systems, both within the garrison and deployed settings, increasing data collection along the service member's period of service and beyond, and fully realizing policy efforts to facilitate access to surveillance and other data by the VA. Regarding DMSS specifically, several relevant military health data sets remain unconnected, thus limiting the full execution of AMSA's surveillance mission and limiting the ability of DoD more broadly to take advantage of the full value offered by DMSS. The highest priorities for new data linkages into DMSS relate to deployment health, especially data derived from deployed settings. Current issues related to classified data systems also need to be overcome. We understand that relevant health surveillance data can possibly be made available to DMSS via the unclassified Theater Medical Data Store. For data that cannot be made available via this system, options for linking classified data into DMSS include time-delayed incorporation of declassified location data or near-real time incorporation of classified data, which would require new secure communications capabilities that DMSS currently does not possess.

Other relevant data linkages to consider are to existing DoD biological specimen archives such as isolates and original nasal swab specimens from the DoD Febrile Respiratory Illness surveillance system and pathology and necropsy specimens maintained by the Armed Forces Institute of Pathology. More robust linkages in both directions between DMSS and the VA health system should also be considered, to the extent that the mission of DoDSR and DMSS are expanded beyond strictly active duty and reserve populations. Also, consideration should be given to whether and how behavioral risk factor data should be collected and fed into DMSS. Because there are many current data sources which might be tapped for deployment health surveillance, and there may be more in the future, the new AFHSC would be better positioned to fully execute its mission if it were included in the Military Health System information requirements process currently managed at the Tricare Management Agency.

In addition to DMSS data content and management is the need for better protection of its physical infrastructure and the integrity of the data themselves, i.e., to resist physical or cyber threats to the DMSS database. In addition to assuring adequate housing of the data system, we recommend that strong consideration be given to systematic and frequent off-site back up and even parallel mirroring of the DMSS database, to assure its integrity in response to any threat that may arise, as occurred in late January 2008.

4. ENHANCE THE UTILITY OF SPECIMENS

The DoDSR serum specimens continue to serve well their original purpose of HIV serosurveillance. However, as early as 1997, the DoD made a decision to use serum as the tissue of convenience for deployment health surveillance. The sera permit examination of deployment-related exposures to and investigations of infectious agents; they are not particularly useful for time-sensitive environmental exposures for which biomarkers are only fleetingly present. And, as military health research becomes broader and more technologically sophisticated, the limitations of current serum specimens become more apparent: Researchers increasingly recognize the importance of genetic material for current

and future research into a range of acute and chronic conditions. Serum specimens as presently stored in the DoDSR at -30°C do not reliably preserve genetic material. The best way to do this is to archive specimens derived from whole blood specimens, e.g., stored in liquid form or as dried blood spots, or storage of buffy coat fractions (see description in Chapter 5) in which the quantity of genetic material is substantially greater. Storage requirements for dried blood spots are modest and incrementally the easiest. Storage of both plasma and buffy coat at -80°C reflects current best industry practices for preservation of genetic material and other relevant blood-derived analytes. However, adoption of this alternative would mean costly new repository requirements for future specimens, i.e., walk-in freezers would not be possible for storage at -80°C. Nonetheless, the near-term expiration of the current repository lease and potential relocation provides a timely opportunity for military leadership to think carefully about the needs of the military health system into future and determine whether new kinds of specimens should be archived, to better serve a broader range of mission areas for this valuable military resource.

5. RAISE AWARENESS OF AND EXPAND ACCESS TO DoDSR AND DMSS

The use of DoDSR and DMSS resources may be limited because of limited awareness across DoD. For example, military clinicians are apparently largely unaware of these resources in support of clinical management. Broad or targeted "educational campaigns" could be undertaken to raise awareness and use of DoDSR and DMSS. Access also may have been limited because of perceived lack of fully transparent criteria for release of specimens. A remedy for this could include development and dissemination of updated and transparent criteria and procedures for accessing DoDSR specimens and DMSS data. In terms of expanding use, the first priority should probably be for military health users within DoD, followed by more robust use by the VA. DoD should carefully consider whether and how to expand use to civilian researchers, while protecting individual privacy, the overall military health mission, and availability of remaining specimens as more users

draw down the number aliquots from a given specimen. Finally, efforts should be made to take better advantage of the longitudinal nature of the DoDSR inventory, e.g., through clarifying the legitimate use of DoDSR for research and sensitizing military health researchers to the availability of these serial specimens and linked data.

6. PLAN FOR THE NEXT REPOSITORY FACILITY

Finally, depending on decisions related to the preceding recommendations, DoD should begin to define the requirements for the next repository, following expiration of the current lease in 2010. Factors to take into consideration include the time horizon for the next repository (e.g., 20 years or more), the annual rate of specimen acquisition (which would increase if specimens are to be collected from members following separation), the types of specimen to be archived (e.g., serum or plasma, buffy coat, whole blood in liquid form or as dried blood spots), and desired storage temperature (e.g., -30°C or -80°C). All of these influence the size and configuration of the future repository and hence the requirements for future repository space.

CONCLUSIONS

The goal of this study was to help identify opportunities to make even better use of DoDSR and DMSS resources in addressing military health needs now and into the future. Our analyses uncovered specific opportunities to better fulfill current requirements, especially to close gaps in the content and efficiency of medical surveillance. The largest gap relates to data from deployed settings, which figures prominently within the strategies we describe in the report and our recommendations. Beyond surveillance, we have also identified specific ways to position the DoDSR and DMSS resources to better serve the military of the future -- planning now for changes that will permit a wider range of uses to improve not only surveillance but also clinical management and research in support of Force Health Protection. Taken as a whole, our recommendations suggest that the DoDSR and DMSS could benefit from improved oversight and management to ensure they function

within the strategic goals of the Military Health System, and have access to the needed data systems as well as other resources they need to fulfill their mission. There are key decisions that need to be made at the Undersecretary of Defense level which will cascade across the recommendations we offer here, affecting the direction of the decisions as well as the magnitude of change.

AMSA has been a responsible custodian for the DoDSR and DMSS, characterized by multiple interviewees as "national treasures" whose full potential has yet to be fully harnessed. Creation of the new AFHSC and relocation of the repository offer the opportunity to consider how the DoDSR and DMSS resources can be used to even greater advantage to support military health now and into the future. This study took a systematic approach to analysis of current characteristics and opportunities for improvement. Some of our recommendations are relatively easy, while others are more ambitious. Nonetheless, we feel that implementation of all of these recommendations will allow the AFHSC to better fulfill its current requirements, serve a broader range of legitimate mission areas, and position the DoDSR and DMSS resources for valuable service well into the future.

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GLOSSARY, LIST OF SYMBOLS, ETC.

Symbol	Definition
AFEB	Armed Forces Epidemiology Board
AFHSC	Armed Forces Health Surveillance Center
AFIOH	Air Force Institute of Operational health
AFIP	Armed Forces Institute of Pathology
AHLTA	Armed Forces Health Longitudinal Technology Application
AMSA	Army Medical Surveillance Activity
ASD(HA)	Assistant Secretary of Defense (Health Affairs)
CDC	Centers for Disease Control and Prevention
CHPPM	Center for Health Promotion and Preventive Medicine
COCOM	Combatant Command
CONUS	Continental United States
DBS	Dried Blood Spots
DEDS	Directorate of Epidemiology and Disease Surveillance within CHPPM
DEERS	Defense Enrollment Eligibility Reporting System
DMED	Defense Medical Epidemiology Database
DMSS	Defense Medical Surveillance System
DNA	Deoxyribonucleic acid
DNBI	Disease and Non-Battle Injury
DoD	Department of Defense
DoDSR	Department of Defense Serum Repository
ESSENCE	Electronic Surveillance System for the Early Notification of Community-Based Epidemics
FHP	Force Health Protection (Policy)
FHP&R	Force Health Protection and Readiness (Division of ASD (HA))
FY	Fiscal Year
GEIS	Global Emerging Infections Surveillance and Response System
HIV	Human Immunodeficiency Virus
ICD-9	International Classification of Diseases, Ninth Revision
IMR	Individual Medical Readiness
IQR	Inter-Quartile Range
IRB	Institutional Review Board
JMeWS	Joint Medical Workstation
JPTA	Joint Patient Tracker Application
MEPS	Military Entrance Processing Stations

Symbol	Definition
MILVAX	Military Vaccine Agency
MRMC	Medical Research and Materiel Command
MSMR	Medical Surveillance Monthly Report
MTF	Military Treatment Facility
NDAA	National Defense Authorization Act
NEHC	Navy Environmental Health Center
NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
NHRC	Navy Health Research Center
NIPRNET	Non-Classified Internet Protocol Router Network (now known as Unclassified but Sensitive Internet Protocol Router Network)
OCONUS	Outside of Continental United States
PDTS	Pharmacy Data Transaction Services
RBC	Red blood cells
RNA	Ribonucleic acid
SIPRNET	Secret Internet Protocol Router Network
SRSV	Secure Robotized Sample Vault
SSN	Social Security Number
TMIP	Theater Medical Information Program
TMDS	Theater Medical Data Store
CHPPM	US Army Center for Health Promotion and Preventive Medicine
VA	Department of Veterans Affairs
WBC	White blood cells
WRAIR	Walter Reed Army Institute of Research

AN IMPORTANT NOTE ABOUT TERMINOLOGY

On February 26, 2008, the Deputy Secretary of Defense issued a memorandum officially establishing the Armed Forces Health Surveillance Center (AFHSC). Based on documents obtained by the RAND study team on February 28, the Center had been in the planning stages since at least September 2005. In anticipation of its imminent formal establishment, the Army Surgeon General's office established a Provisional AFHSC in October 2007, combining two extant organizations: the Army Medical Surveillance Agency (AMSA) and the Global Emerging Infections System (GEIS). Both AMSA and GEIS are described in some detail in this report, and AMSA is in fact the focus of the report. Formalization of this new center occurred at the very end of this study. Because the new Center combines two organizations, and because our study is in fact focused on AMSA, we have used the term AMSA throughout this report to refer to the portion of the new center that contains those activities traditionally performed by AMSA. Specifically, we are referring to the activities and responsibilities that involve management of the DoD Serum Repository and the Defense Medical Surveillance System.

In this report we use three key terms as defined by DoD directives. All three describe population health. "Medical surveillance" as established by DoDD 6490.02E (October 21, 2004) is the collection, analysis and reporting of data resulting from medical care or medical evaluation. "Health surveillance," as defined by the same directive, includes medical surveillance plus occupational and environmental health surveillance. DoD also defines the term "comprehensive military health surveillance" to mean "health surveillance conducted throughout Service members' military careers, across all duty locations, and encompassing risk, intervention, and outcome data" (DoDD 6490.02E, October 21, 2004, para 3.1). While not officially defined by DoD, we usually use the term "deployment health surveillance" to mean "health surveillance" related to deployment, including garrison-based pre- and post-deployment data plus data arising from a deployed setting. When relevant, we are explicit in distinguishing between these two settings.

CHAPTER 1. INTRODUCTION

Protecting the health of military personnel is a strategic component of operational readiness. Force health protection is built upon a foundation of both individual medical care and public health services. In the public health area, the Department of Defense (DoD) provides preventive health services, monitors the health of its members using epidemiological surveillance, and, in the event of a disease outbreak, conducts disease investigation and response. Public health surveillance — i.e., the collection, analysis, and interpretation of health-related data and the dissemination of that information to monitor the health of a population and identify potential risks to health — is particularly important in deployed environments, where surveillance is used to inform operational readiness, track disease and injury, and permit examination of linkages between environmental exposures and health outcomes. Health data are critical to these activities and to ensuring the continuity of medical care over service members' careers.

Over the past 20 years, the DoD has collected blood specimens from both military members and applicants for service, and these specimens and related data have been stored in the DoD Serum Repository (DoDSR) and Defense Medical Surveillance System (DMSS), respectively. The repository currently contains over 43 million specimens taken from more than 10 million active duty and reserve service members of the Army, Navy, Air Force, and Marines, and applicants to these services. The DMSS contains data linked to these specimens. The DoDSR and DMSS are both managed by the Army Medical Surveillance Activity (AMSA).

Although routine collection of blood specimens was first mandated in 1985 to track the virus now known as HIV (with serum remaining after the tests retained in storage), the DoDSR has expanded in size and scope in recent years and is now intended to provide information about a number of deployment-related health issues and, more broadly, the identification, prevention, and control of disease associated with military service. DoDSR and DMSS can provide specimens and population-based information to the surveillance centers in other services as well

as policymakers and researchers, and can also provide individual specimens and data to clinicians for medical management purposes. Since 1997, an important component of deployment health surveillance has been routine pre- and post-deployment health assessment and associated collection of blood specimens that are ultimately archived in the DoDSR for potential future testing.

However, while the mission and requirements of the DODSR and DMSS have expanded, there has not been a commensurate systematic effort to assess how these resources are being managed and used, and whether there are opportunities for improvement in these areas. Therefore, AMSA asked the RAND Corporation to undertake a systematic examination of DODSR and DMSS to help identify ways in which AMSA can make these resources available to meet the current and future health needs of the military as fully as possible.

This report focuses on the current and potential role of the DoDSR and associated DMSS database to support comprehensive health surveillance, epidemiological investigation, research, and clinical management. It describes current requirements and capabilities of both systems, identifies issues and gaps, and assesses specific strategies to increase the capabilities of these vital surveillance resources to serve the needs of the U.S. Armed Forces today and into the future.

PURPOSE AND SCOPE OF RAND STUDY

The purpose of this study is to examine the current capabilities of the DoDSR and associated DMSS database in the areas of surveillance, epidemiologic investigation, research and clinical support and to identify opportunities for improvement. To do this, we addressed five research questions:

- What are current requirements for collection and use of DoDSR specimens and DMSS data?
- What capabilities do the DoDSR and DMSS have to meet these requirements?
- How are the DoDSR and DMSS currently used?

- What are the gaps between current capabilities and current and potential future needs?
- What are strategies for improving capabilities to meet future needs?

We focused our examination of DoDSR and DMSS on consideration of:

- Blood and constituent components of potential use in surveillance, epidemiologic investigation, research and clinical support;
- Infectious disease agents, as well as DNA and RNA, as the main target for testing from blood-derived specimens;
- Existing military data systems that could potentially be linked to DMSS; and
- Existing DoD policy, supporting programs and legacy practices.

METHODS

To answer the research questions, we first analyzed current policies and practices in military surveillance (Chapters 2 and 3), and examined current capabilities of the DoDSR, DMSS, and AMSA (Chapter 4) as well as uses of other biological specimen repositories (Chapter 5). We then compared the current capabilities of DoDSR and DMSS to current and potential future requirements, identified gaps, and suggest priorities for action to close gaps and enhance the utility of these resources in surveillance, epidemiologic investigation, research and clinical support (Chapters 6 and 7).

The identification and assessment of opportunities for improving the capabilities and use of DoDSR and DMSS are based on the following:

- Review of DoD policy, doctrine and other official documents;
- Review of peer-reviewed journal literature and written descriptions of relevant civilian repository programs;
- Comparative analysis of the DoDSR relative to other selected military and civilian biological specimen repositories;

- Interviews with DoD health leadership, other military health experts and other relevant DoD program staff, and civilian health experts; and
- Development of a RAND conceptual framework to guide identification of potential improvements in DoDSR and DMSS system elements and to organize information collection, analysis and presentation (see Chapter 6).

ORGANIZATION OF THIS REPORT

This report is organized as follows. Chapter 2 describes the evolving requirements for DoDSR and DMSS, while Chapter 3 describes selected military medical surveillance systems and organizations responsible for medical and broader health surveillance, to provide a context for the systems that currently do, or could, be linked to DMSS. Chapter 4 describes the current capabilities of AMSA, DoDSR and DMSS. Chapter 5 examines other biological specimen repositories in order to seek insights that may be pertinent to decisions regarding DoDSR.

Chapter 6 then presents a conceptual framework that is used to identify issues, and describes potential strategies to close gaps between requirements and current capabilities and to increase the capabilities of DoDSR and DMSS to meet new needs into the future. Chapter 7 concludes with a description of six overarching recommendations derived from our analyses.

CHAPTER 2. EVOLUTION OF DODSR AND DMSS REQUIREMENTS

In order to evaluate how well the DoDSR and DMSS are able to meet current and future requirements, we need first to understand what those requirements are and how they have evolved since the DoDSR was first created in 1985. This information, together with an understanding of current medical surveillance systems and organizations (Chapter 3), current capabilities of DoDSR and DMSS (Chapter 4), and uses of other biologic serum repositories (Chapter 5) establish the basis for the assessment of existing gaps and identification of potential improvement strategies (Chapters 6 and 7).

We begin by discussing the current mission of the DoDSR and DMSS and the way in which the requirements have evolved over time. Figure 2.1 presented below depicts the main highlights of this evolution, and Appendix 1 presents a more detailed summary of the requirements as they have evolved. We also discuss aspects of DoD's vision for the repository and ways in which its role was intended to develop.

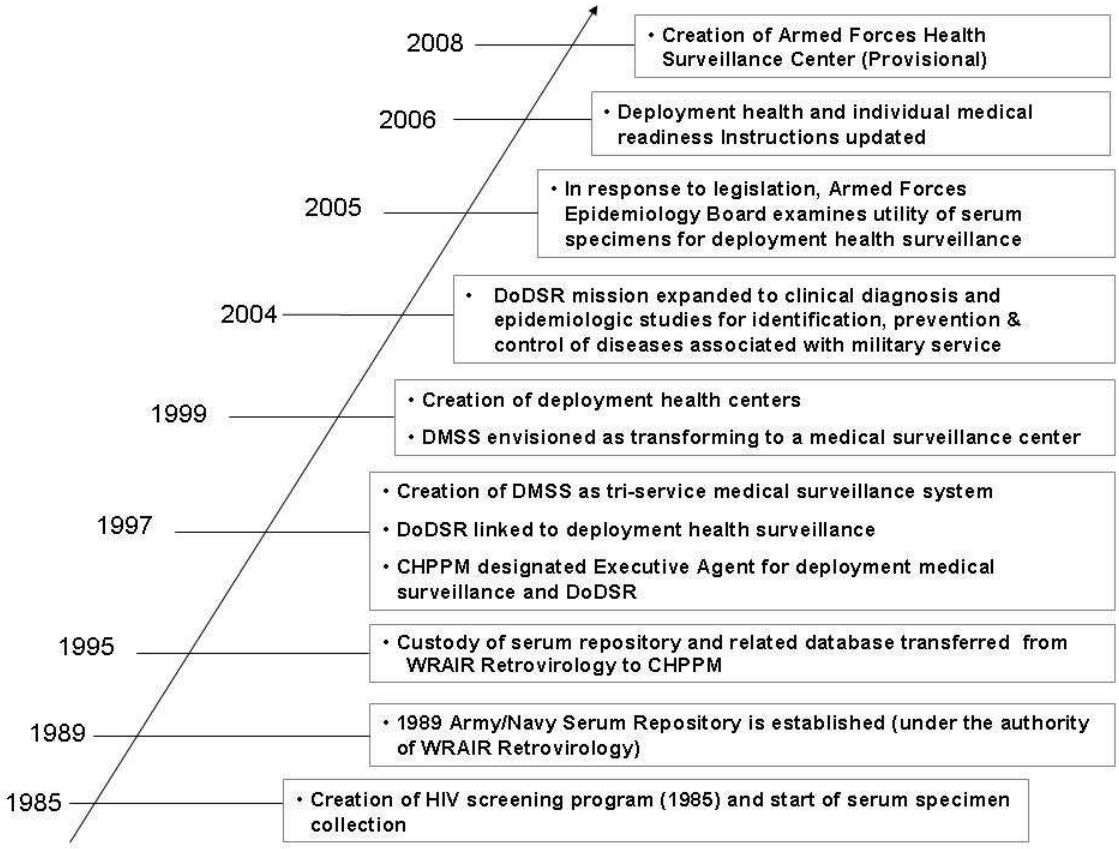
EVOLVING MISSION AND USES OF THE DODSR

The current mission of the DoDSR is to provide support for the identification, prevention, and control of disease related to military service. (DoDD 6490.02E, October 21, 2004) The mission of the DMSS is to serve as a tri-service medical surveillance system.

The uses of the repository have shifted, however. The DoDSR was initially conceived as a resource for routine HIV screening. It subsequently was defined as a resource for deployment health surveillance, and later for the broader purpose of identifying, preventing, and controlling disease associated with all military service.

We describe highlights from this evolution in the following sub-sections. An overview of the main steps in the evolution is shown in Figure 2.1.

Figure 2.1.
Evolution of DoDSR, DMSS and Organizational Requirements



Origins in HIV Screening Program

The serum collection currently maintained in the DoDSR and managed by AMSA started in 1985 as part of the Army's HTLV-III screening program (ASD(HA), December 5, 1985), which began in response to the spread of a new human virus subsequently known as the Human Immunodeficiency Virus (HIV). DoD instituted mandatory collection of blood specimens for screening of all civilian applicants going through Military Entrance Processing Stations.[6] Actual collection and storage of remnant serum occurred as part of contracts between DoD and commercial testing laboratories in which all non-reactive serologic specimens were ordered to remain in frozen storage for the duration of the contract. Although these disparate collections of serum, which would ultimately seed the DoDSR inventory, were stored by the DoD contractors, a specified purpose

for their future use had not been officially articulated. In 1989, a maintenance and management contract was awarded to McKesson to begin consolidating and storing in a single facility the serum specimens that were stored by testing contractors, who had been conducting HIV screening for the DoD since 1985. Under the authority of WRAIR Retrovirology, this contract gave way to the establishment of the Army/Navy Serum Repository, the predecessor to the DoDSR. By 1990, the contractor processing the HIV specimens had collected and stored over six million serum specimens.

The first officially articulated purpose of the repository was documented in a 1991 Army request for proposals to create and maintain the Walter Reed Army Serum Bank Repository: "Sera repository operations are required for retrospective studies in support of current and future retroviral research efforts… Analysis of these sera will be very important." The Department of Retrovirology would require as-needed specimen retrieval up to about 5,000 per year (RFP, DAMD17-90-0181, p5-7).

By 1996, the repository had collected and stored over 17 million serum specimens from Army and Navy civilian applicants as well as from active component service members (Institute of Medicine, 1996). Together with the linked medical information stored in the U.S. Army HIV Data System, the military had developed a rich resource for conducting robust retrospective studies.

Along with the creation of the serum repository, the Army created a data center in 1986 within the Walter Reed Army Institute of Research Division of Preventive Medicine to support HIV-related screening, care, and research activities (Rubertone and Brundage, December 2002). In 1995 the system was transferred to the Army's Center for Health Promotion and Preventive Medicine (CHPPM) and called the Army Medical Surveillance System. (Dr. Rubertone, personal communication, 7 January 2007)

Emergence of Deployment Health Surveillance Requirements

Later in the 1990s, the serum repository was assigned an additional mission related to deployment health, and AMSA was designated

as executive agent responsible for management of the repository and associated data system on behalf of DoD. Many service members returning from the first Gulf War reported illnesses of unknown origin, and many questioned the DoD's commitment to providing health care for military members and veterans. The issues were so serious that in the decade after the war, DoD sought to determine not only the etiology of the illnesses and appropriate treatments, but also sought to establish systems that would ~~.~~assure adequate health data captures in future deployments. This was important because the medical records of deployed Gulf War service members were not adequate either to substantiate or refute the exposures being reported. Public concern was so great that even as late as 2000, the Institute of Medicine published a report criticizing the DoD for not adequately addressing the concerns that had been raised and urging DoD to take "immediate action" to repair the data deficiencies in the medical records of service members(Institute of Medicine, Protecting Those Who Serve, National Academy Press, 2000, page 2, accessed 20 Feb at: http://www.nap.edu/openbook.php?isbn=0309071895).

In response to the concerns over multiple unexplained symptoms reported by Gulf War veterans, also called Gulf War Syndrome, in 1997 Congress mandated that DoD conduct comprehensive health surveillance on service members who deploy overseas (Public Law 105-85, November 1997). In particular, the law required DoD to collect blood specimens before and after military deployments. It also stipulated that DoD maintain a central archive of records and make them accessible across DoD.

Nearly simultaneously, DoD issued new policy related to joint medical surveillance (DoDD 6490.2, August 30, 1997, and DoDI 6490.3, August 7, 1997, see figure 2.1). These policy issuances designated CHPPM as executive agent for deployment medical surveillance and for maintenance of a DoD-wide serum repository whose purpose was "medical surveillance for clinical diagnosis and epidemiologic studies. The repository shall be used exclusively for the identification, prevention and control of diseases associated with operational deployments of military personnel" (DoDD 6490.2, August, 30, 1997, para D7). CHPPM was

also directed to "maintain a medical surveillance system to integrate, analyze, and report data from multiple sources relevant to the health and readiness of military personnel" (DoDI 6490.3, August 7, 1997, para E7); the services, components and COCOMs were mandated to report data to CHPPM.

It is important to note that the serum repository, which had originally been established in response to then-available technology for HIV screening, was simply expanded to also serve as a deployment health surveillance tool, with the serum remaining the specimen of convenience to meet this new requirement. It is also important to note that the 1997 policy appears to limit the use of the serum repository to deployment-related health. These points had many implications, which we will examine in some detail later in this report.

Also in 1997, the ASD(HA) called for the creation of a tri-service medical surveillance system; this became the DMSS at CHPPM.[1] Also at this same time, the Army's Medical Surveillance System changed its name to be the DMSS and was moved from being managed directly by CHPPM to being managed by AMSA, a subordinate agency of CHPPM. (Rubertone and Brundage, December 2002).

Vision for All-Theater Medical Surveillance and Data Collection. In 1998, the Assistant Secretary of Defense for Health Affairs (ASD(HA)) issued a policy memorandum which established that a pre- and post-deployment blood specimen collection (mandated by the NDAA of FY98) could be met by routine participation in the HIV screening program, as long as the pre-deployment specimen was collected within 12 months of the start of the deployment (ASD(HA), October 6, 1998).

In further response to the health problems experienced by the veterans of the first Gulf War, Congress passed the NDAA for FY99 (Public Law 105-261, October 1998), which authorized the Secretary of Defense to establish a center for deployment health in which

[1] We were unable to find the source document, but were able to find reference to it in an ASD(HA) Memorandum from September 30, 1999 which we describe in more detail below.

longitudinal health data would be collected and studied in order to assess the effect of deployment on service members (section 743).

Because of this legislation, the ASD(HA) issued a key policy memorandum in 1999 that established two centers for deployment health – the Deployment Health Clinical Center within the Walter Reed Army Medical Center and the Deployment Health Research Center within the Naval Health Research Center - and specified that the DMSS would serve as the "comprehensive, longitudinal, relational, epidemiology database" for the study of deployment-related health (see Figure 2.1). This memorandum explicitly calls for "all theater medical surveillance and treatment data collected by the Services, Unified and Specified Commands and individual commands…(to be) forwarded to the DMSS." Finally, it stipulates that the "TRICARE Management Activity will provide unrestricted access to applicable Military Health System data and support the DMSS…as appropriate."(ASD(HA), September 30, 1999, all cites from para 6). The same memorandum provides a concept for changing the DMSS into a "DoD Medical Surveillance Agency" that would function as the DoD's deployment health surveillance center (Concept of Operations attachment).

The concept for the future of DMSS was that it would provide access to deployment-related health data and allow for DoD-wide surveillance and research. CHPPM was designated as the DoD repository for all theater medical surveillance data, as described above, and AMSA was described as "the sole link between the DoD Serum Repository and other databases." (ASD(HA) Concept of Operations Document,1999). And finally, DMSS was directed to provide remote access to personnel and health surveillance data to the Navy Health Research Center (NHRC) and other related service surveillance organizations. As we describe in later chapters of this report, not all the provisions of this memorandum were executed.

Therefore, by the end of FY99, DoD had established a deployment-related health surveillance system with the goal of determining the health effects of deployment; established three deployment health centers, each with a distinct deployment-health mission (clinical, research, surveillance); and established a data system in order to

assess deployment-related health data. Most of the major ground work for deployment health surveillance was begun.

Effect of the Global War on Terror. The operations in Afghanistan and Iraq created new demands related to medical surveillance and deployment health surveillance, and these played out in the modifications to the required deployment health assessment forms (DD Forms 2595 and 2596), in the expansion of the surveillance program to cover certain reserve component populations, and in development of quality assurance programs. Importantly, in 2001, ASD(HA) issued a policy memorandum that applied all deployment-related health assessment requirements and specimen collection requirements to the reserve component service members who were activated for 30 days or more. This memorandum stipulated that all pre- and post-deployment health assessment forms (DD Form 2795, and DD2796 respectively) be sent to AMSA and stipulated the content of the forms by providing examples within the memorandum which were mandated across services. Further policy issuances updated procedures for deployment health surveillance and readiness (JCS MCM-0006-002, 2002), enhanced post-deployment assessments (USD(P&R), April 22, 2003), and new requirements for the electronic transmission and capture of pre- and post-deployment health assessment forms (ASD(HA), May 21, 2004).

Broadening of Mission Beyond Deployment Health

The mission and requirements for DoDSR expanded further beginning in 2004, when the use of the repository was broadened beyond exclusive use for deployment-related health to encompass all uses for the prevention and control of diseases associated with military service. This began when DoD issued a major policy document in 2004 describing the overarching guidelines and goals for Force Health Protection within the military health system (DoDD 6200.04, October 9, 2004). This document lays out requirements for annual health assessments, as well as annual assessments of individual medical readiness. Individual medical readiness standards are applied to each individual service member to ensure their ability to deploy worldwide, and are further described in Chapter 3.

Less than two weeks later, DoD issued new policy on Comprehensive Health Surveillance (DoDD 6490.02E, October 21, 2004), updating the 1997 issuance on joint medical surveillance (see Figure 2.1). The 2004 policy document described a broader mission for the repository:

> *4.12 "There shall be a Department of Defense Serum Repository for medical surveillance for clinical diagnosis and epidemiologic studies. The repository shall be used for the identification, prevention and control of disease associated with military service.*

The 2004 comprehensive health surveillance issuance establishes DoD policy to conduct health surveillance across service members' careers, in all duty locations and across the full spectrum of activities encountered within the military. It requires daily review of battle injuries and disease and non-battle injuries in order to detect any health threats; it directs biological monitoring as required; and it directs that tri-service reportable medical events be reported electronically, although neither the reporting system nor reporting destination is specified. That is, the policy directs collection of such data but does not explicitly link this to DMSS. The comprehensive health surveillance issuance also requires the synchronization of data between medical and personnel systems and directs that health surveillance data be transferred to the Department of Veterans Affairs once a service member separates from the service.

In sum, by 2004, the mission and requirements related to DoDSR had evolved beyond simply HIV screening and deployment health surveillance to also include a broader range of purposes - medical surveillance, clinical diagnoses, and epidemiologic studies for diseases associated with military service, i.e., not strictly limited to deployment health surveillance.

Growing Concern About DoD's Ability to Track and Assess Deployment Health Data

By 2005, the Global War on Terror was four years underway and record numbers of reserve component deployments supplemented high levels of active component deployments. Congress in 2005 again addressed the issue of deployment health surveillance. The NDAA of FY05 indicated growing congressional concern with the DoD's ability to track and assess deployment health data, especially data from theater, given the high levels of deployments and complex nature of the contingencies in Iraq and Afghanistan. In particular, the NDAA for 2005:

- required the Secretary of Defense to ensure interim standards that blood specimens needed for the pre-deployment examination of a service member be drawn no later than 120 days prior to the date of the deployment, and that the post-deployment specimens be drawn no later than 30 days after the conclusion of the deployment. (Section 734);
- required DoD to maintain a medical record of all care provided to service members in theater as part of a complete health record;
- required the evaluation of medical tracking and health surveillance in-theater systems with a report due back to Congress within a year. The evaluation was to establish "the efficacy of health surveillance as a means of detecting (i) any health problems (including mental health conditions) of members of the Armed Forces...; and (ii) exposures of assessed members to environmental hazards that potentially lead to future health problems."(para B). Further, Congress required the evaluation to address how the data system could support future research on health issues, to make recommendations for changes to medical tracking and health surveillance systems, and to provide a summary of scientific literature on blood sampling procedures used for detecting and identifying exposures (paras C-E). Congress also asked DoD to determine in this same evaluation whether a need existed for "changes to regulations and standards for drawing blood specimens for effective tracking and health surveillance of the medical conditions of personnel before deployment, upon the

end of deployment, and for a follow up period of appropriate length."(para F);

- required DoD to prescribe a policy on the collection and dissemination of in-theater individual personnel locations, (Section 734, para d);
- required DoD to review and revise the classification levels of data for the use of monitoring and assessing the health tracking and surveillance data in order to make the data more useful.(Section 735).

While deployment health surveillance and medical surveillance, epidemiology and clinical support are not mutually exclusive, it is clear that Congress' interest in assuring that the DoDSR and DMSS met all key needs as a deployment health surveillance tool. Yet neither Congress nor DoD explicitly specified DMSS as the destination for theater medical surveillance data.

Potential Need for Changes in the Process of Drawing Blood Samples. In addition, the NDAA requires the DoD to examine the need for any changes related to the process of drawing blood specimens for effective deployment health surveillance. In order to conduct the evaluation required by Congress, the ASD(HA) requested a study from the Armed Forces Epidemiology Board (ASD/HA January 2005), posing three questions:

- Is there was a sound basis for the continued routine collection of sera pre- and post-deployment for clinical care reasons, public health surveillance or research purposes in order to examine the effects of deployment on health?
- Should any other biological specimens be collected for clinical care reasons, public health surveillance, or research purposes?
- Are there were any valid reasons to change the time frames of specimens of collected biological specimens either pre- or post-deployment for clinical care reasons, public health surveillance, or research purposes?

The study reached four conclusions (Armed Forces Epidemiology Board, April 2005). First, it concluded that there were medically valid reasons to continue the collection of serum specimens for all purposes. Next, the study concluded that there is utility in collecting baseline and periodic blood specimens consisting of serum and white blood cells. Going further, the study suggested that DoD should formalize in rules and procedures and make more clear the accessibility of the repository, to ensure wide access, and that an oversight panel be created to govern access. Finally, the study concluded that sampling of the entire deploying military force, as opposed to a smaller sample of the deploying population, was also appropriate for the purposes of deployment health surveillance, and that the one-year pre-deployment, and 30 day post-deployment collection windows were appropriate.

As provided for in the NDAA FY05, the ASD(HA) changed the legislated interim standards for pre- and post-deployment serum collection per the recommendations of the Armed Forces Epidemiology Board, allowing pre-deployment serum specimens to be collected within 365 days of deployment under routine HIV sampling, unless some reason would indicate a more proximate collection, and post-deployment serum collection within 30 days after arrival at a demobilization site or home station or in-patient medical treatment facility in the case of evacuees (ASD(HA), March 14, 2006).

Establishment of Policy on Individual Medical Readiness. As the conflict in Iraq changed from a major combat operation to a counter-insurgency operation, veterans began to return to the United States with blast injuries from improvised explosive devices. Injuries involving extremities were seen more often, as were blast injuries and psychological traumas that were manifesting themselves months after the deployment in cognitive and mental health problems. In March 2005, the ASD(HA) issued a policy memorandum that required a new post-deployment health reassessment form that was to be completed between three and six months following a deployment. Although the new form was designed to elicit a service member's concern about physical health, its focus was on self-perceived cognitive and psychological health issues. The form

was based on the pre- and post-deployment health assessment forms and was to be ultimately funneled to AMSA for storage in DMSS and inclusion in required analyses of deployment health assessments.

By 2006, the manpower-intensive counterinsurgency efforts in Iraq and Afghanistan demanded new sources of U.S. troops, with Naval personnel being used on the ground in Iraq, for example. Because of the relatively large demand on both active and reserve service members for ground operations, DoD issued new policy on Individual Medical Readiness, establishing six baseline readiness standards across all services (DoDI 6025.19, January 3, 2006). The medical readiness standards for deployment for individuals are: 1) a current periodic health assessment (every 12 months), 2) the absence of deployment-limiting medical conditions, 3) dental readiness to specified standards, 4) immunization standards germane to the theater of operation, 5) current medical readiness laboratory tests, and 6) possession of appropriate individual medical equipment. These new standards eased the confusion that arose from competing standards across services, while also creating a sort of baseline for surveillance of medical readiness across DoD (see Figure 2.1).

In 2006 DoD updated its 1997 deployment health policy to specify policies and procedures for daily monitoring of disease and non-battle injury rates during deployments (the diseases and injuries incurred during a deployment but not from combat), address occupational and environmental health risk, require documentation of occupational and environmental health exposures, and require a record of daily location of personnel (DODI 6490.03, August 11, 2006). This issuance also requires that deployment health data be collected, transmitted and maintained electronically, rather than on paper as had been previously practiced, although the systems were not specified, i.e., DMSS was never mentioned as the destination for such deployment health surveillance data.

The updated 2006 deployment health policy responded to the outstanding requirement from the NDAA FY05 for more complete and accurate individual location data by directing the Deputy Undersecretary of Defense for Program Integration to ensure that the current manpower

data center receive once-daily deployment location records at the Secret level and below. This allows linkages between exposures and patient encounter data. The services are tasked within this instruction to develop a data collection system that would record the location data of all deployed individuals. The services are further tasked to ensure post-deployment health assessment and reassessment forms are submitted to DMSS, and to conduct occupational and environmental health surveillance (section 5). The COCOMs are tasked to coordinate occupational and environmental and medical surveillance, and to provide timely reporting of disease and non-battle injuries, battle injuries and other medical events (section 5).

The updated 2006 deployment health policy reiterates the maintenance of DMSS and DoDSR by AMSA, and the timelines for pre- and post-deployment serum sampling and process. It tasks AMSA with providing individual-level and aggregated data from the pre- and post-deployment health assessment forms as well as the reassessment form. It also directs AMSA to integrate tri-service reportable medical events data from across the services and make such data available to the services for further analyses and reporting. It further directs the Army to maintain and provide analyses from the occupational and environmental health data system. Yet, while DMSS is explicitly mentioned in the context of ongoing pre- and post-deployment health assessment forms, there is no mention that directs theater surveillance data be sent or ultimately linked into DMSS.

CHAPTER HIGHLIGHTS

There are several points to be emphasized from this discussion of requirements to inform the future of DoD's medical and deployment health surveillance, the serum repository, and DMSS.

- In terms of current missions:
  - The current policy-directed mission for AMSA is to manage the DoDSR and DMSS and to act as the organization carrying out the Secretary of the Army's executive agency responsibility for DoD-wide deployment medical surveillance;

  - The current policy-directed mission of the DoDSR is to provide support for the identification, prevention and control of disease related to military service;
  - The current policy-directed mission of the DMSS is to act as a tri-service medical surveillance system that is to transform to a medical surveillance center, share data across services with related surveillance agencies, connect to all relevant personnel and medical systems, and receive all theater medical data. Yet, no policy specifies that theater medical surveillance data be transmitted to DMSS.
- The use of the repository has shifted since its inception in 1985. Initially a resource for routine HIV screening, it subsequently became a resource for deployment health surveillance, and later as a resource for the broader purpose of identification, prevention, and control of disease associated with all military service, for both the reserve and active components.
- As early as 1997, DoD determined that it would continue to store the sera that had already been collected and also expand the use of serum specimens to fulfill new deployment health surveillance requirements. Pursuant to legislation in 2005, the ASD(HA) requested an evaluation of the soundness of the continued use of sera for surveillance and for clinical care purposes as well as research. The Armed Forces Epidemiology Board conducted the evaluation and reported that there was utility in continuing this practice, but suggested that archiving of an additional blood fraction - white blood cells - might also be appropriate in order to preserve genetic material for testing now and into the future. As we discuss later in this report, with the technological advances presenting new opportunities for health surveillance, the benefits of storing whole blood, or other blood fractions, may now outweigh the simple convenience of continuing to rely upon sera to meet

deployment health surveillance requirements now and into the future.

- In 1997 the ASD(HA) envisioned DMSS as a tri-service medical surveillance data system that would be connected to health data collections in a theater of operation. ASD(HA) further suggested that DMSS would migrate toward a "DoD Medical Surveillance Agency" that would function as the DoD's deployment health surveillance center. As we discuss later in our report, this suggestion has never been realized. Data collected from theater systems have not been fed into DMSS, but instead these data are being analyzed by an agency within ASD(HA). Further, the collection of individual location data has been addressed both by Congress and DoD, yet as we discuss later, these data are still elusive. In fact, the connection of the DMSS system to relevant and timely data systems is a significant issue that can be addressed by DoD since there appears to be regulatory guidance available and the data systems themselves are evolving to make such connections more feasible.

In this chapter we have discussed the statutory and DoD policy directives relating to AMSA, the DoDSR and DMSS. In the next chapter, we will describe selected DoD medical surveillance systems and organizations.

CHAPTER 3. DEPARTMENT OF DEFENSE MEDICAL SURVEILLANCE

We now discuss DoD surveillance systems. Understanding relevant medical surveillance activities helps place the role of DoDSR and DMSS into context. The summaries of relevant surveillance components and activities also set the stage for potential strategies to improve the capabilities of DoDSR and DMSS by leveraging, integrating or streamlining existing DoD activities and resources.

DoD distinguishes between "medical surveillance" and "health surveillance." Medical surveillance involves the collection, management, and analysis of health and medical information, including biological specimens, from members of all services stationed in both garrison and deployed environments in the United States and around the globe. Health surveillance is broader: it includes medical surveillance as well as occupational and environmental health surveillance. The military operational tempo since 2001 has led to updates in DoD policy related to deployment health, including deployment health surveillance.

Guided by department policy, the services carry out routine public health surveillance activities such as HIV testing (DoDD 6485.1, August 10, 1992), notifiable disease reporting (ASD(HA), November 9, 1998), and disease and non-battle injury reporting (DoDI 6490.03, August 11, 2006). Independently, services support more specialized public health programs based on the needs of their member population and operations. Specific service components have been designated to support DoD-wide public health program elements.

Our focus in this chapter is on medical surveillance within the broader context of health surveillance in DoD. The goal is to describe the scope of these activities across DoD along with the current systems executing them. We discuss selected medical surveillance systems and the organizational components responsible for medical and broader military health surveillance. We begin with a discussion of relevant definitions and principles established by DoD policy, then highlight relevant surveillance systems, and finally discuss key service agencies that conduct military health surveillance.

KEY DEFINITIONS

Department of Defense policy has defined different kinds of military health surveillance, based on the source, content and scope of the data. These definitions begin to establish the context for the role of DoDSR and DMSS. The following definitions are cited in DoDD 6490.02E, October 21, 2004, with key distinctions across definitions highlighted:

(3.1) Comprehensive Military Health Surveillance.

*Health surveillance conducted throughout **Service members military careers, across all duty locations, and encompassing risk, intervention, and outcome data**. Such surveillance is essential to the evaluation, planning, and implementation of public health practice and prevention and must be closely integrated with the timely dissemination of information to those who can act upon it.*

(3.2) Health Surveillance.

The regular or repeated collection, analysis, and interpretation of health-related data and the dissemination of information to monitor the health of a population and to identify potential risks to health, thereby enabling timely interventions to prevent, treat, or control disease and injury. It includes occupational and environmental health surveillance and medical surveillance.

(3.3) Medical Surveillance.

*The ongoing, systematic collection, analysis, and interpretation of **data derived from instances of medical care or medical evaluation**, and the reporting of population-based information for characterizing and countering threats to a population's health, well-being, and performance.*

(3.4) Occupational and Environmental Health Surveillance.

*The regular or repeated collection, analysis, archiving, interpretation, and dissemination of **occupational and environmental health related data** for monitoring the health of, or potential health*

hazard impact on, a population and individual personnel, and for intervening in a timely manner to prevent, treat, or control the occurrence of disease or injury when determined necessary.

MEDICAL SURVEILLANCE SYSTEMS ACROSS DOD

This section describes a range of DoD's medical surveillance systems and activities. Not surprisingly, data systems are stovepiped within services. Moreover, as noted in Chapter 2, the regulatory context for deployment health has developed separately from the garrison, or non-deployment context. Data collection systems have likewise developed within those two general contexts, as we describe below.

We identified relevant systems that collect, analyze, and report medical data used to monitor the health of service members and prevent, treat, or control disease and injury. For each surveillance system, we describe the main purpose and relevant doctrine and also present brief descriptions of the data collected in support of the surveillance mission, reports generated by the systems, and whether or not these data are sent to DMSS. A high-level summary of the information discussed in this chapter is provided in Table 3.1. A detailed description of the capabilities of DODSR and DMSS is provided in Chapter 4.

Table 3.1.
Summary of Elements within Selected Military Medical Surveillance Systems

System	Specimens	Data	Reports	Data in DMSS?
HIV screening	Serum (DoDSR)	Date, service, SSN	HIV trends	Yes
Deployment health assessment	None	DD Forms 2795, 2796, 2900	Monthly MSMR reports	Yes
Reportable medical events	None	70 specified diseases and conditions	Daily reports monitored by services	Garrison: Yes Deployed: No
Mortality	None (for surveillance)	Cause-specific mortality, near real-time	Weekly casualty reports	No (discontinued in 2003)
Disease and non-battle injury	None	Inpatient & outpatient, ICD-9 codes, individual	Aggregate data reports, through JmeWS	No
Individual medical readiness	(HIV, forensic DNA)	Six standard indicators	Visibility at service level; reported to OSD	Immunizations, HIV: Yes Others: No

Human Immunodeficiency Virus-1 (HIV-1)

DoDD 6485.1, issued in 1992, assigns responsibility to the Secretary of the Military Departments to establish policies and programs for the identification, surveillance, education and administration of personnel infected with HIV-1. Presently, the interval for periodic screening of personnel through the collection and testing of serum specimens is not to exceed 24 months.

Specimens collected by the Army and Navy are tested and processed by ViroMed, a contract laboratory. Specimens drawn for Air Force personnel are tested and processed by the Air Force Institute of Operational Health (AFIOH). Specimens collected from all services are shipped to DoDSR for frozen storage.

Deployment-Related Health Assessments

Pre- and Post-Deployment and Health Assessment Forms, DD Forms 2795 and 2796, and associated blood specimens are the basis for the deployment health surveillance currently carried out by AMSA. The forms are completed by all military personnel before and after serving in major overseas deployments in compliance with DoD Instruction 6490.03, "Deployment Health" August 2006. All deployment-related health assessment forms are submitted electronically to DMSS and permanently archived. A post-deployment health reassessment requirement was added in 2005, instituting collection of health information and a medical review of service members 3-6 months after returning from deployment. The program uses DD Form 2900 to collect information on health concerns, with particular emphasis on mental health; the latest version of the form is dated September 2007.

The pre-deployment process generally involves self-disclosure by a service member of any recent health events, medicines being taken, and any health concerns. Once the form is completed, medical personnel will review the form and if needed interview the service member to determine fitness for deployment or if the service member needs any treatment to prepare for deployment. The post-deployment assessment process starts with the completion of the form by a service member. When a concern is noted on the form or the service member screens positively for potential mental or physical health issues, that member is immediately seen by medical personnel who will determine whether referral to a medical provider for further attention is needed. The post-deployment reassessment process is similar to the post-deployment process, but is focused on capturing cognitive and mental health problems, which typically appear in the three- to six-month window following a deployment. Again, should a service member screen positive or indicate health concerns in their reassessment, he or she will be seen by medical personnel and referred as appropriate.

The deployment health assessment forms are intended to describe the service members' perceptions of their own health, health exposures, psychological problems, and health related concerns, the post-deployment health assessment and reassessment forms in particular. However, some

limitations exist in these forms, restricting their use in robust population-level analysis. Information intended to describe in-theater health and exposure concerns is captured post-deployment through self report, introducing the opportunity for recall bias and limited specificity. The questions differ between pre- and post-deployment forms and different versions of the forms have been used over the years. In addition, the response categories to questions addressing health and exposure concerns are broad and restricted to self-report. Analyses have been conducted using these data: MSMR publishes monthly tabulations of self-assessed health status, including mental health referrals. The forms are currently undergoing validation by the military health system.

Reportable Medical Events Surveillance

There are two separate systems for reportable medical event surveillance. In a deployment setting, the Joint Staff sets the tri-service surveillance reporting requirements for deployments, which currently include 70 types of medical events to which others can be added by COCOMs and joint task forces as needed (JCS MCM 0028-07, 2007). Theater-based information is reported through the Joint Medical Workstation (JMeWS).

For the garrison setting, the services participate in a Joint Preventive Medicine Policy Group which establishes the list of required medical events that must be reported. Reporting requirements are established under the authority of the ASD(HA) and published by AMSA (ASD(HA), November 6, 1998). In garrison, current reporting of selected medical events relies on a passive approach based on identification and coding by physicians during medical encounters. Over 70 specific diseases and environmental exposures are reported to each service's independent reportable event system, which captures these and additional service-specific medical events. For each of the reportable events, a clear case definition, laboratory criteria for diagnosis, and associated ICD-9 code are specified to standardize reporting across DoD. Information on select medical diseases, exposures, and conditions is reported to AMSA and incorporated into DMSS, with the aim of enabling timely and adequate response, identification of emerging or re-emerging

diseases, and estimation of disease distribution, trends and risk across the military population.

Mortality Surveillance

The Global Emerging Infections Surveillance and Response System (GEIS) and the Armed Forces Institute of Pathology (AFIP) established a Mortality Surveillance Division in the Office of the Armed Forces Medical Examiner. The Division was created in 2001 to track mortality among all military personnel and monitor cause-specific mortality among service members in near real-time. It does not collect specimens on a routine or systematic basis for the purposes of surveillance. This system tracks DoD personnel casualty data, integrated from the four services, in close to real time through the Defense Casualty Information Processing System. Additionally, the Armed Forces Medical Examiner's Tracking System provides data for epidemiologic analysis and real-time surveillance of casualty trends. The system also archives all military personnel death certificates and autopsy reports.

Disease and Non-Battle Injury (DNBI) Surveillance

Disease and Non-Battle Injury (DNBI) surveillance is required by the Joint Chiefs of Staff and performed by the COCOMS to document non-combat related health events occurring in a theater of operations. Outpatient data are collected by Field Medics/Battalion Aid Stations (i.e., Level I), Division Level Health Support (i.e., Level II) and Corps Level Health Support (i.e., Level III). Inpatient data are collected by Levels II-III. Data are collected through patient encounter modules, and fed into JMeWS. Patient encounter modules (e.g., within the Armed Forces Health Longitudinal Technology Application - Theater system), are used to capture data such as individually-identifying information (name, Social Security Number, unit, etc.), and ICD-9 diagnostic codes. Data are generally aggregated for reporting purposes. Although there are instances where it is not feasible (e.g., where classified data transmission lines are not available, or in systems that cannot capture patient encounters), generally, JMeWS is considered the primary source for data reporting. Because JMeWS is a

classified information system, it is precluded from direct connection and data sharing with the DMSS, which is currently an unclassified system. The COCOM surgeons monitor DNBI trends and report threats to the Joint Staff and the services and components. (JCS MCM 0028-07, 2007, Enclosure C). Further, personnel at the ASD(HA) review DNBI data on a daily basis (personal communication, October 15, 2007).

Individual Medical Readiness (IMR)

DoD policy assigns responsibility and establishes procedures to improve medical readiness through monitoring and reporting of a common set of indicators for all services (DoDI 6025.19, January 3, 2006 and DoDD 5124.2, 1994). The medical readiness of active component service members and select reserve component military personnel is assessed continuously and provides the basis for ensuring a force that is medically ready to deploy.

The six elements identified for monitoring medical readiness for deployment, and the standard for each, are: 1) a periodic health assessment (annual), 2) the absence of deployment-limiting conditions, 3) dental readiness (class 1 or 2 per annual dental exam), 4) immunization status (current for total force/all services vaccines), 5) medical readiness laboratory tests (HIV test results on file within past 24 months, and a one-time DNA specimen), and 6) individual medical equipment (nuclear, biological and chemical protective mask inserts for deployable members needing visual correction) (DoDI 6025.19, January 3, 2006, para 6.1). Services may enhance these basic requirements, although they are not required to report any of the data derived from enhanced monitoring.

The services report their data to the ASD(HA), which oversees the entire program and has the responsibility to issue periodic medical readiness reports (DoDI 6025.19, January 3, 2006, para 5.1.4). Services currently report IMR via the Status of Resources and Training System, though this is expected to migrate to the new readiness reporting system called the Defense Readiness Reporting System, once available. Individual service commanders have full visibility and access to

respective force medical readiness data through service-specific IMR program applications.

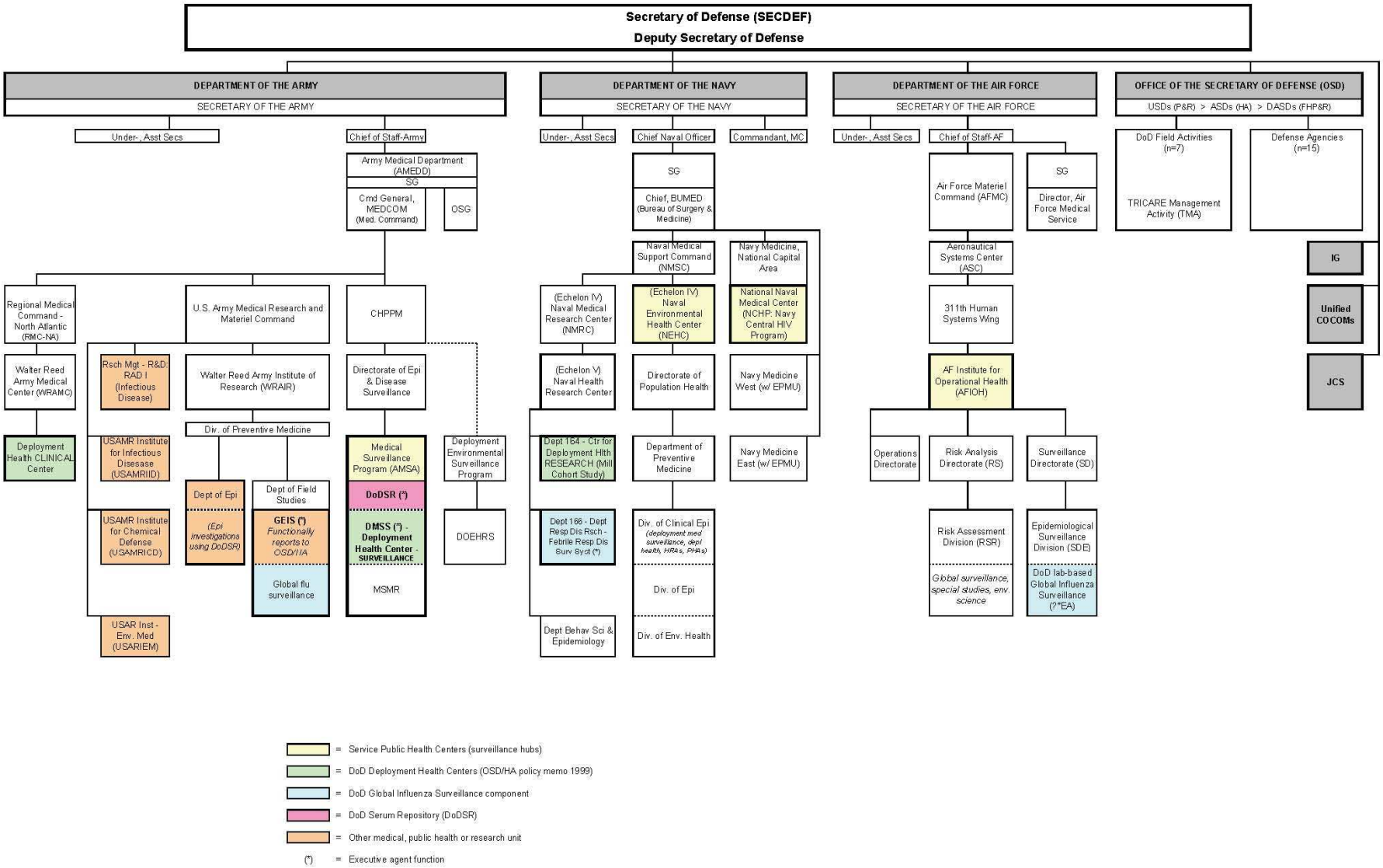
KEY ORGANIZATIONAL COMPONENTS AND PROGRAMS

To understand the current and potential utility of DoDSR and DMSS to surveillance, investigation, and research activities, the RAND team gathered information about ongoing surveillance by DoD organizations that play key roles in military public health activities. We interviewed military public health leaders and reviewed official documents and scientific publications to complement interview data.

The following sections provide brief overviews of the organizations, their respective roles in DoD medical surveillance, activities related to influenza specifically, and collaborations with or use of the DoDSR and/or DMSS. Figure 3.1 depicts these organizational components within the overall DoD organizational structure.

Figure 3.1.

Organizational Context for Military Health Surveillance



Global Emerging Infections Surveillance and Response System (GEIS)

The Global Emerging Infections Surveillance and Response System was created as a tri-service organizational entity located within the U.S. Army. The origins of GEIS trace back to a September 1995 inter-agency report on global emerging infectious diseases (NSTC 1995) and an August 1995 memorandum from the Commanding General of the Army Medical Research and Materiel Command[2]. (Patrick Kelley, personal communication, April 22, 2008) On October 10, 1995, the ASD(HA) announced the assembly of a Global Surveillance and Response Committee to develop a charter and provide oversight for a DoD global surveillance and response capability. (Patrick Kelley, personal communication, April 22, 2008) The system was subsequently formalized by Presidential Decision Directive NSTC-7 (Emerging Infectious Diseases) in 1996 (PDD NSTC-7, 1996), which expanded the role of DoD in worldwide surveillance and response to emerging infectious diseases.

Citing the HIV/AIDS pandemic and the reemergence of tuberculosis, cholera and pneumonia, the directive stipulated that "the mission of DoD will be expanded to include support of global surveillance, training research, and response to emerging infectious disease threats" (para 8). It further specified that DoD centrally coordinate the effort, improve its preventive health and epidemiologic capacities, and increase the use of existing CONUS and OCONUS facilities. Further, DoD was directed to use its overseas facilities to train foreign epidemiological staff. The goals of GEIS include surveillance and detection, response and readiness, integration and innovation and cooperation and capacity building.

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[2] Memorandum included the following: "In response to the Office of Science and Technology Policy within the Executive Office of the President and to a request by the Office of the Assistant Secretary of Defense (Health Affairs), the US Army Medical Research and Material Command and the Naval Medical Research and Development Command are initiating a program on global surveillance for emerging infectious diseases. This initiative relies heavily on the overseas laboratories."

GEIS supports health surveillance programs and activities focusing on the following conditions: respiratory illnesses (including influenza), other febrile illnesses (malaria and dengue), enteric illnesses (acute diarrhea), antimicrobial resistance, and sexually transmitted infections. The GEIS-sponsored Mortality Surveillance Division is run by the AFIP Medical Examiner's Office and collects tri-service casualty information in near-real time. The ESSENCE syndromic surveillance system, an outbreak detection tool monitoring daily garrison-based outpatient medical encounters, also receives support from GEIS.

Influenza surveillance programs sponsored by GEIS are primarily laboratory based. They focus on collection and characterization of viral isolates sampled from military and civilian populations from approximately 273 participating sites in 56 countries in FY06, with an additional 38 sites in nine countries that were added in FY07. Permanent overseas medical research laboratories are located in Egypt, Indonesia, Kenya, Peru and Thailand and serve as collaborative centers with host nation research entities, the World Health Organization and the Centers for Disease Control and Prevention. These research centers host the GEIS surveillance functions for DoD.

GEIS and DoDSR, DMSS. GEIS's collaborative efforts with AMSA and the DoDSR and DMSS resources under AMSA management have focused on supporting research and "threat assessments" or investigations. A number of studies involving military and civilian researchers have been sponsored by GEIS (DoD-GEIS Annual Report for FY 2006) For example, a recent suspected outbreak of Q-Fever among Army service members stationed in Iraq was investigated drawing on historical serum specimens from the DoDSR. In addition to collaborative work, GEIS used Avian/Pandemic Influenza funding in late 2007 to provide infrastructure support to the DoDSR, through the purchase of a specimen transport truck for the use of a contractor to enable more timely shipment of serum specimens from contract testing facilities to the DoDSR.

Center for Health Promotion and Preventive Medicine (CHPPM)

The U.S. Army Center for Health Promotion and Preventive Medicine (CHPPM) acts as the Army's public health center and is the designated executive agent for health surveillance (DoDD 6490.2, October 21, 2004). Its mission is "to provide worldwide technical support for implementing preventive medicine, public health, and health promotion/wellness services in all aspects of America's Army and the Army Community anticipating and rapidly responding to operational needs and adaptable to a changing world environment". Designated CHPPM in 1994, the organization provides scientific expertise and services in clinical and field preventive medicine, environmental and occupational health, health promotion and wellness, epidemiology and disease surveillance, toxicology, and related laboratory sciences.

CHPPM is organized into eight directorates, with the Directorate of Epidemiology and Disease Surveillance (DEDS) providing the central epidemiologic resource for the Army; AMSA is one of five programs within DEDS. Other directorates specialize in Environmental Health Engineering, Health Promotion & Wellness, Health Risk Management, Laboratory Sciences, Occupational & Environmental Medicine, Occupational Health Sciences, and Toxicology.

As described in other sections, AMSA manages and oversees DoDSR and DMSS.

CHPPM and DoDSR, DMSS. According to AMSA analysts, there are limited formal mechanisms for making data within DMSS available for use by CHPPM personnel outside of AMSA. Further, CHPPM and its component directorates do not regularly utilize the contents of the DoDSR for surveillance purposes. Given DMSS and the DoDSR's current physical set-up and geographic remoteness to most of CHPPM staff and facilities, use of these resources requires on-site staff in order to access data and specimens.

Air Force Institute of Operational Health (AFIOH)

The Air Force Institute of Operational Health (AFIOH) acts as the public health center for the U.S. Air Force and provides occupational,

environmental, and public health expertise to operational decision-and policy-makers. AFIOH is the executive agent for the laboratory-based component of the virologic surveillance activities supported by GEIS and is under the command of the 311th Human Services Wing.

The AFIOH consists of five divisions, of which two are directly engaged in surveillance: the Risk Analysis Directorate and the Surveillance Directorate. The Risk Analysis Directorate collects and analyzes environmental, safety and health data in order to enhance performance and protect the force. The Surveillance Directorate collects data on personnel health such as HIV status and drug testing for the Air Force. The Surveillance Directorate also provides chemistry services for air, soil and water analysis as well as expertise and analytic services for surveillance of radiation.

The AFIOH laboratory-based surveillance program collects specimens from participating care facilities and sentinel sites around the world. A total of 43 U.S. Military Treatment Facilities (MTFs) located worldwide collect specimens from DoD beneficiaries attending hospitals, health clinics, emergency clinics and pediatric clinics; other sentinel sites include two military hospitals in Hungary serving foreign military beneficiaries and multiple treatment facilities in 13 allied countries serving foreign military and civilian patients. Overseas GEIS laboratories also work closely in support of the AFIOH lab-based surveillance program, through specimen collection and testing.

AFIOH and DoDSR, DMSS. Currently, the AFIOH sends remnant serum from HIV screening, HIV test results and reportable medical events captured in garrison to AMSA's DoDSR and DMSS.

Navy Environmental Health Center (NEHC)

The Navy Environmental Health Center (NEHC) serves as the public health center for the U.S. Navy and Marine Corps and is under the Navy Medical Support Command. NEHC's mission is to "provide leadership and expertise to ensure mission readiness through disease prevention and health promotion in support of the National Military Strategy" (NEHC, 2008). NEHC is made up of the five following directorates: Environmental

Programs, Expeditionary Preventive Medicine, Industrial Hygiene, Occupational and Environmental Medicine, and Population Health. Thus, NEHC addresses the full range of health surveillance components, including medical surveillance and occupational and environmental surveillance.

NEHC's EpiData Center provides epidemiologic services in support of the Navy's disease and injury prevention programs. The Center conducts infectious disease surveillance, deployment health surveillance and provides clinical epidemiology, occupational and environmental epidemiology and injury epidemiology analytic services.

Currently the EpiData Center receives HL-7 data feeds of pathogen laboratory results from medical specimens, blood chemistry results, and pharmacy data and has the capability of linking these data streams to health outcomes within the electronic medical record system. The Center plans to test the integration potential of these HL-7 data sources to the ESSENCE syndromic surveillance system to provide validation of diagnoses coded by outpatient ICD-9 codes.

NEHC and the DoDSR, DMSS. Currently, NEHC sends remnant sera from HIV screening, HIV test results and reportable medical events captured in garrison to AMSA's DoDSR and DMSS. Further, NEHC provides data to the DMSS, though has had little need for DMSS analysis or specimens to date.

Naval Health Research Center (NHRC)

The Naval Health Research Center is the research hub for the U.S. Navy and Marine Corps. NHRC is made up of the following six departments: Medical Modeling, Simulation & Mission Support; Warfighter Performance; Behavioral Sciences and Epidemiology; Deployment Health Research; HIV/AIDS Programs; and Respiratory Diseases Research (RDR). NHRC is one of three designated deployment health centers – the center for deployment health research (ASD(HA), September 30, 1999).

NHRC serves as the Navy node for GEIS and conducts active surveillance of febrile respiratory illness (FRI) in recruit training centers DoD-wide, on board ships, and in local border areas (San Diego – Mexican border). Additionally, as part of the Febrile Respiratory

Illness surveillance program, NHRC collects and tests throat swabs for adenovirus and influenza virus, employing molecular techniques for pathogen isolation, characterization and preservation. NHRC archives throat swab specimens and isolates from this surveillance program in frozen storage at -80°C.

The Naval Respiratory Disease Laboratory, part of the DoD Center for Deployment Health Research at NHRC, has culture and molecular testing capabilities for approximately 21 bacterial, viral and other respiratory pathogens including *Streptococcus pneumoniae*, *Streptococcus pyogenes*, influenza, adenovirus, and coronavirus. This laboratory also conducts serologic testing and is currently running serology for adenovirus, chlamydia and *M. pneumoniae.*

NHRC and DoDSR, DMSS. NHRC collaborates closely with AMSA on ad-hoc research studies and has utilized DoDSR serum and DMSS data for studies of special interest (e.g., acute respiratory infections among military recruits). No formal standing mechanism exists between NHRC and AMSA for purposes of exchanging data or conducting surveillance.

CHAPTER HIGHLIGHTS

- Medical surveillance within the DoD is accomplished at many levels, across all services, and through numerous different systems. Not surprisingly, data systems are stovepiped within services and segregated by garrison or theater context, with classification problems compounding connectivity issues.
- There is strong evidence that medical surveillance within DoD is hampered by lack of data sharing, lack of timely data, and even missing data such as the location of individuals in a theater of operations. In spite of the fact that Congress has directed DoD to solve the location data problem, the DMSS is not yet receiving any feeds at the individual level because the one service-specific system with this information is classified and DMSS is not.

- Further, there appears to be a difference between policy and practice in terms of which DoD surveillance system and organization should be tracking this information.

CHAPTER 4. CURRENT CAPABILITIES OF AMSA, DODSR AND DMSS

In this chapter we highlight the current operations and capabilities of AMSA, DoDSR and DMSS. For DMSS in particular, we examine capabilities against the requirements described in Chapter 2. Together with the examination of other biological specimen repositories, which is the focus of the next chapter, this information establishes the basis for the analysis of issues, gaps and opportunities to improve the capabilities of AMSA, DoDSR and DMSS, which is the focus of Chapter 6.

THE ARMY MEDICAL SURVEILLANCE ACTIVITY TODAY

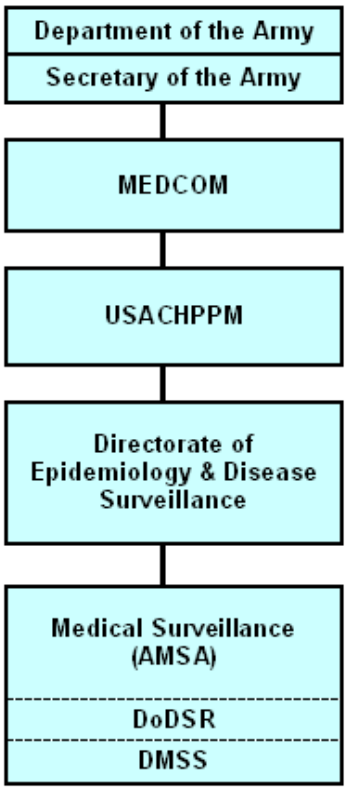
AMSA, a component of CHPPM (see Figure 4.1), is the DoD's source for medical surveillance information and analysis. AMSA's budget is approximately $4 million per year, according to our interview sources, and covers the cost of AMSA staff, the DoDSR and DMSS management and operations. AMSA's most current mission statement is as follows:

> *The Army Medical Surveillance Activity's (AMSA) main functions are to analyze, interpret, and disseminate information regarding the status, trends, and determinants of the health and fitness of U.S. military (and military-associated) populations and to identify and evaluate obstacles to medical readiness. AMSA is the central epidemiological resource for the U.S. Armed Forces providing regularly scheduled and customer-requested analyses and reports to policy makers, medical planners, and researchers. It identifies and evaluates obstacles to medical readiness by linking various databases that communicate information relevant to service members' experience that has the potential to affect their health. (AMSA Mission, personal correspondence, 28 January 2008).*

Deployment medical surveillance is not included in AMSA's mission statement. Although the Executive Agency for AMSA clearly describes the organization's mission in terms of deployment medical surveillance, these assigned requirements do not appear in AMSA's own mission. In

fact, AMSA's mission seems focused on medical readiness and the "health and fitness" of military populations. In order to determine what guidance AMSA received from higher organizations either within DoD or within the Army, we asked AMSA whether it received any prioritized written guidance or any other form of formalized guidance, to direct its efforts within the greater DoD surveillance context. We learned that AMSA apparently receives little if any guidance from any organization for its medical surveillance activities. AMSA is also positioned quite low in the CHPPM chain of command. Together, these facts could make AMSA less than fully transparent to any parent organization.

Figure 4.1.
Chain of Command for AMSA



AMSA staff include assigned military officers, civilian General Service staff, and contractor personnel working for the five principal

contracts. Of military officers, there are positions for a Chief (Army O5-6 Preventive Medicine Physician), Preventive Medicine Officers (2 Army O3-4 Preventive Medicine Physicians), and Service Liaison Officers (currently 1 Air Force O5 Preventive Medicine Physician, with one Navy position unfilled).

As we have already established, AMSA has responsibility to manage both the DoDSR and the DMSS. It also manages a data tool called the Defense Medical Epidemiology Database (DMED) that provides remote access to a subset of DMSS data. AMSA supports a number of contracts to help manage the repository, DMSS and analyses:

- DMED contract: responsible for maintaining AMSA's internal applications (the DoDSR inventory management application, the DMSS management tool application) and its external user applications, as well as facilitating AMSA's providing technical data extracts to external customers
- DMSS contract: responsible for maintaining and developing DMSS, which includes acquisition and loading of data, software development, and maintenance of hardware
- DoDSR contract: responsible for maintenance of the DoDSR freezers and supporting infrastructure (e.g. compressors, backup generators), and the daily operations of the DoDSR which include processing of new specimens, and the retrieval of specimens and their aliquoting for external study. This contract is also responsible for specimen pickup from the sources, which involves use of a specialized transport truck.
- Two separate analysis contracts: support staff analysts for internally directed analyses and external research requests, including serum studies.

To summarize, the important issues we found were:

- Assigned requirements for AMSA did not match its stated mission

- AMSA receives little if any formal guidance concerning its activities in relation to the total DoD health surveillance effort.

DOD SERUM REPOSITORY

The DoDSR stores sera from service members' blood. The basic serum storage process stems from the original purpose of the repository which was to collect and store sera collected as a result of HIV testing. Currently, AMSA runs the serum repository via contracts, which involve specimen collection, transport, and storage. AMSA makes serum available to military and civilian researchers for "purposes of conducting military relevant investigations" and regulates the use according to official AMSA guidelines (AMSA, 2003).

The repository contains specimens received from two main sources: the department-wide HIV screening programs (DoDD 6485.1, August 1992) and deployment-related health assessments (DoDI 6490.03, August 11, 2006). The repository has received remnant serum from Army, Navy, and Military Entrance Processing Stations HIV testing programs since 1985 and serum specimens from the Air Force HIV testing program since 1996.

On average, the repository grows by an additional 1.9 million specimens per year and includes specimens collected from service members stationed domestically and in Europe. As of December 2007, the repository included a total inventory of over 43 million serum specimens collected from approximately 10.5 million individuals (see Table 4.1). Currently, of the total number of specimens within the DoDSR (43.1 million), approximately 2,628 HIV positive specimens. However, most positive specimens are retained by the services or by the Army's Retrovirology Laboratory.

Of the 43.1 million specimens, approximately 37.6 million are linked to personnel data and are available for immediate physical retrieval from frozen storage. Of those, approximately 13.7 million specimens are from the 2.2 million individuals currently in the service (as of 31 Oct 2007).

As a result of storage space restrictions at the current DoDSR facilities, approximately 5.5 million specimens for which no linked data currently exist (i.e., the specimen is not linked to an individual SSN) have been placed in "compressed configuration." Much of the information needed to link these specimens to individual SSN exists currently on paper manifests, which are awaiting either verification of manual transcription or initial manual transcription. Entry of these data is awaiting contract award. Of the approximately 5.5 million specimens in "compressed configuration," only 244,876 are from the 2.2 million individuals currently in the service (as of October 31, 2007).

Also as of 2007, serum specimens are shipped to the DoDSR from three laboratories: ViroMed Laboratories (Minnetonka, MN), with whom the Army and Navy each have a contract, and the Air Force Institute for Operational Health (San Antonio, TX). Specimens from COCOMs, such as those coming from the Landstuhl Regional Medical Center (Ramstein, Germany), are shipped to the serum repository via the Walter Reed Army Institute of Research. Specimens from ViroMed and AFIOH have been transported routinely by a contract carrier to the DoDSR approximately six times per year.

Specimens are stored in 25,000 ft^2 of leased walk-in freezers at -30 degrees Celsius, which are now nearly full. The lease for this space expires in 2010, and we learned from our interviews that AMSA is in the process of defining its future storage requirements.

Table 4.1.
Description of DoDSR Serum Inventory and Source of Specimens

DoDSR Contents	
Total number specimens*	43,194,251
Total number of individuals	10,418,551
Acquisition rate	1.9 million per year
Source of Specimens	
Current active duty**	1,402,589
Current reservist members	375,012
Current National Guard	456,183
Former military members	5,001,228
Dependant beneficiaries	898,358
Median no. of specimens per service member**	
Current active duty	6 (IQR 3,9)
Current reservists	6 (IQR 3,9)
Current National Guard members	5 (IQR 2,7)
No. of HIV+ specimens	2,628

* As of 31-December 2007
** As of 31-October 2007

Source of Specimens

Seventy-five percent of service members have provided three or more specimens. Serial collection of serum specimens is an important feature of the repository because it permits longitudinal studies capable of assessing temporal trends as well as long-term health effects in

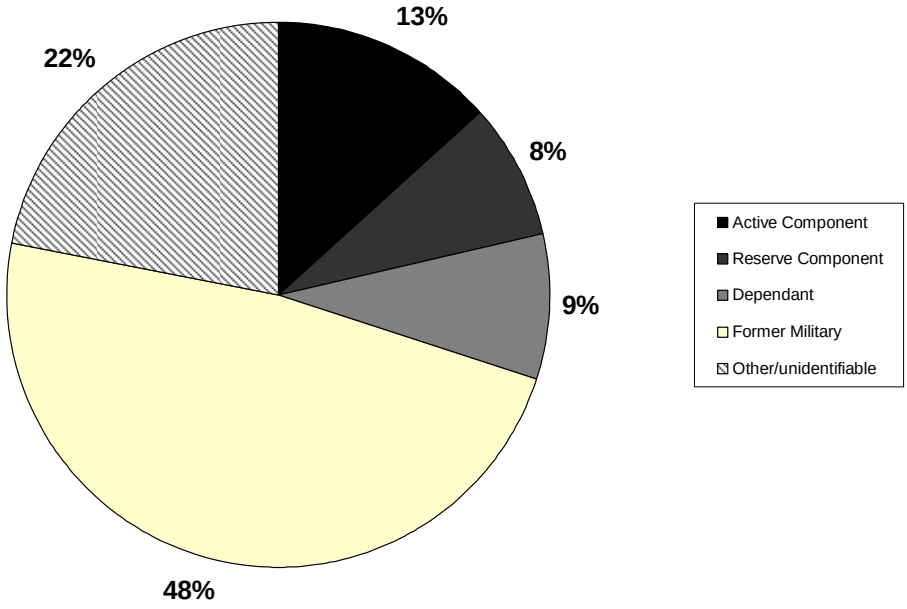
individuals and population cohorts. Thus, the number of consecutive specimens contributed by a given service member determines to a great extent the epidemiologic utility of the stored specimens. As shown in Table 4.1, as of October 2007, the median number of specimens per active component and reserve component service member was 6 (inter-quartile range, IQR, 3, 9). Thus, approximately 75% of active component and reservist service members had provided three or more specimens. For the National Guard, the median number of specimens contributed was 5 (inter-quartile range 2, 7).

Over half the specimens are traceable to service members who have been on active duty after 1990. According to AMSA analysts, over half of the serum specimens in the DoDSR are traceable to a service member who has at some point been on active duty after 1990. As previously discussed, this subset of the population captured by the DoDSR is of high value because of the availability of linked longitudinal medical and personnel information. The total number of former and current military members represented in the DoDSR, including the current active component and reserve component members (as of October 31, 2007) is 7.2 million, and is the largest subpopulation making up the full pool of contributors to the serum repository (see figure 4.2).

Specimens for civilian military applicants are also stored in the DoDSR. In addition to military service members, beneficiaries and civilian military applicants also contribute serum specimens to the DoDSR. Civilians applying for military service are required to be tested for serologic evidence of HIV-1 infection (DoDD 6485.1) as a criterion for eligibility for service. These specimens are stored in the DoDSR because testing contracts include packaging and shipment of all specimens tested for HIV-1 irrespective of military duty status. Since 1998, reserve component members have had have the same blood collection requirements as active component members, including routine HIV screening and pre- and post-deployment specimens (ASD(HA), October 6, 1998). Approximately 2.3 million individuals with specimens in the repository are classified as unidentifiable (see Figure 4.2). According to AMSA analysts, the majority of unidentifiable specimens are from civilian applicants who did not join the military and a small number of

affiliated civilians who had received HIV testing pre- or post-deployment.

Figure 4.2.
Contributors to the DoDSR (as of October 31, 2007)



Consent forms are not needed when the sample is taken. Consent issues arise twice: first at the time of the taking of the blood specimen, and second when uses of stored sera are proposed. Blood is drawn from service members for both HIV testing and for pre- and post-deployment specimens, with the HIV test specimen serving as the deployment-related specimen when it meets certain criteria described in DoDI 6490.03. According to our interviews, there are no consent forms needed from service members at the time of these specimens since the specimen collections are done for public health surveillance and as a condition of employment in the service. Second, serum specimens are stored in perpetuity in the DoDSR, with no apparent guidelines governing appropriate handling and/or disposal of sera from separated or deceased members. Our interviewees suggested that service members know that

their serum specimens are stored in perpetuity; however, we could find no evidence of explicit communication to that effect.

Guidelines address uses of stored serum specimens, but consent rules are not fully articulated. For uses of the serum specimens, AMSA's "Guidelines for Collecting, Maintaining, Requesting, and Using Specimens Stored in the Department of Defense Serum Repository," (29 May 2003) establish "research" as an activity conducted with the primary intent to create, extend or validate generalizable knowledge, or knowledge that extends beyond the individual (or populations directly associated with the individual). "Non-research" is an activity conducted in order to develop specific knowledge of an individual or directly associated population. Within these two categories, the guidelines address four primary uses of the stored serum specimens: research, patient care, public health/force health protection, and criminal investigations. The issue of consent is addressed by determining whether the sera are identifiable to an individual (or, linked), or un-identifiable.

- For research purposes, linked specimens would require consent documents, and unlinked specimens would not require consent;
- For patient care purposes, a consent must be obtained prior to specimen release;
- For public health/force health protection, linked specimens would not require consent if the use is "non-research," and if the use is to examine a threat to or intervention for a military population. The guideline does not describe when linked specimens might require consent for the purposes of public health/force health protection. However, it does describe the potential use of an unlinked specimen, although it is not explicit about whether this use would or would not require consent (presumably it would not);
- For criminal investigations and prosecutions, the guidelines are quiet concerning the need for consent although specify the use of counsel.

It appears that the guidelines could be improved upon by specifying consent issues relating to public health/force health protection. Further, from the discussion above, since the specimens are drawn without consent, then there seems to be no way to use the sera for any purposes other than "de-linked" or certain public health/force health protection uses.

Guidelines for use of institutional review boards could be expanded. We learned from our interviews that AMSA relies on the IRBs of requesting agencies to determine the appropriateness of the protections stipulated within the proposed protocols, although the current trend among repositories is to have an internal IRB or an established affiliation with an IRB (see chapter 5). As in our discussion of informed consent above, because recent technological innovations allow for detection of DNA in sera, it is questionable whether sera can actually be "de-linked". The AMSA guidelines specify the following IRB requirements for proposed uses of sera:

- For research purposes, AMSA requires an IRB approval;
- For the purposes of patient care, the AMSA guideline is silent on the matter of IRB approval;
- For the purposes of public health/force health protection, the guidelines are silent with regard to IRB approval, although this category of use in particular may warrant an IRB;
- For the purposes of criminal investigations and prosecutions, the guidelines are also silent, although stipulate the use of counsel.

Therefore, guidelines articulating the protections offered by an IRB review may be improved upon by further detailing when an IRB is going to be used, and which IRB will be used (i.e. either an AMSA-affiliated IRB or the requesting organization's IRB).

There appear to be several opportunities for improvement in the treatment and description of the requirements for an IRB as well as informed consent, and this suggests that an updated examination might

provide benefit both to the service member as well as to the military health system.

To summarize the key points of this discussion regarding informed consent:

- Specimens are being drawn for two legally-mandated and regulated purposes: HIV testing and pre- and post-deployment surveillance;
- Specimens are stored in perpetuity with no evidence of communication of that to service members;
- Specimens can be used for purposes other than that for which they were drawn (namely research, clinical care, public health and criminal investigation), but research uses require either de-linking from individually identifying information or express informed consent;
- The consent rules are apparently not fully articulated in current guidelines;

And, for the use of IRBs:

- Repositories either tend to be affiliated with existing IRBs or they constitute their own internal IRBs. In contrast, AMSA relies exclusively on the determination of requesting organization IRBs;
- The guideline articulating the need for IRBs is silent in the case of using sera for public health/force health protection. Because this category of use is large, it may benefit DoD to revisit this use of serum specimens and further specify the appropriateness of if, when and how to use an IRB.

Timing of Specimen Collection

The events associated with specimen collection and subsequent storage by the DoDSR include: application for military service, routine HIV screening, deployment related health assessments (both before and after) and separation from military service. Individual medical readiness requirements (DoDI 6025.19, January 3, 2006) also include compulsory HIV screening for all active component and reserve component

members with screening intervals not to exceed 24 months. Pre-deployment specimens must be collected no more than one year before deployment and post-deployment specimens within 30 days of redeployment home. Notably, specimens collected as part of medical encounters, in between deployment or in theater are not stored or sent to the DoDSR. Furthermore, blood collected as part of medical care provided by the Veterans Health Affairs system is not currently required to be stored by the DoDSR.

Specimens

Specimens are kept in frozen storage. All domestically collected blood specimens are drawn at medical treatment facilities (MTF, military care sites), where they are spun down for serum extraction. The serum is packaged and shipped from MTFs to either ViroMed or AFIOH at a temperature of 4-8°C (usually 24-48hrs after blood draw). At the testing laboratories, specimens are processed and tested for evidence of HIV antibody, using ELISA-based identification methods. Specimens are maintained at 4-8°C during the preparation and testing process. After testing, specimens are placed in frozen storage at -30°C at ViroMed and AFIOH testing facilities. From testing laboratories, remnant serum specimens from HIV screening are transferred by truck at -30°C to DoDSR six times per year.

Specimens collected from service members stationed overseas in Europe and Iraq are sent to Landstuhl Regional Medical Center, Germany. At Landstuhl, specimens are processed to serum, if not already done, and then frozen and shipped in batches to the HIV Diagnostic Reference Laboratory in the Division of Retrovirology at the Walter Reed Army Institute of Research. There specimens are processed and tested for HIV infection. After testing, specimens are frozen and delivered on dry ice to the DoDSR on a weekly basis. Upon arrival at the DoDSR, they are scanned to verify arrival and entered into the DoDSR inventory program.

The HIV Diagnostic Reference Laboratory also acts as the quality assurance laboratory for the ViroMed contract. Management personnel in the HIV Diagnostic Reference Laboratory review digital images of all of the HIV positive specimens from ViroMed. If they do not concur on the diagnosis, verification testing is requested. The HIV Diagnostic

Reference Laboratory also review any incident reports generated by ViroMed describing conditions or incidents occurring during the shipping and testing processes with the potential to influence diagnostic test results.

Currently, the HIV Diagnostic Reference Laboratory has no way to verify the cold chain for the serum specimens drawn in either the United States or Germany. Once a specimen is drawn, no standing mechanism exists to verify appropriate handling along the specimen's trajectory towards the ViroMed testing laboratory. The HIV testing protocol that is followed requires that specimens are tested within 2 to 7 days of being drawn, if the specimens are not frozen.

Uses of the Serum Repository

As of early February 2008, DoDSR had distributed specimens for over 170 different studies and clinical support needs. For non-military related researchers to receive specimens, they must collaborate with a military principal investigator and go through the military IRB process. Costs associated with specimen use by non-military researchers are $20 per specimen. Uses of the specimens for military related research are exempt from the $20 fee. Approved research studies can receive only unidentified serum specimens. Use of unidentified serum specimens for research purposes precludes the linking of specimens to other individual level demographic, medical, and personnel data stored in the DMSS database.[3]

[3] Research activities involving human subjects that are exempt from IRB review and the requirement for informed consent are identified in 45CFR 46.101(b)(1)-(6). In particular, 45CFR 46.101(b)(4) is relevant to the use of stored human specimens. It states: "Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects." Therefore, as long as certain identifiers have been removed (i.e., the 18 identifiers specified under HIPAA at section 164.514(b)(2) of the regulations -- i.e., name, social security number, medical record number, telephone number, e-mail address, health plan beneficiary number, etc.), the specimen and any accompanying data can be considered de-identified and may be exempt from needing IRB oversight and informed consent.

AMSA has not published a description of its decision making process for approving use of the sera. According to this AMSA guideline, authority over the release of specimens and compliance with stated requirements is determined solely by the Director of AMSA. To our knowledge, AMSA has not published the criteria or process it has used in approving release of serum specimens. As specified in AMSA's *Guidelines for Collecting, Maintaining, Requesting and Using Specimens Stored in the Department of Defense Serum Repository* (AMSA, May 29, 2003), access to specimens is based on consideration of the following factors: nature of intended use, DoD affiliation, and number/size of specimens. Categories of intended use include: "research", "patient care", "public health/force health protection: community and military preventive care", and "criminal investigations and prosecutions". There is no separate category for "deployment health". Specific logistical and technical requirements are described in detail according to the category of intended use of the specimens.

To date, most uses of DoDSR have been for research rather than surveillance. According to DoD policy (ASD(HA), January 2005 and DoDD 6490.2, October 21, 2004), serum collection and storage is intended to contribute to deployment-related surveillance, although the ability of serum to provide information regarding agents or exposure markers has yet to be explicitly defined or systematically evaluated. Further, there appears to be no ongoing body that systematically evaluates potential new exposure threats and improvements in technology to detect those threats in biological specimens against available resources.

Specimens stored at the DoDSR together with the service members' linked health and personnel information supply a robust resource for supporting surveillance and outbreak investigations, addressing research questions, and supporting clinical management. The number of distinct requests for serum specimens by year is presented in Table 4.2, and the number of requests by type of use is presented in Table 4.3.

Of note is that, from January 2001 to January 2008, specimens from the DoDSR were requested fewer than 200 times. The various uses of serum specimens are described in more detail in the following sections.

Table 4.2.
Number of DoDSR Specimen Requests (Military and Civilian), 2001- 2008[4]

Year	# of approved serum requests
2001	11
2002	17
2003	6
2004	11
2005	12
2006	19
2007	43
2008	3

[4] Through February 2008

Table 4.3.
Uses of the Serum Inventory, 2001-February 2008[5]

Uses of Serum	# of approved serum requests
Vaccine	27
Clinical support	19
Deployment related	12
Miscellaneous	9
HIV	8
Epidemiologic Investigation	7
Influenza	3
Seroprevalence	3
Forensic	2
Research (n=32)	
Non-communicable disease	18
Infectious Disease	4
Miscellaneous	3
DNA	3
HIV	2
Drug	1
Chemical	1

Surveillance. The only routine surveillance use of DoDSR remains the HIV screening program, despite what is called for by department policy regarding deployment health and the DoDSR's role. No other tests or analyses are routinely or systematically carried out on DoDSR specimens. According to AMSA analysts, AMSA is not resourced or funded to support regular or systematic analysis of pre- and post-deployment serum specimens (paired or otherwise) for the purpose of performing biological surveillance of deployment-related health threats. AMSA has supported many external requests for relatively small numbers of such paired specimens, focusing on specific time periods and locations and

[5] Through February 2008

testing for specific exposures of interest, but this process has not resulted in a robust or systematic infrastructure for such biological surveillance. AMSA currently lacks the laboratory capability to support such testing. This may trace back to the origins of the DoDSR as a repository for specimens already tested for HIV, rather than as a surveillance laboratory.

Investigation. AMSA is not currently resourced to conduct independent detection or response investigations to disease or injury outbreaks. AMSA's role in epidemiologic investigations has historically been one of providing data and/or specimens in support of such investigations. A recent example is a Q-Fever outbreak among US military troops returning from Iraq, in which AMSA was able to provide historical serum specimens as well as demographic and personnel information to assist in the investigation of the outbreak. Other examples include epidemiological investigation of outbreaks caused by influenza and adenovirus.

Research. To date, military public health and medical research account for the largest number of requests for specimens from DoDSR. Research projects for which specimens have been requested span a wide range of medical topics, including infectious diseases, cancers, diabetes, multiple sclerosis and schizophrenia. Civilian and military researchers in the fields of immunology, infectious disease, cancer, cardiovascular epidemiology, nutrition, environmental health, and maternal/child health have tapped into this unique biological resource, as evidenced by the list of published reports found in Appendix 2 to this report. As discussed in prior sections, use of the serum for research purposes is stated in AMSA guidelines and must meet specific requirements for approved use. From 2001 through early February 2008, AMSA received approximately 175 distinct requests for serum specimens, including approximately 30 research projects. Two research projects focused specifically on avian and/or pandemic influenza. Appendix 2 is a bibliography of peer-reviewed scientific publications utilizing the DoDSR serum specimens or DMSS database.

Clinical Support. Less taxing requests on specimens are made by clinicians for HIV test result validation or to obtain patient medical

history information. Specimens requested to meet this need typically require less time and effort to process.

Avian and Pandemic Influenza. A particular focus of this study was use of the repository to address issues related to influenza.[6] Routine uses of the DoDSR and DMSS specific to influenza have not been established; however, beginning in FY06, three serologic studies investigated the utility of the DoDSR's serum inventory for surveillance of avian and pandemic influenza. We describe these in further detail below.

Seroprevalence of H5N1 antibody among service members deployed to countries with human H5N1 infections. Utilizing pre- and post-deployment health assessment forms and deployment rosters, AMSA was able to identify a cohort of 1000 service members who deployed to Thailand, Indonesia, Vietnam, or Cambodia during periods when there were avian and human H5N1 cases among the local population. AMSA linked the deployment data to specimens in the repository for which the pre-deployment specimen was drawn prior to the deployment and the post specimen was drawn within 365 days from deployment return. Specimens were sent to the Southern Research Institute where hemagglutination inhibition assays and confirmatory microneutralization assays for H5N1 Clade 1 and 2 viruses was performed. Results showed approximately 1 percent of the study population was seropositive to H5 antibody prior to deployment, likely due to cross-reactive antibody. Out of the 1000 subjects tested, only 2 subjects seroconverted during deployment to Thailand using a 1:40 antibody titer cutoff. No known exposures or respiratory illnesses were reported for these two subjects during or after the deployment. These cases of seroconversion may be due to cross-reactive antibody or false positives. Overall, AMSA investigators found no significant risk of H5N1 infection during deployments to countries with human H5N1 activity.

Evidence of prior immunity against influenza among recruits. A random sample was identified with 1000 recruits who had a MEPS specimen

[6] The study was supported by pandemic influenza preparedness funds.

collected in 2005. Serum specimens were tested for evidence of previous infection by the influenza H3 and H1 strains circulating during the previous year. The Southern Research Institute tested the specimens by hemagglutination inhibition assay. Results showed approximately 43 percent and 66 percent of recruits were seropositive for H1 and H3 antibody, respectively. Thirty-two percent of recruits were seropositive for antibody to both viruses. No seasonality for seropositivity to either virus was found. Assessment of demographic and geographic factors associated with seropositivity was reported ongoing through February 2008.

Prolonged cough in service members deployed to Afghanistan. In early 2007, anecdotal reports from U.S. health care providers in Afghanistan surfaced that a large number of U.S. service members were experiencing prolonged episodes of cough. These reports led to the consideration of widespread administration of the new acellular pertussis vaccine. In response, Preventive Medicine assets at CENTCOM and Afghanistan asked AMSA and GEIS to conduct serological testing to determine the likely etiology prior to determination of vaccine policy. A study was initiated using pre and post deployment serum specimens to determine the seroconversion due to common respiratory pathogens during deployment to Afghanistan. Specifically, seroprevalence of IgG and IgA antibody to *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Bordetella pertussis*, and Para-Influenza virus (PIV), the seroprevalence of IgG and IgM antibody to Adenovirus and Respiratory Syncytial Virus (RSV), and the seroprevalence of hemagglutination inhibition antibody to Influenza among U.S. military service members before and after deployment is being determined.

The results will serve to inform military vaccination and force health protection policy and should serve as a basis to set priorities among DoD respiratory pathogen research in the future.

Military and civilian researchers are main users of the DoDSR. In addition to AMSA analysts and service public health surveillance hubs,

military and civilian researchers make up the main user group of DoDSR specimens. Within the DoD, researchers and policy makers from the following organizations have used specimens from the serum collection: Walter Reed Army Institute of Research, the US Army Medical Research Institute for Infectious Diseases, the Military Vaccine Agency, the Global Emerging Infections Surveillance and Response System, the Air Force Institute for Operational Health, the Navy Environmental Health Center and the Navy Health Research Center. Because remote access to DMSS is not authorized, nor is it technically efficient with existing architecture, requests for data or specimens submitted by both internal (i.e., AMSA) and external (i.e., unaffiliated) entities and specimens are subject to the same review and handling process.

DEFENSE MEDICAL SURVEILLANCE SYSTEM

As described earlier, DMSS was created in 1997 to provide tri-service medical surveillance out of the existing Army Medical Surveillance System. DMSS is a relational database that links individual health, personnel and serologic data together to support department-wide public health and preventive medicine operations, and which is to receive "(a)ll theater medical surveillance and treatment data collected by the services, the Unified and Specified Commands, and the individual commands with the Services…" (ASD(HA), September 30 1999, para 5).

The DMSS is a longitudinal surveillance database. As such, it is a unique tool because it relates service member-level information from various Department sources and retains a longitudinal record spanning an individual's service career. The Defense Medical Epidemiology Database (DMED) is derived from DMSS, providing select DMSS data which are de-identified and remotely accessible to DoD members outside of AMSA. A description of the chronology over which the various data elements became integrated into the DMSS is depicted in Figure 4.3.

DMSS has gradually integrated a broader range of data. The Army Medical Surveillance System (AMSS), the predecessor system to DMSS, was brought online in 1990; it became the DMSS in 1997. Since 1990, the

database has gradually integrated a broader range of data from individual service members into a permanent central longitudinal data store and to date includes 401 million rows of information including:

- personnel and demographic (all persons in the active and reserve components, and civilian applicants),
- deployment rosters for the first Gulf War and major deployments since then,
- health assessment questionnaires administered before and after major deployments (DD2795, DD2796, DD2900),
- results from HIV tests,
- information on applicants and inductees to military service from Military Entrance Processing Stations (MEPS),
- inpatient and outpatient medical encounter data for active component,
- activated reservists and National Guard service members,
- immunizations,
- reportable medical events (in garrison),
- characteristics of the serum repository specimens,
- casualty information and heath risk appraisals collected by CHPPM for the Army until 2003. (According to AMSA analysts, transmission of casualty data to DMSS was discontinued in 2003 because of security concerns related to Operation Iraqi Freedom.)

As of January 2008, 311 million rows of data in the aforementioned categories have been validated as belonging to identified military service members (the remaining data are from separated service members, beneficiaries and non-military member applicants).

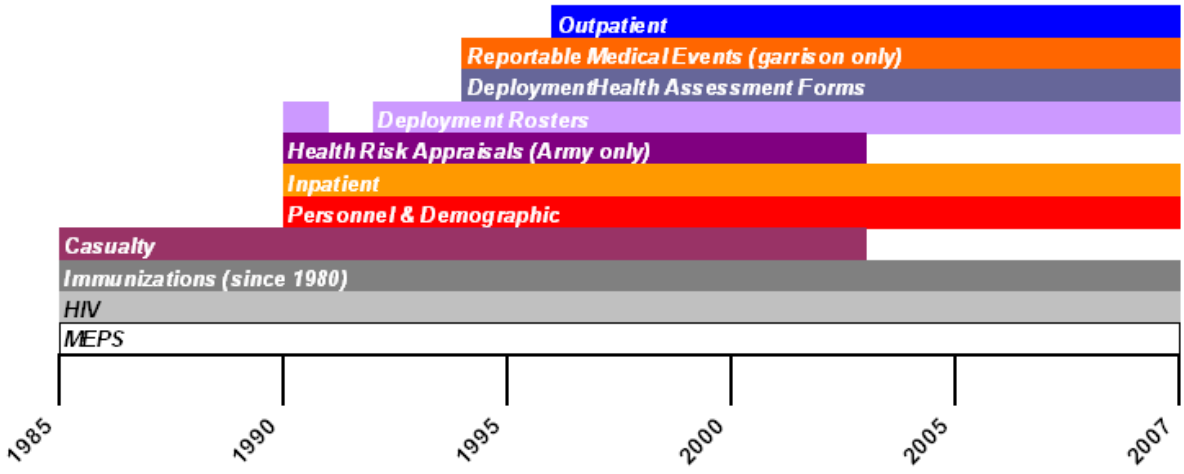
The Defense Manpower Data Center provides monthly feeds to DMSS of personnel and demographic information and deployment roster files for all services from 1990-2007. DMSS receives its information on military applicants and inductees from the Military Entrance Processing Command for all services on a monthly basis and has data archived starting in 1985 (and continuing to the present). DoD's Executive Information Decision Support sends inpatient and outpatient data files to DMSS on a daily basis for all services and has these data archived from 1990 and

1996, respectively, with outpatient data arriving on a monthly basis for outsourced care. Health assessment forms completed pre- and post-deployment have been included in DMSS since 1994 for all services.

Military Treatment Facilities have provided reportable medical events data captured in garrison to DMSS daily since 1994. HIV test results from contract testing laboratories are fed into DMSS weekly and the data reach back to 1985.

The Defense Enrollment Eligibility Reporting System has provided immunization data to DMSS for all services on a monthly basis since 1990 and data were retrospectively loaded, reaching back to 1980. Lastly, health risk appraisals administered by the CHPPM to Army members only, have been archived and stored by DMSS for the years between 1990 and 2003.

Figure 4.3.
Data Integrated into DMSS from Inception to December 2007



Comparison of Surveillance Data Requirements and DMSS Capabilities

A review of DoD policy (DoDD 24, October 24, 2004; DoDI 6490.03, August 11, 2006) reveals only very limited detail regarding the exact data elements required to fulfill all medical surveillance requirements.

To review quickly, the mission of the DMSS was articulated in 1999 as being a tri-service *medical surveillance* tool (ASD(HA) memorandum). Also, according to 2004 policy on comprehensive health surveillance, the definition of "medical surveillance" is "the ongoing, systematic collection, analysis, and interpretation of data derived from instances of medical care or medical evaluation, and the reporting of population-based information …."(DODD 6490.02E, October 21, 2004, para 3.3). The mission obviously drives the types of data that should be collected, analyzed, interpreted and reported. In order to assess the full range of medical surveillance data requirements, we combed current DoD policy regarding deployment health surveillance and comprehensive health surveillance and formulated the following list:

- instances of disease or injury ([a], para 4.4)
- patient encounters - inpatient and outpatient (DoDI 6490.03, para 4.2)
- reportable medical events ([b], para 4.2)
- medical treatments ([a], para 4.4)
- preventive medicines ([a], para 4.4)
- immunizations ([a], para 4.4)
- deployment location data ([b], para 4.2)
- lifestyle data ([a], para 4.4)
- combat casualties ([a], para 4.5.1)
- stress-induced casualties ([a], para 4.5.1)
- individual health status ([a], para 4.4)
- disease and non-battle injuries ([a], para 4.5.1)

[a] DoDD 6490.02E [b] DoDI 6490.3

According to DoD policy on comprehensive health surveillance, surveillance data must span the entire period of service of military members, and must be transferable to the VA. The data must be timely, and analyses from the data must inform commanders about the health of the force in order to appropriate determine risk and countermeasures. Finally, health surveillance activities must be prioritized based upon

the greatest benefit to Force Health Protection planning, response and decision-making (DODD 6490.02E, October 21, 2004, paras 4.4 and 4.5).

In addition to the items described in the list above, all captured in DoD policy, the AFHSC Concept of Operations also specifies that Individual Medical Readiness reporting will now also be encompassed by AFHSC, with the implication that such data would be linked to DMSS. Also, our interviews suggested additional data elements that are not included in current policy but that could be valuable for medical surveillance and other purposes, e.g., laboratory data from medical records.

DMSS provides a robust database for surveillance data in garrison settings but does not capture all data elements needed for deployment surveillance. Table 4.4 provides a detailed comparison of medical surveillance data requirements specified in DoD policy and the data capabilities currently resident in DMSS, in both the garrison and deployment-related context. It also depicts potential new surveillance data items (boxed areas on the table).

Table 4.4.
Medical Surveillance Data Required by DoD Policy and Contained in DMSS

Type of data	Garrison		Deployment	
	Required?	In DMSS?	Required?	In DMSS?
Demographic, administrative	YES	YES		
Location	YES	YES	YES	**
Inpatient	YES	YES	YES*	NO
Outpatient	YES	YES	YES*	NO
Pharmacy	YES	YES	YES	NO
Laboratory	NO	NO	(N/A)	
Reportable Medical Events	YES	YES	YES	NO
Individual Medical Readiness (TMR)				
Immunizations	YES	YES		
Periodic Health Assessment	NO	NO		
Dental readiness	NO	NO		
Deployment laboratory tests	NO	NO		
No deployment limiting condition	NO	NO		
HIV test result	YES	YES		
Casualty	YES	NO		
Deployment health forms				
Lifestyle	NO	NO		

** Includes DNBI*

***Deployment rosters (unit locations) are included in DMSS; specific individual location data are not.*

As indicated by the table, DMSS is a robust longitudinal surveillance database, particularly for data collected in garrison settings. Much of this information is relevant to deployment health, e.g., the deployment health assessment forms and medical encounters that may follow deployments. In terms of garrison-based data:

- The sources of demographic, administrative and location characteristics in DMSS (starting at the top of the box in Figure 4.4) are described in earlier in this chapter.
- Garrison patient encounter information is generated by DoD's Composite Health Care System and stored by DMSS in the form of Standard Inpatient Data Record files describing inpatient medical diagnostic information and Standard Ambulatory Data Record files for clinical diagnostic information from ambulatory care visits. There are additional data available from such records but not yet linked to DMSS, e.g., vital signs, nurses' notes.
- Information on garrison-based preventive medicines is captured in medical records and pharmacy claims data by AHLTA, the military's current electronic health record and the Pharmacy Data Transaction Service (PDTS), respectively. DMSS acquisition of pharmacy data was just underway at the time of this study.
- Laboratory data are not captured in DMSS.
- Reportable medical events in garrison are captured in service-specific systems and fed into DMSS.
- Individual medical readiness indicators (see Chapter 3 for further details of this system) are captured and tracked in service data systems, and all but immunization data (which resides in DEERS) are unavailable to DMSS. DEERS data feed into DMSS.
- The HIV test result for a service member is captured by the HIV testing laboratories and is fed into DMSS.
- Casualty information was fed into DMSS through 2003, though is no longer captured because of security issues.
- Lifestyle factors are captured by service-specific systems, although these are not fed into DMSS.

There are opportunities, nonetheless, to capture more garrison-based data to enrich the medical surveillance and other applications of DMSS, e.g., laboratory data (if these can be standardized sufficiently), additional individual medical readiness indicators, and information related to lifestyle (e.g., behavioral risk factors); most of these are indeed specifically cited by policy as relevant for purposes of medical

surveillance. Policy from 1999 specifically calls for the TRICARE Management Activity to provide "unrestricted access to applicable Military Health System data"(ASD(HA) memorandum, 1999, para 6) for DMSS. The same memorandum also called for DMSS to receive "all theater medical surveillance and treatment data…"(para 6). Beyond these medical surveillance data elements are the array of additional occupational and environmental surveillance data (comprising the other piece of "health surveillance"), which are also not captured by DMSS. The Concept of Operations for the new AFHSC specifies that such data should ultimately be linked for robust comprehensive health surveillance purposes.

Moreover, measurements of theater-based disease and non-battle injury, reportable medical events, medical treatments, and deployment locations are required in established DoD policy but not currently captured in DMSS. We find for deployment-related data:

- DMSS stores deployment rosters (general theater locations, by unit) for all major deployments since the first Gulf War. However, the location of individuals is not guaranteed from unit-level location data. Detailed individual location data is stored in classified data systems (JMeWS).
- Deployment medical encounter information from a theater of operations – including inpatient, outpatient and disease and non-battle injury - comes from the Armed Forces Health Longitudinal Technology Application – Theater (AHLTA-T) and the Joint Medical Workstation (JMeWS), which are classified, and hence the data are not available to DMSS.
- No pharmacy or laboratory data are linked from theater into DMSS.
- In theater, reportable medical events and disease and non-battle injury (DNBI) data ultimately archived by the JMeWS system. The DNBI system generates daily counts of illness and injury by individual and diagnostic code and aggregates these into broad medical categories determined by the Joint Chiefs of Staff. The use of a classified information system, Theater Medical Information Program, within JMeWS, to store DNBI data has been cited as precluding connection and data sharing with the DMSS since DMSS currently resides in an unclassified environment. Yet,

we learned from several of our interviewees that the only data fields that are actually classified are those relating to daily locations and not health and DNBI data fields.

- Theater-based casualty information is considered sensitive and is not made available to DMSS.
- Deployment health forms are all sent to AMSA via the services and components, for both the pre- and post-deployment health assessment form as well as the post-deployment health reassessment form, as described in Chapter 3.

Uses and Users of DMSS

Access to DMSS appears to be limited to users physically located at AMSA. Written AMSA guidelines and procedures for accessing and general use of DMSS data apparently do not exist. Data within DMSS are obtained from many sources and some are used subject to the restrictions of various data use agreements, which may be interpreted to restrict the further use or sharing of this data with external customers. According to AMSA analysts, no formal policies have been developed or articulated regarding use and access of data sources for which DMSS is the sole custodian (e.g., deployment forms data).

In an article describing the DMSS and DoDSR (Rubertone and Brundage, December 2002), data access is described as being limited to on-site members of AMSA staff, including AMSA responses to telephonic or written requests for special analyses. According to AMSA analysts, the use of DMSS data by affiliated analysts, under current technical limitations, functionally requires co-location of the affiliated analyst with AMSA staff. The Deployment Health Support Directorate, a sub-directorate within the structure of the ASD(HA)'s Force Health Protection and Readiness Division, maintains an on-site analyst who performs queries of DMSS data and who is able to perform analyses of data that reside principally on the ASD(HA) systems by manually transporting the data across facilities. Another affiliated analyst from WRAIR is analyzing mental health data from DMSS.

Specific analyses have been conducted in support of information required to inform policy decisions by the Defense Health Board, Office

of the Army Surgeon General and the Army Proponency Office for Preventive Medicine.

Several of those interviewed outside of AMSA remarked that it was extremely difficult to get data back from DMSS once it was provided by the services, and this situation potentially has caused missed opportunities. It must be noted that the ASD(HA) Memorandum of 1999 called for data sharing between DMSS and the services.

A wider range of military users can access the more limited derivative online DMED database. Analyses of DMSS data are also available through hard copy and on-line AMSA publications, i.e., AMSA's Medical Surveillance Monthly Report. The MSMR provides routine summary analyses of select data captured by DMSS, including monthly updates of deployment health assessments, reportable medical events, febrile respiratory illness in military training centers, and medical conditions of surveillance interest as reported by MTFs. The MSMR also includes reports of recent outbreaks, quarterly force health reports and other military health related topics of special interest.

CHAPTER HIGHLIGHTS

To summarize some key findings regarding both DoDSR and DMSS, we found that:

- The main uses of the DoDSR have been for research, and the main users of the repository and data assets have been limited to a relatively small number of DoD and civilian researchers.
- While DoDSR and DMSS have been used for other important purposes such as special HIV surveillance studies, public health investigation and clinical support, our interviews and analyses suggest the potential for far more robust use: in particular for deployment medical surveillance that includes data from deployed settings, and broader health surveillance (i.e., to include medical and occupational and environmental health surveillance in both garrison and deployment settings).

To summarize some key findings about the serum repository in particular, we found that:

- From 2001 through January 2008, specimens from the DoDSR were requested fewer than 200 times;
- The missions of the serum repository as defined by DoD policy include medical surveillance, clinical diagnosis and epidemiological studies of all illness relating to military service, yet the staff at AMSA perceive its main mission to be one of surveillance;
- The serum repository has a large number of specimens that have become de-linked from the individual donor; there is no apparent policy in place to determine how long to store the specimens or what to do with them;
- The repository has no apparent guidelines explaining the decision making process for allowing use of the sera;
- The sera are stored at -30 degrees Celsius rather than at a colder temperature more consistent with current industry standards, e.g., -80 degrees Celsius (a point that becomes more important in our comparison to other repositories);
- Most uses of the repository to date have been for research studies (as opposed to surveillance uses);
- The ability of the sera to support the repository's given missions has not been evaluated since the Armed Forces Epidemiology Board recommendation of 2005 (which recommended archiving of WBC for preservation of genetic material), and action has not been taken in response to this recommendation
- There does not appear to be a mandate for any joint body to routinely and systematically evaluate the value of the sera for surveillance possibilities balancing against resource constraints and emerging threats to the force.

To summarize some key points related to DMSS, we found that:

- There is a disparity between the mission of DMSS as defined in policy and its actual functioning. Specifically, the mission of

DMSS is to provide tri-service medical surveillance. In order to do this, DMSS needs adequate data elements fed in a timely manner and across a service member's career. DMSS is not currently receiving many relevant data elements, which would be necessary though not necessarily sufficient to address all deployment health needs. For example, theater-level data are not being provided to DMSS because of classification issues, in spite of the fact that Congress called on DoD to re-examine the most appropriate level of classification. And we have presented other examples of this disparity.

- DMSS was to share data across all services; yet we see no evidence that this is being done except in a very limited way through DMED, and several military interviewees complained about the inadequacy of what they perceive as incomplete DMED data;
- Access seems to be limited to users physically located at AMSA, although the data set is unclassified and could ostensibly reside on the NIPRnet. Further, there appear to be no published guidelines explaining why access is limited, to whom it is limited and so forth.

CHAPTER 5. EXAMINATION OF OTHER BIOLOGICAL SPECIMEN REPOSITORIES

To better evaluate potential improvements to the DoDSR, the RAND team examined the characteristics of other repositories in the United States and abroad. Repositories are typically associated with organizations that have specific research interests or surveillance mandates that necessitate storing of biological specimens. Specific details of each repository are a function of their general purpose, the sponsoring organization and underlying research design that led to the repository. Depending upon these factors, the collection, processing, testing and storage of specimens varies across the repositories. The volume and storage conditions of specimens can also be dictated by the purpose and function of the repository.

To understand examine the different repositories, the RAND team developed a framework for the collection, processing, testing and storage of specimens (Figure 5.1). The framework consists of four components – Collection, Processing, Testing, and Storage – each of which includes key variables that affect the usefulness of specimens for different purposes (e.g., research, surveillance). Surrounding each of the components is a colored box representing overarching elements associated with that component. Each of these components is described in more detail below.

In the remainder of this chapter, we first describe the different major blood fractions and the types of standard tests that can be performed with them. Then we describe the framework used in this analysis and discuss each of the repositories.

BLOOD FRACTIONS AND TESTING

As mentioned in Chapter 2, Congress legislated in 1997 that DoD collect blood specimens pre- and post-deployment. Because DoD was already collecting blood for HIV testing and storing sera, it decided to use the extant repository as currently configured to fulfill the newer legal requirement. Since then, both Congress and DoD have questioned the continued use of the repository to fulfill pre- and post-deployment

health surveillance functions. The ASD(HA) asked the Armed Forces Epidemiology Board to investigate whether or not other specimens should be stored, and the board concluded that there may be utility in storing white blood cells (for preservation of genetic material).

As described in this section, white blood cells can be either purified and stored as the buffy coat fraction or captured in whole blood; whole blood can be stored either dried or liquid. In all of these cases, DNA and RNA can be captured in adequate amounts for today's technology, and even perhaps tomorrow's, to use in genetic testing.

As further discussed, dried blood spots have several advantages, one being simple collection, processing and storage along with long term stability of DNA. Whole blood provides buffy coat which in turn provides even larger amounts of DNA and RNA for genetic testing than dried blood spots.

Blood is one of the most common biological specimens collected and used for diagnostic tests, and is also commonly used for surveillance and research purposes. Blood is a complex mixture of cells, proteins, metabolites, and many other substances. Cells make up approximately 45 percent of the total human blood volume. Plasma, the liquid component of blood in which the blood cells are suspended, makes up about 55 percent of total blood volume. Serum is blood plasma without fibrinogen or the other clotting factors. The vast majority of blood cells – more than 99 percent – are erythrocytes (red blood cells, RBC). Thrombocytes (platelets) make up approximately 0.5% of cellular blood components, and leukocytes (white blood cells, WBC) make up approximately 0.3%. The only human blood cells that contain nuclei and are suitable for use in preparation of genomic DNA are WBC.

Which specimens are collected, and how they are stored, is often driven by the purpose of the collection or the purpose of the original study that collected the specimens. Depending on the intended use of the specimens, biological repositories store either whole blood or purified blood components (i.e., blood fractions). Whole blood can be collected and stored either in liquid form or as dried blood spots (collection on filter paper). Repositories also store purified fractions from whole blood, which can commonly include serum, plasma, and WBC. During

separation, WBC and platelets typically are collected together in a fraction called the buffy coat and are often stored in this form. In some cases, repositories also store RBC.

Blood tests can be grouped into a range of categories, including clinical biochemistry, hematology, immunology, microbiology and genetic. In general, serum and plasma can both be used for a wide range of biochemistry, immunology and microbiology tests, although serum is often the preferred fraction, since the clotting factors in plasma can complicate some tests. Plasma is required for blood clotting tests and for some other specific tests like the fasting plasma glucose test for diabetes. Whole blood is required for some hematology tests such as complete blood counts and can also be used for a variety of biochemistry, immunology and microbiology tests.

Genetic-based tests require DNA or RNA, depending on the type of test. This generally requires collection of WBCs, either in purified form or in whole blood. Both dried blood spots (DBS) and liquid blood can be used for genetic studies. DBS have long been used for newborn screening and large population-based repositories (Schafer et al., 1996; Hsu et al 1992). DBS have the advantage of simpler collection, processing and storage requirements (-20°C, humidity control, small space requirements) and long-term stability of the DNA (Ref: UK Biobank specimen handling and storage group protocol and recommendations) but supply a smaller quantity of DNA. Since the size of DBS specimens is typically small, yielding limited amounts of DNA, they may not be suitable for whole-genome amplification (Steinberg et al., 2002).

The buffy coat from processed whole blood can be stored or further processed to purify specific subsets of WBCs, DNA, or RNA. Buffy coat provides more volume of material than DBS for genetic studies. Finally, WBCs can be turned into immortal cell lines to provide long term, high volumes of genetic material. This can be done on freshly purified WBCs or on blood properly stored with cryoprotectant in liquid nitrogen.

FRAMEWORK FOR SPECIMEN COLLECTION, PROCESSING, TESTING, AND STORAGE

As shown in Figure 5.1, the framework for understanding the characteristics of repositories consists of four components: collection, processing, testing, and storage.

The specimen collection component of the framework consists of who the specimens are collected from, when and where they are collected, the purpose for which they are collected (i.e, why), and the collection method used (i.e, how). The overarching elements associated with the collection component of the framework are informed consent and Institutional Review Board (IRB) approval. The system of federal protections pertaining to the ethical involvement of people as participants in medical research, including research with biological specimens, involves review of the proposed research by an IRB and a determination of the need for the informed consent of the research participant (see HHS regulations at 45 CFR part 46 and DoD Directive 3216.02).[7] The IRB looks after the participants' rights and the ethics of the research study. The IRB process can vary across institutions and nations, with some countries having a single national board that address all research studies involving human participants. IRB approval can be implemented at different points in the life of a specimen. Most often an initial IRB approval is required prior to the start of a research study, but additional IRB reviews can occur to provide periodical review of the study to ensure that appropriate steps are being taken to protect the participant's rights and welfare. Once specimens are stored in a

[7] 45 CFR part 46 is the Common Rule that addresses the protection of human research participants in the federal government. It is a set of identical regulations codified by 15 agencies, of which DoD is one. (The Office of Science and Technology Policy (OSTP) is a signatory to the Common Rule, but did not codify it because it does not conduct or sponsor research. The Common Rule also regulates research conducted or sponsored by two other agencies that are not signatories but are bound to HHS regulations and therefore the Common Rule: the Social Security Administration and the Central Intelligence Agency.) The Common Rule has to be upheld and is enforceable by law. DoD Directive 3216.02 is the Department of Defense codification of the Common Rule and is equivalent to it.

repository, IRB approval is also usually required for the distribution of specimens for new research studies and to investigators who were not part of the original study. In addition, some repositories have established their own IRBs to oversee access and storage conditions of specimens, and other general repository functions.

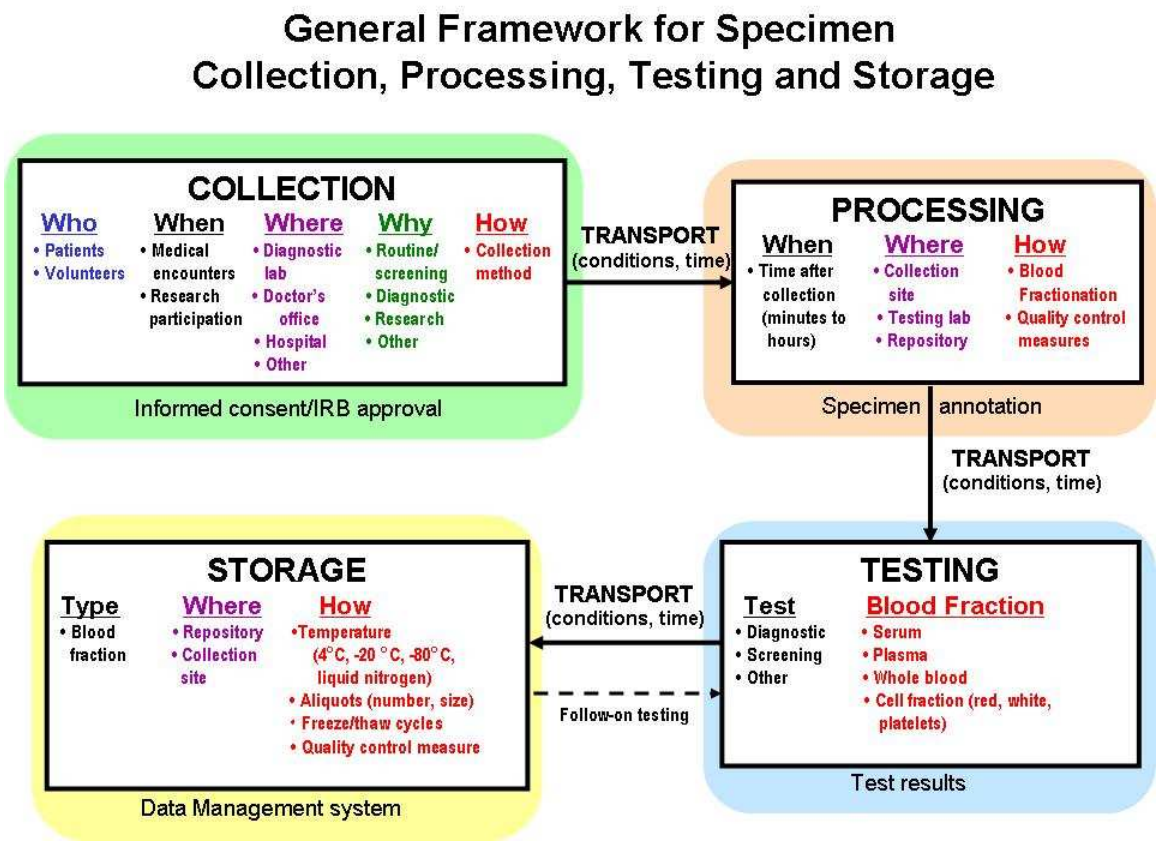
The specimen processing component of the framework includes the processing method (e.g., how blood is fractionated), as well as when and where the specimens are processed. Some specimens may need to be transported from the collection site to the laboratory/facility where they will be processed. The over-arching element associated with specimen processing is the annotation that accompanies each specimen.

Once the specimen has been processed, testing may be conducted to acquire information about the specimen and the person from whom it came. In some cases, the testing is done at the same facility as the processing; in other cases, testing is done at a different site. The results of tests done on specimens are the over-arching element associated with testing.

Finally, once the specimen has been processed and all of the initial testing has been completed, the specimen is put into storage at a biological specimen repository. The storage component of the framework includes the type of specimen being stored, and where and how the specimen is stored. The data management system at a repository is the over-arching element associated with storage. The conditions and time involved in the transport processes between collection, processing, testing, and storage introduce additional variables to the framework.

We chose a variety of different repositories that collect blood products to compare with DoDSR, to cover the variables described here.

Figure 5.1.
Framework for the Evaluation of Serum Repositories



SIX REPOSITORIES FOR COMPARISON

We collected data from six repositories to compare with the DoDSR. These include:

- NHANES: A U.S. federally-funded biological specimen repository for clinical, epidemiological and genomic research, drawn from a nationally representative population sample
- UK BioBank: A non-U.S. government- and foundation-funded prospective epidemiological study designed to include biological specimens and study morbidity and mortality of chronic and other diseases
- NHLBI: A U.S. federally-funded repository storing specimens from multiple individual research projects

- Two U.S. military repositories with purposes of HIV research (US Military HIV Research Program Repository at Walter Reed) and remains identification (DoD DNA Remains Identification Registry at the Armed Forces Institute of Pathology)
- deCODE: A private repository designed to develop drugs and diagnostics based on genomic studies of the population of Iceland.

This section summarizes the general characteristics of each repository, including information connected to the framework presented previously (Fig. 5.1). A summary of the general characteristics across the repositories is presented in Table 5.1 and a summary of the storage and retrieval conditions of each repository is presented in Table 5.2.

National Health and Nutrition Examination Survey (NHANES)

Mission. The Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS) conducts the National Health and Nutrition Examination Survey (NHANES). NHANES began in 1959 after the National Health Survey Act of 1956 (NHANES, 2008) established a continuing health survey of the people of the United States. The mission continues to be to collect information about the health and diet of the American people, including population-based information on diseases and associated risk factors, e.g., nutritional, behavioral, environmental, genetic. (CDC NCHS, 2008) It provides an in-depth survey and assessment of health status of Americans through personal interviews, standardized physical exams, and laboratory tests. NHANES is the only nationally representative health survey with linked biological specimens in the United States.

Collection. Currently, the NHANES surveys collect information over the course of two years on a nationally representative sample (approximately 5,000-7,000 participants per year). Initially NHANES was a periodic survey, but as of 1999, NHANES has become a continuous annual survey. NHANES collects specimens annually but only releases data files every two years (mostly due to disclosure and reliability issues), thus the data release cycle for the continuous studies is described as NHANES

1999-2000, NHANES 2001-2002, etc. Though the survey content can change every two years, the laboratory methods are held as constant as possible across cycles to be consistent with the data release cycles; and to provide the potential for combination of two or more 2-year cycles for greater statistical reliability (CDC NCHS, 2008).

Individuals are recruited from various counties and geographic locations. A mobile examination center (MEC), which includes a laboratory, travels to each location throughout the 2-year survey period to interview participants, conduct a physical examination, and collect the specimens. Currently, NHANES collects blood, urine, other specimen types (such as vaginal swabs from consenting females) from each participant. Between three to eleven blood collection tubes (number and size/type of tubes differ by age) are collected from each individual and are processed in the MEC into serum, plasma, and whole blood aliquots. Whole blood specimens for DNA purification are collected from consenting adults age 20 or older.

Storage and Processing. Some of the vials are stored at 4°C depending on the intended laboratory test, while most serum/plasma vials are stored at -20°C or -30°C till shipment to CDC or a contract laboratory. Most specimens are shipped once a week. There are currently 23 contract or CDC laboratories that conduct a variety of laboratory tests. In the current cycle, three to fifteen vials of serum (0.5-1.0 mL aliquots) and plasma (0.5 mL aliquots) per survey participant are sent to the CDC and ASTDR (the Agency for Toxic Substances and Disease Registry) Specimen Packing Inventory and Repository (CASPIR) in Lawrenceville, GA for long term storage in liquid nitrogen (-196°C). CASPIR has approximately five million specimens in storage, of which approximately 550,000 are from NHANES. Specimens that have been sent from laboratory testing during the survey are returned to a Fisher BioService Repository (located in the DC metro area) operated under NCHS contract. These specimens have gone through at least two freeze-thaw cycles and are subsequently stored at -80°C. Researchers who submit proposals for use of the NHANES specimens are requested to utilize these specimens, if possible. Those who need pristine never

thawed specimens must justify the use of these specimens that are stored at CASPIR.

Testing. NHANES conducts a standard set of approximately 550 laboratory tests on different blood fractions and other biological specimens.[8] These tests include standard clinical assessments such as biochemical, hematology and immunology based tests. Results from these tests are provided to the participant in a hard copy report of findings, other laboratory tests are for research purposes and include a variety of public health topics (such as environmental health). During the second phase of NHANES III (1991-1994), NHANES 1999-2002, and NHANES 2007 to present, the laboratory protocols has included the collection of DNA specimens. The NHANES III specimens (cell lysates from Epstein Barr transformed cell lines) are stored in liquid nitrogen at CASPIR. Purified DNA specimen aliquots from NHANES 1999-2002 and 2007 onward are stored at -80°C at the National Center for Environmental Health Molecular Biology laboratory, which is the processing laboratory for NHANES DNA specimens. These specimens are being used for genetic research proposals with proposals accepted twice a year. [9]

Use of Specimens. Starting in 1999, all participants must complete a separate informed consent form allowing for the use of their specimens in future research. Separate consent for genetic research is obtained from individuals age 20 and older. All proposals for use of the NHANES specimens must undergo a technical review and a CDC Ethics Review Board review. Proposals for DNA specimens must also be reviewed by a Secondary Review Panel which performs a programmatic review. NHANES usually approves 5-8 non-genetic proposals a year from CDC, other federal agencies, and non-federal investigators, with approximately 5,000-10,000 specimens distributed with each proposal.

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[8] Tests vary by the age and gender of participant. For general tests, see http://www.cdc.gov/nchs/about/major/nhanes/testcomp.htm

[9] http://www.cdc.gov/nchs/about/major/nhanes/reserach proposal guidelines.htm

Laboratory test results are publicly released at the end of the two year data collection cycle with the questionnaire and examination data; unless the results are determined to be a disclosure risk (i.e., sexually transmitted infection test results for adolescents are considered a disclosure risk). Results that are considered a disclosure risk can be accessed in the NCHS Research Data Center. Results from the stored specimen are also released publicly on the NCHS/NHANES website. Genetic test results can only be accessed in the NCHS Research Data Center[10].

The NHANES results are usually available one year after a two-year data collection cycle. There is a nominal fee to investigators of $2 per serum/plasma/urine specimen sent by the repository. For a NHANES III DNA specimen the cost is approximately $6 and $8 for NHANES 1999-2002 specimen. The specimen fee recoups some of the costs associated with the collection and storage of the specimen, and collection and processing of the accompanying data.

United Kingdom BioBank

Mission. UK BioBank is a repository funded both by government (United Kingdom Department of Health and National Health Service) and by private charities (Wellcome Trust, British Heart Foundation and Cancer Research UK) (UK BioBank, 2008). The concept of the BioBank was initially discussed in 1999, with feasibility studies completed in 2001. The BioBank is a research initiative with the goals of improving the prevention, diagnosis, and treatment of a wide range of serious life-threatening chronic illnesses, such as cancer, heart diseases, diabetes, arthritis and forms of dementia. The UK Biobank is intended to be used as a prospective epidemiological resource, in part to support a variety of different types of studies, including nested control studies, case control studies, etc. The UK BioBank posts its main protocol online and

[10] A list of currently available NAHNES III SNPS for secondary data analysis can be obtained from: http://www.cdc.gov/nchs/about/major/nhanes/research proposal guidelines.htm

many of the details presented here are available in this protocol (UK BioBank, 2008).

Collection. In April 2007, the UK BioBank began the main phase of recruitment, collecting data and biological specimens from a large sample of people in the UK. The goal is to recruit up to 500,000 people between the ages of 40-69 from all over the UK. The UK BioBank identifies individuals through the UK National Health Service Records, once an "assessment center" is set up, UK BioBank invites all appropriate individuals living within a 10 mile radius to participate. Over the initial course of the study (2007-2010), 35 centers will be set up, with six centers being open at any given time and each center being open for six months. Participants are reimbursed for any travel costs. Personnel at the clinics complete an informed consent process with potential participants, and then conduct a health questionnaire, and collect physical measurements and biological specimens from each participant in a process that takes approximately 90 minutes. There are also provisions that allow researchers to ask and obtain additional specimens from particular participants in the future, depending on research objectives.

Processing. The study collects blood and urine from each participant. Six different bar-coded vacutainer tubes of blood and one container of urine are collected. At the assessment center, prior to shipping, one tube of blood is centrifuged to separate plasma and one tube is centrifuged to separate serum. All of the tubes are sent daily, via overnight courier, to a centralized processing center. Five of the blood specimen tubes and the urine tube are stored and transported at 4°C until further processing on the next day. Temperature integrity is maintained by a temperature sensor that records temperature every ten minutes, while the specimen is in transit. One blood specimen tube is collected in acid citrate dextrose and transported at 18°C. At the central processing center, each tube is processed and then immediately tested or stored. Hematology tests are run on one tube, since those tests cannot be completed on stored specimens. The rest of the tubes are separated into specific fractions (plasma, buffy coat, RBC, serum, whole blood), split into 1.4 ml aliquots, and stored at either -80°C or in

liquid nitrogen, usually a 60/40 split respectively. The tube collected in acid citrate dextrose is processed with a cryoprotectant and stored in liquid nitrogen with the intention of potentially purifying the lymphocytes and converting them into immortal cell lines.[11]

Storage. The BioBank repository is a "two archive" system. The first archive is the "working archive" and can hold up to nine million specimens at -80°C, and has an automated, robotic, retrieval system. The automated retrieval system operates such that specimens are never exposed to temperatures above -20°C until after retrieval. In addition, the robotic retrieval system helps with accurate storage and retrieval of specimens. The system includes a computerized inventory, and when the robotic system retrieves a specimen, it checks that specimen against the bar code and verifies it is the correct specimen. The second archive is the "storage archive" which stores specimens in liquid nitrogen (-196°C) and has a storage capacity of six million tubes. These specimens are manually retrieved.

One of the goals of the UK BioBank is to facilitate genetic research, including studying the relationship between genes and the environment.[12] As a result, the working group that developed guidelines for specimen collection and storage considered many different sources of genetic material. The buffy coat fraction containing WBC is the primary fraction being stored for genetic testing. The blood stored in cryprotectant in liquid nitrogen offers a potential to study very large quantities of genetic material by making the cells immortal, thereby giving researchers an unlimited supply of genetic material for research. However, that process is expensive and will only be performed on specific specimens of interest.

Use of Specimens. Researchers from academic, commercial, charity and public sector organizations, both nationally and internationally, can request access to specimens stored at the BioBank. Currently, UK

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[11] Immortalized cell lines offer the greatest opportunity to harvest large amounts of genetic material for research studies.

[12] Sample Handling & Storage Subgroup Protocol and Recommendations (March 31, 2004)

BioBank scientific protocols and operational procedures, as well as proposed uses of the repository specimens, are reviewed by an appropriate ethics committee, e.g., Central Office of Research, National Health Service Research Ethics Committee (UK BioBank Ethics and Governance Framework, 2007). As a part of the access policy, researchers will be charged a nominal fee for specimens. During the 2006 fiscal year (during which UK BioBank conducted pilot studies), UK BioBank had a total operating cost of £4,038,748 (approximately $8 million as of the writing of this report) of which £22,041 (approximately $43K as of the writing of this report) was governance costs. The operating cost covered some of the development costs and the pilot studies (recruitment, collection, testing and storage of specimens).

National Heart, Lung, and Blood Institute (NHLBI)

Mission. The National Institutes of Health's National Heart Lung and Blood Institute (NHLBI) supports programs in basic research, clinical investigations and trials related to diseases of the heart, lung, blood vessels, blood, and sleep disorders. Within NHLBI, the Division of Blood Diseases and Resources manages the NHLBI Biologic Specimen Repository (Biorepository). The NHLBI Biorepository acts as a central repository for specimens collected by NHLBI studies that are performed around the country by various research institutions. The purpose of the NHLBI Biorepository is to facilitate research in the areas of heart, lung, and blood. The mission of the biorepository is to acquire, store and distribute biological specimens to the scientific community using standardized processes and procedures described in the NHLBI Biorepository Operational Guidelines. There are approximately four million plasma, serum, cellular or tissue specimens. Eighty percent of the specimens are from blood transfusion safety programs[13] and the remaining 20% are from various other NHLBI cardiovascular and pulmonary

[13] NHLBIs Division of the Blood Diseases and Resources, Transfusion Medicine and Cellular Therapeutic Branch has supported various prospective and retrospective studies on blood donors and recipients since the 1970's in an effort to keep the US blood supply safe for transfusions.

programs; with individual study inventories ranging from 4500 to 2.5 million specimens (NHLBI Factbook, 2008). In 2006, $1,031,572 was allocated to the NHLBI Biorepository contractor for repository operations (NHLBI Factbook, 2008). More background information on the repository and the various studies can be found on the NHLBI web site (NHLBI Bio Specimen Repository, 2008).

Collection and Storage. Because the NHLBI Biorepository contains specimens from a variety of different clinical studies, the material type, collection, processing, testing, longitudinal parameters and storage of specimens is varied. Study collections contain different combinations of material types (whole blood, plasma, serum, WBC, platelets, RBC, bronchoalveolar lavage, urine and tissue). Specimens are stored in mechanical freezers at -80°C, in the vapor phase of liquid nitrogen (-135°C to -190°C), or at room temperature depending on the material type and storage medium. In addition, the specimens might be linked to a variety of health information including clinical and laboratory tests result parameters.

For a study collection to be housed in the NHLBI Biorepository, informed consent must be received from all the study participants with specimens in the collection. NHLBI supplies individual studies with language for their informed consent documents to help the studies develop appropriate language for storing of specimens for future research in a repository. In addition, NHLBI provides assistance to research investigators on the information that should be included in an informed consent document regarding the storage and future use of specimens by the scientific community. In addition, NHLBI reviews study documents on describing specimen collection, aliquots, storage, shipping and tracking to assist investigators build study collections that will be of use to the general scientific community.

Use of Specimens. Access to data and specimens at NHLBI depends on which of two study periods a given collection occurs in. The proprietary period lasts until NHLBI receives the study data following a posted limited access data policy (NHLBI Limited Access Dataset, 2008). The open period follows the proprietary (limited access) period -- the duration varies by study type. During the proprietary period, outside

investigators can gain access to a study only by collaborating with the study investigators. During the open period, the specimens are available to the all qualified investigators in the wider scientific community. NHLBI staff initially screen all applications to ensure that the proposals are complete and have the required IRB approval from their home institutions. The NHLBI Biorepository Allocation Committee reviews all requests for specimens during the open period while the parent study (usually the Steering Committee) reviews requests for specimens during the proprietary period. The Allocation committee includes a chair and co-chair with experience in biorepository, the laboratory and epidemiological methodologies, an ethicist, and two ad-hoc members who have expertise in the specific research area under review, and one investigator from the original study that collected the specimens. The committee is a virtual committee, which does not meet in person, and the ad-hoc and original study investigator can change for each new request, or set of requests, for a given study. From 1999-2004 a total of 67,715 specimens were distributed to various investigators.

Division of Retrovirology at Water Reed Army Institute of Research

Mission. WRAIR conducts research intended to support the US Army and DoD to improve biomedical knowledge and technologies. The main mission of the Retrovirology Division within WRAIR is the prevention of HIV-1 disease in the active component. As part of this, they study the epidemiology of HIV globally; develop diagnostic and immunologic assays to support vaccine development; are involved in HIV vaccine development and testing; and conduct research on treating and caring for HIV-infected individuals (US Mil HIV Research Program, 2008) The US Military HIV Research Program Repository stores specimens from patients who have participated in various HIV clinical trials run through WRAIR.

Collection, Processing, and Storage. Currently the retrovirology laboratory has multiple research sites in Africa, South America and Asia. These research sites focus on conducting vaccine trials, with most of the participants being local residents. At each site, whole blood is collected from patients and fractionated into plasma, serum, and WBC, within six hours of collection. These specimens are processed

and stored at -80°C at each research site, after which they are batched and shipped to the United States in liquid nitrogen. Upon arrival they are cataloged and stored in liquid nitrogen in the US Military HIV Research Program Repository. Once specimens arrive at repository they are aliquoted into 1.8mL cryovial tubes. WBC aliquots are stored in liquid nitrogen, while plasma and serum aliquots are stored at -80°C. The repository has approximately 1 million specimens, with 310,000 stored in liquid nitrogen and the rest stored at -80°C. The yearly acquisition rate for WBC is between 15,000 and 20,000, and between 30,000 and 60,000 for plasma and serum specimens.

Use of Specimens. The clinical data associated with each specimen are dependent upon the research protocol. However, generally, demographic and HIV status is collected, and further testing parameters dependent on the research hypothesis. For most studies, longitudinal specimens are collected (baseline, prior to vaccine, post vaccine, etc.) and a variety of tests (HIV, other viral tests, etc.) are completed on the specimens depending on the study protocol.

All the participants in the vaccine and other research trials sign an informed consent form, which includes consent to use their specimens in research, and all of the research study protocols undergo an IRB approval process in the host country. The repository does not have a separate IRB to oversee the storage of specimens. If outside collaborators (those not initially included in the original study protocol) want access to data or specimens, they must propose amendments to the study protocol which would have to undergo an additional IRB review from their home institution and the IRB in the host country, as well as receive consent from principal investigator. Of the few requests granted, the average number of specimens distributed for a given study ranged from 40 to 300. Records are kept of all requests and transactions.

Armed Forces Institute of Pathology - Department of Defense DNA registry

Mission. The Armed Forces Institute of Pathology (AFIP) is a tri-service DoD agency specializing in pathology consultation, education and research as well as a referral center for expert pathology diagnostics

for the U.S. Armed Forces (AFIP, 2008). AFIP houses the DoD DNA Registry, which is used for the identification of human remains. The DoD DNA Registry consists of a laboratory (the Armed Forces DNA Identification Laboratory) and a repository (the Armed Forces Repository of Specimen Samples for Identification of Remains). The DoD DNA registry provides scientific consultation, research and education services in the field of forensic DNA analysis, with the goal of ensuring that "the United States would never again have to entomb the remains of an unknown American" (AFIP DoD DNA Registry, 2008). While the specimens in this repository are not used for research, the repository is included here as another example of a military repository and because of its expertise in the storage and testing of specimens for genetic information.

Collection and Processing. The AFIP DNA repository was established in 1992 and, under DoD Directive 5154.24, collects and maintains blood specimens suitable for DNA analysis from all active component service members, reserve component service members, US Coast Guard personnel, as well as some DoD civilian employees and DoD contractors who support the military in hostile foreign environment (AFIP DoD DNA registry, 2008). To date, the repository has collected and stores over 5 million specimens. Blood is collected either via finger prick or venipuncture and two spots are collected on Whatman filter paper. The specimens are allowed to dry for at least 20 minutes at room temperature prior to packaging in individual shipping pouches with desiccant for shipping. All specimens are supposed to be shipped to AFIP within 10 days of collection.[14] Once they arrive at the repository, specimens are checked for completeness of the personal information provided, to include signature of the donor, to attest to the identity of the donor at collection and acknowledge the reading of the informed consent and privacy act statement. The service member's information is checked against the Defense Eligibility Enrollment Reporting System

[14] See collection instructions available at http://www.afip.org/Departments/oafme/dna/afrssir/

(DEERS) to determine they are eligible for Department of Defense benefits enrollment prior to the specimen being vacuum sealed in individual pouches with a desiccant to keep them dry and are stored in a two-story freezer at -20°C (Gillert, 1998). The specimens are assigned a unique accession number that serves as a location identifier within the repository. Currently, a quality assurance plan is being reviewed to determine if specimens can be stored at room temperature without effecting the yield and quality of the DNA on the cards.

Informed consent, in the form of Privacy Act Statement acknowledgement, is obtained prior to specimen collection. On a case by case basis service members can request to not have their DNA stored based on religious reasons. The blood is stored to be used only in case of remains identification and cannot be used for any other purpose per federal law except in support of a criminal investigation, which requires specific criteria to be met, to include the issuance of a federal court order. In the event of a service member's death, disposition of the card becomes the responsibility of the primary next of kin.

deCODE

Mission. deCODE, a private biopharmaceutical company headquartered in Reykjavik, Iceland, was founded in 1996. The goal of the company is to discover genetic variants associated with increased risk of common diseases, and to applying these discoveries to develop DNA-based tests predicting disease risk, as well as drugs targeting the biological pathways that are affected by these genetic variants. The company conducts genome-wide, population-based gene discovery work using the population of Iceland as its primary study cohort. Approximately 60% of the adult population of Iceland – or 140,000 people – have taken part in one or more or deCODE's gene discovery studies, which covers more than 50 common diseases. Informed consent is obtained from all participants who are asked to participate in research on specific diseases areas, though most also sign an informed consent for their genetic data to be used in cross-disease studies as well. All of deCODE's research protocols are reviewed by the Icelandic medical ethics

committee, a government body that serves in the capacity of a national IRB. All data on individuals used in deCODE's research is anonymized by the Icelandic Data Protection Authority (DPA), a government body; using an encryption system that generates discrete PIN numbers for individuals in order that genetic, medical, and genealogical data can be correlated but protecting the privacy of participants as set out under European Union directives.

Collection. Specimens are typically collected from patients with particular illnesses or disease characteristics, as well as from family members with and without the disease in question. deCODE frequently runs encrypted patient lists from Iceland's national health care service against a nationwide genealogical database built by the company (encrypted using the same key) to select patients who would be most informative for genetic analysis. The PINs of these patients are then sent back through the DPA, decrypted, and the names sent to doctors in the health service who contact individuals and ask them if they would be willing to participate in a particular study. Participants go to an offsite, deCODE-sponsored clinic, where, after signing an informed consent form, five vials of blood is collected and a health questionnaire is administered. The health questionnaires are typically focused around the particular disease/study, with a few broad application questions. Physicians who are involved with a given research program customarily also take detailed and standardized clinical data relevant to the condition under study. All biological specimens and medical information is anonymized via the DPA before being sent to deCODE.

Processing and Storage. deCODE currently stores over 500,000 biological specimens from both Icelanders and foreigners taking part in its studies via collaborations with clinicians in many countries. Virtually all of these specimens are in the form of whole blood and/or purified DNA. From each participant, five vials of whole blood are collected. One vial is processed into purified DNA and aliquoted into an average of ten 2 milliliter tubes that are stored at 4°C. There is no time restriction on storage length for the purified DNA, but the general rule of thumb practiced by deCODE is that if a aliquot of purified DNA

has been stored for less than a year at 4°C, then it can go directly into the research cohort. If an aliquot has been stored longer than a year, it must go through a quality control test before being included in the research cohort. The other four other vials are stored as whole blood in 10 milliliter tubes in their repository, called the Secure Robotized Sample Vault (SRSV), at -25°C. All specimens are bar-coded and encrypted. The SRSV can store tubes in a variety of sizes, in customized racks. A robot pulls specimens from the racks and delivers them through an access port in the side of the SRSV, which helps maintain the specimens at a constant temperature.

deCODE adds anywhere between 12,000 and 60,000 new specimens each year from Icelandic and outside participants. They have created three cross-referencable databases that enables the company to analyze correlations between genetic variations and medical data from participants, in the context of comprehensive nationwide genealogical data assembled from public domain sources. deCODE collects informed consent from all participants. deCODE has longitudinal aspects to its research but it is not standard practice, it is very research project dependent. deCODE does not send out specimens to outside researchers or share raw data with other research organizations. deCODE researchers do, however, provide services to outside researchers in genotyping and structural biology, and the company markets certain technologies and know-how it has developed for protecting, analyzing, and storing large quantities of specimens and data.

COMPARISON OF DODSR AND OTHER REPOSITORIES

As described above and summarized in Tables 5.1 and 5.2, there are a number of important similarities and differences between the DoDSR and other biological repositories. We highlight the following comparisons:

- The DoDSR is by far the largest of all the repositories examined here: its total size and annual rate of specimen acquisition are at least ten times those for the civilian repositories described in this chapter.

- The DoDSR has a wide range of purposes, whereas most of the other repositories serve largely research purposes; only NHANES also has a surveillance mission.
- Similar only to NHANES (general population) and the AFIP DNA Registry (military population), the DoDSR contains specimens that are statistically representative of a defined population, i.e., beyond a research study population; of these, only DoDSR has serial specimens collected from the same individuals, i.e., longitudinal specimen collection and is linked to medical records.
- All six of the comparison repositories, but not DoDSR, store blood-derived specimens from which genetic material (DNA or RNA) can be retrieved reliably; storage requirements are different for such specimens (less rigorous temperature requirements for DBS and, in general, colder temperature requirements for all other relevant blood fractions – only deCODE stores whole blood and purified DNA at higher temperatures than the -30 degrees Celsius temperature at which the DoDSR stores its serum specimens).
- Only DoDSR specimens are collected without at least reading an informed consent and privacy statement (even the DoD DNA specimens are collected following reading of these statements); only specimens in the two DoD repositories are collected without prior IRB approval, however, an appropriate IRB must approve use of DoDSR specimens for research purposes.

CHAPTER HIGHLIGHTS

Key points from this chapter include the following:

- As described in this chapter, white blood cells can be either purified and stored as the buffy coat fraction or captured in whole blood; whole blood can be stored either dried or liquid. In all of these cases, DNA and RNA can be captured in adequate

amounts for today's technology, and even perhaps tomorrow's, to use in genetic testing.

- Also as we describe here, dried blood spots have several advantages, one being simple collection, processing and storage along with long term stability of DNA. Whole blood provides buffy coat which in turn provides even larger amounts of DNA and RNA for genetic testing than dried blood spots.
- A comparison of the repositories we selected for this study (Table 5.2) shows that the DoDSR is unique in that it stores sera at a relatively warmer temperature than the others, it is the only repository that stores only sera, it is very large compared to the others, and does not require informed consent. While each of these differences does not indicate that the DoDSR is not meeting the current "best practices" of the industry, it does indicate that DoD has opportunities to address each of these issues within its unique context to deliberately assess whether or not it is functioning as intended. The DoDSR will soon be forced to consider how it is going to acquire more space, and as we discuss in the next chapter, this presents an opportunity for DoD to determine whether or not changes are warranted.

Table 5.1.
Comparison of General Repository Characteristics

	NHANES	UK BioBank	NHLBI	WRAIR: Division of Retrovirology	AFIP: DoD DNA Registry	deCODE	DoDSR
Purpose	Surveillance, research	Research	Research	Research	Forensics/Identification	Research & drug development	Surveillance, investigation, research, clinical support
Population represented	Representative sample of U.S. population	Prospective cohort	Clinical research subjects	Clinical trial subjects	All military service members	Family disease clusters	All military service members
Specimens archived	Plasma, serum, purified DNA	RBC, plasma, serum, buffy coat, purified DNA	Whole blood, plasma, serum, buffy coat, purified DNA	Plasma, serum, buffy coat	Whole blood (dried blood spots)	Whole blood, purified DNA	Serum
Longitudinal specimen collection	No	Yes	Study-dependent	Study-dependent	No	No	Yes
Health survey data	Yes	Yes	Yes	Yes	No	Yes	No
Link to medical records	No	Yes	No	No	No	Yes	Yes

Current inventory (2007)	>550,000	~100,000	~3.5 million	~1 million	>5.1 million	>500,000	43 million
Acquisition rate (per year)	~50,000	~175,000	80,000-130,000	~70,000	~300,000	12,000-60,000	1.9 million
Repository funding	Public (HHS)	Public/ Private	Public (HHS)	Public (DoD)	Public (DoD)	Private	Public (DoD)
Informed consent	Yes	Yes	Yes	Yes	Yes	Yes	No
Specimens collected with IRB approval	Yes	Yes	Yes*	Yes	No	Yes	No
Specimens requested for use with IRB approval	Yes	Yes	Yes	Yes	No	Yes	Yes**
Year Established	1988***	2001	1975	1986	1992	1998	1989

* Also has an additional IRB, conducted through the repository, to address storage of specimens
** IRB approval required for research uses
*** Established in 1956, but storage of specimens started during NHANES III (1988-1994)

Table 5.2.
Repository Specimen Storage Characteristics for Blood-Derived Specimens

Repository / Blood Fraction	NHANES	UK BioBank	NHLBI	WRAIR: Division of Retrovirology	AFIP: DoD DNA registry	deCODE	DoDSR
Blood Fractions							
Whole Blood			-80°C / Liq N_2			-25°C	
Red Blood Cells		-80°C / Liq N_2					
Plasma	-80°C / Liq N_2	-80°C / Liq N_2	-80°C / Liq N_2	-80°C			
Serum	-80°C / Liq N_2	-80°C / Liq N_2	-80°C / Liq N_2	-80°C			-30°C
Buffy Coat		-80°C / Liq N_2	-80°C / Liq N_2				
Purified DNA	-80°C / Liq N_2	-80°C / Liq N_2	-80°C / Liq N_2	Liq N_2		4°C	
Dried Blood Spots					-20°C		
Retrieval Mechanism							
Automated		X				X	
Manual	X	X	X	X	X	X	X

CHAPTER 6. IDENTIFICATION OF POTENTIAL IMPROVEMENT STRATEGIES

In this chapter we present the main findings from our analysis. This discussion draws upon our analysis of the material covered to this point in the report. We developed a conceptual framework to bring together the findings from our assessment and identify potential improvements to system elements.

The chapter first describes a conceptual framework that we used to organize our analytic process. Next, we identify and assess potential improvement strategies, grouped according to the various domains of the framework. For each, we summarize relevant current characteristics of the DoDSR-DMSS system (described in greater detail elsewhere in this report), describe issues or problems derived from our analyses and key informant interviews, and finally present potential strategies to address those issues. Potential improvements are described in terms of the questions to be addressed, strategies to address them, approach to implementation, and potential advantages and disadvantages. In Chapter 7, we package the most promising strategies into practical recommendations for action.

CONCEPTUAL FRAMEWORK

Chapter 4 describes in detail the capabilities of the DoDSR and associated DMSS system in terms of their functional and structural elements -- management, timing of specimen collection, specimens, data, and users/uses. We used these concepts as the basis for organizing a systematic process to capture current characteristics of these systems, discuss them with persons interviewed both inside and outside the military, and identify potential improvements. These system elements are described briefly below and depicted in Figure 6.1. The conceptual framework organizes the domains, depicts their logical relationship to one another and facilitates identification of opportunities for improvement in the DoDSR-DMSS system.

- **Management***:* This domain includes the organization and staffing of AMSA (which oversees the DoDSR and DMSS), the overall program direction and oversight, and management of the physical repository facility.

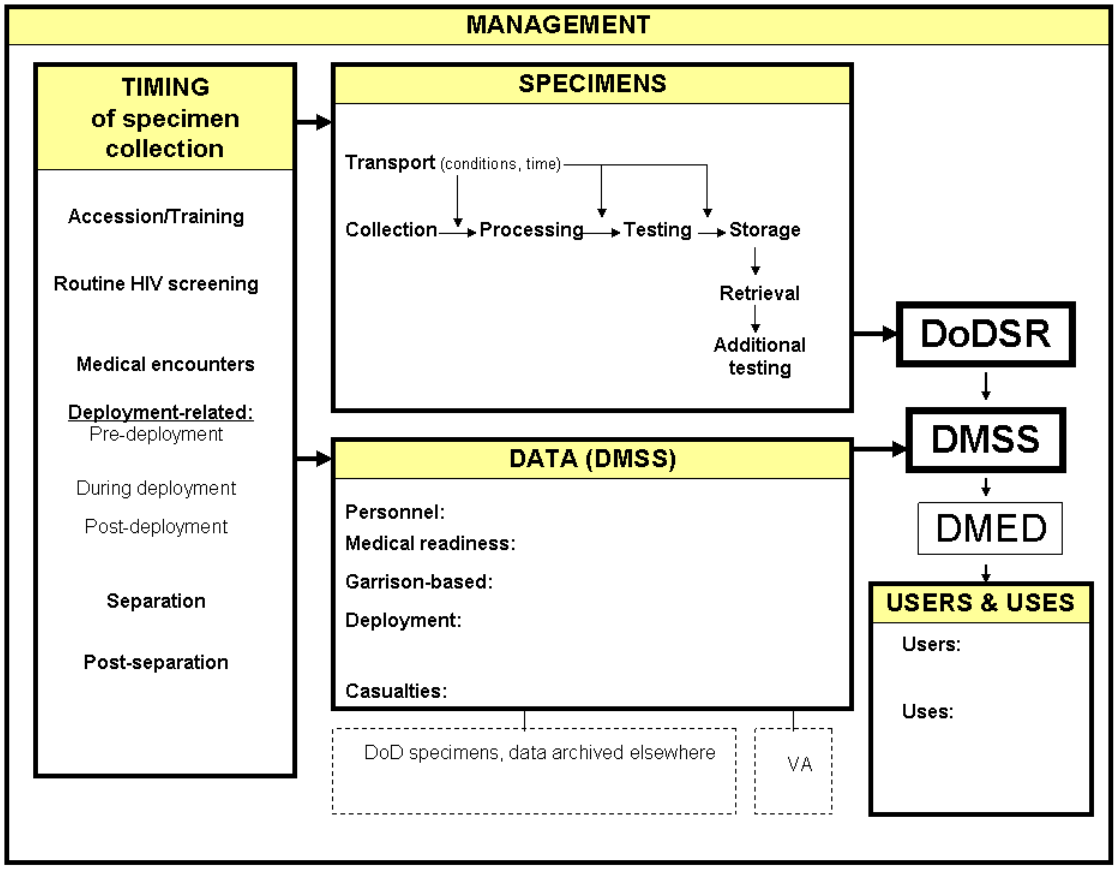
- **Timing of specimen collection***:* Specimens are typically collected and archived from military service members. Figure 6.1 reflects a number of administrative milestones that already do, or could, trigger specimen collection over the term of a member's service.

- **Specimens***:* Processes related to specimens include collection, processing, transport, initial testing, storage, retrieval, and additional testing.

- **Data***:* This domain includes linkages of data into DMSS and access to the data.

- **Users and uses***:* This domain includes the range of military and non-military users of DMSS data and/or DoDSR specimens, and the range of potential uses of these resources.

Figure 6.1.
Conceptual Framework to Help Identify Potential Improvements to System Elements



POTENTIAL IMPROVEMENT STRATEGIES

We now present our discussion of issues raised by the current system and potential improvement opportunities. Current system characteristics, as described in detail in Chapter 4, and issues raised about them during our interviews, are summarized in the discussions that follow. Figures 6.2 and 6.3 represent populated versions of the conceptual framework shown in Figure 6.1, depicting current DoDSR-DMSS characteristics and potential improvements, respectively.

Management

Current Status. AMSA is the designated as the Executive Agent for military health surveillance (DoDD 6490.2, August 31, 1997) and as such is the U.S. military's central epidemiological resource. AMSA manages the DoDSR and DMSS systems and the associated DMED database that can be accessed by military users outside of AMSA. Consistent with AMSA's own guidelines, access to repository specimens is ultimately the decision of the AMSA director. AMSA's guidelines provide information about submitting requests, but do not address the precise decision-making process. Under current institutional requirements, specimens are housed in leased space in Silver Spring, MD (lease expires in 2010). The 25,000 ft^2 facility accommodates the current inventory of approximately 43 million specimens, some of which have been reconfigured into "compressed" space due to storage space limitations and are thus less readily accessible.

Issues Identified.

AMSA's mission statement has no explicit reference to "deployment health surveillance" nor to epidemiological investigations, clinical support or research. In interviews, AMSA staff and leadership frequently alluded to their surveillance mission, suggesting it is the sole, or at least primary, mission for which they are resourced. However, the AMSA mission statement describes very general surveillance activities without using the term "surveillance" or referring to "deployment surveillance":

> *The Army Medical Surveillance Activity's (AMSA) main functions are to analyze, interpret, and disseminate information regarding the status, trends, and determinants of the health and fitness of U.S. military (and military-associated) populations and to identify and evaluate obstacles to medical readiness. AMSA is the central epidemiological resource for the U.S. Armed Forces providing regularly scheduled and customer-requested analyses and reports to policy makers, medical planners, and researchers. It identifies and evaluates obstacles to medical readiness by linking various databases that communicate information relevant to service*

members' experience that has the potential to affect their health. (AMSA Mission, personal correspondence, 28 January 2008).

DoD policy has defined a broader set of mission areas for DMSS and DoDSR: medical and deployment health surveillance, including clinical diagnosis and epidemiological studies (DoDD 6490.02E, October 21, 2004) and deployment-related data (from both garrison and deployed settings) for DoD-wide surveillance and research (ASD(HA), September 30, 1999). Thus, policy seems to suggest that AMSA, as Executive Agent for DMSS and DoDSR, must support the missions of not only medical and deployment health surveillance but also clinical management, epidemiologic investigations, and research toward development of measures for the "prevention and control of diseases associated with military service" (DoDD 6490.02E, October 21, 2004). Although AMSA's mission statement does not refer explicitly to deployment health surveillance or even surveillance more broadly, AMSA's "Guidelines for Collecting, Maintaining, Requesting, and Using Specimens Stored in the Department of Defense Serum Repository" reflect the full range of mission areas with the exception of "deployment health" as a category for use of requested serum specimens.

It is important to note that CHPPM does not have the lead responsibility for research within the Army. That lies with the Medical Research and Materiel Command (MRMC), which is responsible for medical research, development, and acquisition; medical information management and information technology; medical logistics management; and health facility planning. MRMC is headquartered at Fort Detrick, MD, and supports 14 laboratories and separate organizations throughout the United States. Six of the MRMC medical laboratories and institutes perform core science and technology research specializing in infectious diseases, combat casualty care, operational medicine and chemical and biological defense. The military infectious disease research program focuses on vaccine development against diseases which threaten military personnel, prophylactic and treatment drugs for infectious diseases, techniques for identification of disease organisms and diagnosis of disease, studies of vector controls and collection of epidemiological

data relevant to disease. Serum specimens stored in the DoDSR and managed by AMSA/CHPPM are relevant to military research, which is managed by a separate command, MRMC.

Analysis of our interviews suggests that there is lack of shared understanding within the Army and across DoD of both the mission and appropriate uses of the repository. Some interviewees felt that there is no explicit vision for the repository, perhaps reflecting the lack of common understanding of its full range of missions. There is also lack of common understanding of the meaning of such missions/terms as "surveillance" and "research." To our knowledge, critical nuances related to the definition and allowable scope of "medical surveillance" and "research" have not been clarified by central (or even Army) guidance. However, AMSA's Guidelines do begin to tease this out, distinguishing between "research" and "non-research" studies. Thus the specific research mission for DMSS and DoDSR may be a source of conflict for AMSA, whose name, funding stream and work to date suggest it is a surveillance entity, yet it is the designated Executive Agent for DoDSR and DMSS programs that serve mission areas beyond surveillance alone, including research. Thus, to the extent that DoDSR and DMSS are used for research purposes, AMSA must have at least a research support mission, and the connections between research policy components, e.g., MRMC, and AMSA, must be reconciled.

This confusion plays out in the management of the Serum Repository. The DoDSR has a set of published guidelines, which define research as studies with "the primary intention to create, extend, or validate generalizable knowledge—that is, knowledge that applies to individuals, populations, or settings external to and not directly associated with the donors of specimens from which the knowledge is generated…."(DoDSR, May 29, 2003, pg. 7). Non-research is defined as studies that are specific to identified individuals or populations or settings that those populations represent. The same guidelines signal that non-research study requests will be responded to "more quickly" than research, indicating some sort of prioritizing. (DoDSR, May 29, 2003, pg. 7) AMSA's definition of "non-research" studies may help legitimize work undertaken by its own staff in response to requests for

DMSS data analyses; however, even so, there are true "research" studies that have also made good use of DMSS data and/or DoDSR specimens (see chapter 4). It is unclear if AMSA staff feel conflicted about their authority to support such efforts, given their surveillance mission and operational funding stream.

AMSA's organizational position potentially limits use of the repository. AMSA is buried deep within the Army's Medical Command. Some interviewees commented on the organization and leadership of AMSA as potentially limiting optimum use of the repository. Interviewees expressed hope that creation of the new AFHSC will offer opportunities to overcome real or perceived organizational factors that may have impeded robust use of DoDSR and/or DMSS in the past.

There is currently no process in place to systematically review and integrate promising new technologies of relevance to the repository. We found no evidence of such a process in our review of documents and interviews across the military.

Small AMSA staffing size may challenge AMSA's ability to fulfill even its primary surveillance mission. Requests for support to other mission areas also put pressure on AMSA's limited staff. AMSA staffing comprises mainly Army and civilian personnel. Also according to AMSA, the deployments of at least three AMSA military staff in recent years have led to more frequent staff turnover than usual, leading some AMSA staff to comment on issues of staffing strategies, e.g., longer term billets or more civilian staffing, that might better serve institutional continuity. Finally, the almost exclusive military staffing by Army personnel raised questions among some interviewees about the true tri-service nature of AMSA and the DoDSR-DMSS system it oversees; some contrasted AMSA to GEIS, whose staffing was often perceived as more diverse across services.

Some interviewees expressed concern about a lack of transparent procedures concerning access to specimens. DoDI 6490.03 (August 2006)

calls for the Secretary of the Army to "establish procedures to respond to requests" for data and specimens. While some interviewees noted that they had had no problems in accessing repository specimens, others expressed concern about what they perceived as difficult access or lack of transparent procedures. AMSA, for its part, was open to considering a new mechanism that improves its oversight of the approval process for release of specimens. In addition, they noted concerns that time-sensitive requests for specimens cannot be met consistently, for example if recent pre-deployment specimens needed for an ongoing outbreak investigation have not yet arrived at the repository.

The mixing of uses and long-term storage of specimens, without apparent communication to donors, could be problematic for human subjects protection. The protection of human subjects with regard to the serum repository generally involves two practices: the use of an IRB, and the gaining of informed consent, where appropriate, from service members. We have described in detail the intricacies of both practices as they relate to the collection, storage and research or non-research use of stored sera (see chapter 4). One of the key issues is that specimens are drawn for either HIV testing or pre- and post-deployment surveillance, and then later could potentially be used for research, patient care, public health/force health protection, and even criminal investigations. Related to this, the sera are stored in perpetuity and there appears to be no explicit communication of this to the individuals donating the specimen. The mixing of uses and the enduring storage of the specimens, all with no apparent communication to the donors, could be problematic. Finally, the AMSA guidelines that describe the various practices pertaining to each type of use of the sera are not explicit in all cases about whether consent is needed or even whether an IRB is needed.

The current repository facility is not sufficient to support future growth. Approximately 43 million specimens have accumulated over the years. Of those, approximately 5.5 million cannot be linked to records in DMSS, and most of these unlinked specimens have been placed in

"compressed" configuration in response to growing limitations in repository storage space. The current repository facility does not provide sufficient space for further growth. At present, no specimens are discarded. AMSA staff noted that selective culling of such specimens would be tedious and not necessarily result in major gains in storage space, since sera are stored in boxes with multiple specimens each. Potential culling of older specimens was called into question by other interviewees, who described the value of military serum specimens from the 1950s-1960s, stored elsewhere, that had been very useful in studying the emergence of hepatitis C. In any case, the upcoming relocation of the repository once the current lease expires provides a timely opportunity to consider space (and other repository) requirements into the future.

The DMSS physical infrastructure and lack of back-up pose a risk of system malfunction or failure. The facility used to house the DMSS hardware and operations center is characterized by AMSA analysts as not meeting industry standards and as containing vulnerabilities posing serious risk to system malfunction or failure, such as leaks in the roof of the room housing the DMSS server. An incident in late January 2008 involving the DMSS server emphasized the need for both physical protection of DMSS hardware and facilities and robust back-up mechanisms for the DMSS database itself.

Some AMSA interviewees commented on the fragmented nature of HIV testing. This testing is conducted by AFIOH, the Army Retrovirology Laboratory, and ViroMed. No interviewee expressed dissatisfaction with the performance of any of these laboratories.

Potential Improvement Strategies. Based on the problems identified, there are several key questions related to aspects of program management:

- Could the use of DoDSR-DMSS be improved through a clarification or redefinition of the mission of AMSA and DoDSR-DMSS, a different organizational structure, a different size or skill set of AMSA

staff, and/or different procedures for accessing serum specimens or data?

- Given the current storage space constraints, what requirements for space should be sought for the new repository facility following expiration of the current lease? Should archived specimens be selectively culled?
- What improvements can or should be made to current DMSS operating facilities and hardware, given the risks posed by the poor condition of the facilities that house the system?
- Should HIV testing be consolidated within DoD?

The strategies described below address these questions.

Strategy 1: Clarify or redefine the mission of AMSA and appropriate uses of DoDSR, and define relevant terms clearly

This strategy involves clarification by appropriate military authorities of the scope of "surveillance" and "research" functions, the full range of missions authorized for DMSS and DoDSR, and implications for AMSA. Does the mission of AMSA itself need to be more explicit to include medical surveillance and deployment health surveillance (including near-real time medical surveillance from deployment areas), and should it also explicitly include support to clinical management, epidemiological investigations and research? Or, is AMSA's current mission of DoDSR and DMSS oversight sufficient to support other DoD entities in these additional mission areas?

After clarification at the policy level, this information should be shared widely and incorporated into practice by AMSA and its chain of command, and shared with all current and potential users of DMSS and DoDSR DoD-wide. This strategy may or may not require new policy/doctrine in and of itself, but the creation of the new AFHSC and attendant requirements for updating relevant DoD policy offers opportunities to be more explicit in describing and aligning the missions of DoDSR, DMSS and their oversight organization, the new AFHSC. Communications will also require leadership to help assure clearer common understanding across DoD of the full roles and responsibilities of AMSA, DMSS and DoDSR,

which in turn should lead to more robust and efficient use of these important military resources. There appear to be few if any disadvantages, other than to note that supporting a functionally expanded set of missions may require additional staffing, discussed in Strategy 3 below. Perhaps AMSA's guidelines distinguishing between "research" and "non-research" studies using DoDSR specimens were aimed at least in part at reconciling their support to "research" studies, as well as potential human subjects protection issues.

Strategy 2: Change the organizational structure

In late February 2008 the Deputy Secretary of Defense issued a memorandum officially establishing the Armed Forces Health Surveillance Center (AFHSC), consolidating AMSA and GEIS within an elevated single organizational unit whose director reports directly to the CHPPM Commanding General. The final structure of the organization is to become tri-service. This is an effort to further integrate military health surveillance, both in terms of bringing together the complementary functions of AMSA and GEIS and other surveillance organizations. While the organization now officially exists, we hope its name – which suggests a primary "surveillance" mission – will not confuse potential users or impede the broader use of its assets as described throughout this report. Also, while organizational restructuring may be deemed desirable, broad experience with organizational restructuring suggests that it will likely not be sufficient to fully integrate surveillance and optimize use of the DoDSR-DMSS resources. Also needed are continued strong leadership, efforts to attract strong multi-service military staff, and efforts to create normative change across the military in which the new AFHSC helps the DoDSR-DMSS achieve its full potential through clear mission and successful implementation perceived as timely and helpful by users. Further, as technology advances and the needs of the services change, the AFHSC could play an ongoing oversight and monitoring role to manage a process to determine when relevant new technologies, such as those for collecting, processing, testing and storing biological specimens, are ripe enough for practical use in the services.

Strategy 3: Align staffing with mission

Expansion of the mission or uses of the DoDSR-DMSS resources may require changes in the staffing pattern, e.g., in terms of size and skill mix or expansion of relevant AMSA contracts, most notably the data analysis contracts. Beyond adding billets to AMSA's staff or resources to AMSA contracts, there may be low-cost ways to augment AMSA's staffing, such as offering rotations to military Preventive Medicine Residents and/or epidemiology students from USUHS. Regardless of change in mission, however, drawing its highly qualified professional staff from across all services (as GEIS has done, for example) may contribute to the positive perception and enhanced use of the repository across DoD. There may also be a role for longer military tours for AMSA analysts and/or civilian staffing of relevant staff or leadership positions (e.g., deputy director) to optimize institutional continuity.

Strategy 4: Improve transparency in access to specimens

The most reasonable approach to implementation of this strategy is probably a consensus planning effort culminating in doctrine disseminated across DoD. As a practical matter, this could involve revision and reissuance of AMSA's current guidelines, to add criteria for release of repository specimens, or issuance of a separate document with this information. Based on suggestions from various interviewees, such procedures should also include an administrative fast-track mechanism for approval and release of specimens needed on a time-sensitive basis, such as investigation of an ongoing outbreak or for urgent clinical support. Such procedures should be thoroughly vetted, captured in appropriate doctrine, disseminated widely, and followed in practice.

Strategy 5: Improve internal AMSA oversight of DoDSR specimen release

AMSA in particular expressed interest in an appropriately constituted group to help oversee the approval of release of repository specimens as well as independent (of service IRB's) oversight of

ethical/human subjects issues relevant to the repository. In fact, such a mechanism was suggested in the Armed Forces Epidemiology Board Memorandum of April 2005, but apparently was never acted upon. Oversight of human subject protections is particularly important if use of repository specimens expands significantly beyond the original intended uses of its specimens, e.g., research or other uses judged to require informed consent. AMSA may wish to consider establishing its own IRB if it feels that an additional layer of human subjects review is warranted. In addition to IRB review, the U.S. National Heart, Lung and Blood Institute has constituted an allocation committee that reviews requests for specimens (see Chapter 5). This allocation committee may provide a relevant model for AMSA for dealing with requests for serum specimens.

Strategy 6: Collect specimens with informed consent

The current AMSA guidelines are not explicit about all cases when consent may or may not be required. In the cases when consent is not required, guidelines specify that the specimens be "de-linked" from individually identifying information. Currently, and consistent with the waiver provision in existing legislation on privacy protection and informed consent, specimens stored in DoDSR are collected without informed consent. For that reason, in part, specimens that are sent to researchers for research purposes are de-linked from any identifiable information. This also limits the utility of the specimens in the repository since there is no way for researchers to request more of the same specimen, and restricts research to strictly retrospective studies since it is not possible to obtain specimens from the same individual in the future once it has been de-linked from identifiable information.

Sera are drawn for either HIV testing or pre- and post-deployment surveillance, but can be used for other purposes and are stored in perpetuity. None of this is apparently explained to service members. As concerns about protecting the privacy of human subjects continue to be raised, and to broaden the usefulness of the specimens in the repository, DoDSR should consider obtaining informed consent for the storage and research use of specimens in DoDSR.

Also, the DoDSR is charged with the storage of specimens from service members and civilians in the military community. The current AMSA guidelines do not address the use of an IRB in all described cases of use, and when it does it relies on the IRB approval of the requesting agency. There is a trend among repositories to either have an internal IRB or to be closely affiliated with an outside IRB. Therefore, AMSA may wish to pursue a strategy to establish its own IRB for the DoDSR or become affiliated with a tri-service IRB that would protect not only service members' interests, but ensure that protocols take in to consideration the protection of the military health system and the DoDSR while still allowing for the conduct of appropriate research and non-research.

Strategy 7: Determine requirements for the new repository

Once any modifications are made to plans for future collection and/or archiving of specimens, planners must determine the time horizon and associated requirements for space in the new repository facility. For example, if the current 25,000 ft^2 repository accommodates approximately 43 million specimens, with some redundancy to mitigate potential equipment failure, and with an acquisition rate of approximately 1.9 million new specimens per year, then a new repository configured similarly but with double the capacity should suffice for the next 23 years. However, if specimens are to be collected more frequently or for an extended period of time, e.g., following separation, then space requirements and planning horizon must take these new requirements into account. This is a timely juncture for undertaking such planning, however, since the current repository lease expires in 2010, and any new space requirements must be established soon.

Strategy 8: Protect the physical infrastructure and back up DMSS

An incident in late January 2008 involving a DMSS server emphasized the potential vulnerabilities of both the facility housing the DMSS operation as well as the system hardware on which the DMSS system currently operates. An in-depth assessment of the current facility and potential risks posed by the physical state of the facility should be

undertaken. At the very least, planning requirements for the new AFHSC facility should provide for adequate housing and protection of the integrity of the database itself. Off-site back up systems as well as data mirroring are important ways to secure the continuity of DMSS operations and maintain the integrity and utility of service member information. Securing the maintenance and integrity of DMSS data is paramount to AMSA's ability to meet its stated mission objectives and continue to support military health in a consistent and reliable manner.

Strategy 9: Consider consolidation of HIV testing

From a systems perspective, DoD could consider potential efficiencies to be gained by consolidating HIV screening in a single (e.g., military or contract) laboratory. However, our analyses did not yield compelling justification for this strategy.

At present, the laboratory with the highest throughput capacity is that of AFIOH; and at present the WRAIR HIV laboratory currently performs all HIV testing for the European Command. Under the Base Realignment and Closure plans, AFIOH is scheduled to be relocated to Wright-Patterson AFB in Ohio. Several of those interviewed across the services commented on the potential desirability of co-locating the laboratory and the repository, including the possibility of establishing a new laboratory for purposes of HIV screening and potentially other testing. Another option would be to co-locate the AFIOH laboratory and new serum repository, whether at the new AFIOH site in Ohio or the new repository site in the National Capital Region (where the new AHFSC will also reside). If any co-location strategy is to be seriously considered, decisions should be made relatively soon – since both AFIOH and the serum repository facility will be relocated within the next few years. Further, any benefits in either co-location of the laboratory and repository or consolidation of HIV screening in a single military laboratory (e.g., potential cost savings, improved management efficiency, increased military laboratory surge capacity) should be weighed against the costs and administrative requirements associated with deviations from current plans. Military leadership will likely wish

to make any relevant planning decisions within the near-term planning frame for the new AFIOH and repository facilities.

Timing of Specimen Collection

Current Status. In general, blood specimens are collected according to administrative milestones. Specimens are routinely collected and archived at accession, pre- and post-deployment, and at separation, as well as every two years for HIV screening. No specimens collected from routine medical encounters, during deployments, or post-separation are archived.

Issues Identified.

Most military interviewees were satisfied with the current frequency and timing of specimen collection from service members. Indeed, the Armed Forces Epidemiology Board (now the Defense Health Board) endorsed in 2005 continuation of the universal sampling and current timing of pre- and post-deployment specimen collection. Most of the military interviewees did not see good reason to collect routine HIV specimens more frequently or on dates tagged to birth month, nor to collect and archive additional specimens from routine medical encounters (other than those from which specimens are already required) or theater operations.

Interviewees expressed divergent views regarding the desirability of ongoing specimen collection from separated members enrolled in the VA health system. This group represents an estimated 8 million of the approximately 25 million eligible. According to the VA, such individuals tend to remain within the VA health care system for life, thus extending the longitudinal coverage of service members for years or decades beyond their active duty. Policy makers in OSD and the VA expressed strong support, while at least one AMSA staff member expressed reservations, seemingly based on perceived administrative complexity. AMSA did suggest, however, that they would be supportive of continued specimen collection from separated military members treated at MTFs.

Potential improvement strategies. Based on the issues discussed, the key questions related to the timing of specimen collection concern the frequency of specimen collection and the extension of collection beyond active duty:

- Is there any reason to change the frequency of specimen collection?
- Is there justifiable benefit in extending specimen collection from separated service members followed in MTFs and/or the VA health system?

The strategies described below address these questions.

Strategy 10: Change the frequency or timing of specimen collection

From a purely systems perspective, factors that could potentially be changed are the timing or frequency of specimen collection, e.g., tying HIV screening systematically to birth month rather than more random two-year sampling, or collecting specimens annually rather than every two years. However, as with any potential change, the potential merits and justification must be weighed against the administrative or other drawbacks. Most interviewees did not advise any change – they feel that the HIV screening and pre- and post-deployment specimens meet current needs. The RAND team also found no compelling justification for changes in the timing or frequency of specimen collection.

Strategy 11: Extend routine specimen collection beyond separation

Two implementation options, not mutually exclusive, include extending systematic specimen collection on a voluntary basis from separated military members followed at MTFs -- an estimated 2 million members separated from active duty currently enrolled in TriCare Prime or eligible for TriCare for Life combined (DoD Task Force, December 20, 2007) and doing the same for the even larger group of separated service members followed by the VA health system -- estimated 8 million currently enrolled (CBO, December 2007). A decision regarding this strategy should be made relatively soon, however, so that planning for the new repository space can accommodate any new space requirements. It is also possible that specimens collected through the VA system could be

archived elsewhere, e.g., through the VA, but in any case both specimens and data collected by the VA and MTFs should be linked to DMSS to assure the seamless longitudinal nature of data and specimens from service members through their years of active duty and post-separation. If such a strategy is contemplated, DoD should also consider the epidemiologic value of such "specimens of convenience" as compared to more methodologically rigorous establishment of cohorts of separated service members, which would be considerably more complicated from a practical point of view.

Specimens

Current Status. Currently, specimens that ultimately reach the repository are collected in a single tube and usually processed within 24-48 hours of collection. Shelf time before initial processing may vary depending on individual versus mass specimen collection. Serum is extracted and tested for HIV. Initial HIV testing is performed by ViroMed (the laboratory contractor for U.S.-based Army and Navy/Marine specimens), AFIOH (for all Air Force specimens), or the Army's Retrovirology Laboratory (for specimens coming from Europe). The Army and Navy/Marines have separate contracting processes, but currently both employ ViroMed. Serum remaining after HIV screening, usually about 2-3 cc, is sent to the repository. Shipping temperature requirements are in place, but they are not rigorously monitored.

The AMSA transport contractor picks up specimens approximately every two months from the ViroMed in Minnesota and from AFIOH in Texas and then transports them in a refrigerated truck to the repository in Maryland. Specimens are shipped and stored frozen in walk-in freezers maintained at -30°C. Specimens are retrieved manually from the walk-in freezers. Upon first request for a specimen from the repository, there is a single freeze-thaw cycle for aliquoting. The specimen is thawed, divided into multiple 0.5cc aliquots, and then used for further analyses or frozen and stored at -30°C until it is needed. Serum specimens are released as 0.5cc aliquots to approved users for approved testing purposes.

Issues Identified.

Variations exist in specimen processing and transport conditions. There are significant variations and a lack of standardization in the length of time specimens sit at the MTF before being processed (i.e., spun down) to obtain serum, and the transport time (24 – 48 hours) of serum from the MTF to the testing laboratory. In addition, several interviewees, from both AMSA and across military services, commented on problems of timeliness in the repository's receiving recently obtained specimens, e.g., accession or pre-deployment specimens needed for investigation of outbreaks. The two-monthly schedule for transport of specimens to the repository contributes to delays in the accessibility of such specimens, e.g., to support real-time outbreak investigations.

The finite size of the archived serum specimens limits the number of uses from a single specimen. This point was noted by a number of interviewees. The current 0.5cc aliquot size means that a given 2-3cc serum specimen can only be used 4-6 times.

At DoDSR, storing the specimens in 2-3cc vials requires a free-thaw cycle before the specimen reaches the end user. Freezing and thawing biological specimens can impact the measurement of many components of the specimen, including biomarkers and genetic material. Some other repository models minimize the freeze-thaw cycles of their specimens.

Some interviewees noted the utility of archiving other blood fractions. Most of the specimen-related discussions with interviewees focused on the utility of serum specimens as currently stored and the desirability – or not – of archiving other blood-derived specimens, most notably fractions that would retain adequate genetic material. Indeed, in 2005 the Armed Forces Epidemiology Board recommended the preservation of WBC for this purpose, but there has been no apparent action on that recommendation. There are clearly considerations related to policy, logistics and cost associated with any such change. Several interviewees expressed interest in collecting dried whole blood spots on filter paper. Such specimens offer promising opportunities to retain genetic

material and are associated with only modest requirements for space and storage conditions. The inclusion of new types of specimen in the repository would most certainly mean different storage requirements and perhaps also different retrieval processes, both of which should be considered in light of the anticipated relocation of the repository.

If new types of specimens are contemplated, alternate storage conditions must also be considered. The current repository stores serum specimens at -30° C, which also permits the use of large walk-in freezers. If new types of specimens or different storage conditions for serum specimens are contemplated, associated new requirements must also be considered, as AMSA secures a new repository facility within the next several years. For example, storage at a colder temperature such as -80°C would not permit walk-in freezers.

Some interviewees supported the possibility of conducting screening beyond HIV. Some AMSA interviewees raised the possibility of running a routine panel of tests on serum specimens before they are (re)frozen and stored.

Potential Improvement Strategies. Based on the issues discussed, the key questions related to blood specimens concern the cold chain maintenance of specimens, timeliness of transport to the repository, finite size of archived sera, number of required freeze-thaw cycles, the potential for other routine screening tests, the desirability of retaining additional blood fractions that would permit a wider range of testing, and storage temperature of the specimens:

- How could the cold chain be monitored better?
- How can accessibility to recently collected specimens be improved?
- Given that it may be impractical to collect and store larger specimens (greater volume of serum), should smaller aliquots be considered?
- Can the number of freeze-thaw cycles be reduced, as another way to preserve testable analytes in the specimens?

- Should new routine screening tests be added?
- Should additional blood fractions be retained, and if so, are potential new requirements justified?
- Should specimens from other studies be archived in the central repository, or at least be accessible through links into DMSS?

The strategies described below address these questions.

Strategy 12: Improve the cold chain custody of specimens

Specimens are collected throughout the country and world at MTFs, clinics, hospitals, etc and shipped to AFIOH, WRAIR HIV laboratory or ViroMed for testing. However, laboratory personnel do not have adequate cold chain custody for specimens. There is no way to determine if the specimens were maintained at controlled temperatures before they arrive at the testing facility. There are simple devices that can track the temperature of a shipment continuously or track the highest temperature that a package reached during transit. Either of these options would allow laboratory personnel to know whether the specimens have been compromised by reaching high temperature levels. Once tested, specimens from AFIOH and ViroMed are frozen and shipped to the repository in a refrigerated truck. Specimens from WRAIR HIV laboratory are delivered to DoDSR weekly on dry ice. It would also be useful to maintain records of the refrigerated truck temperature as AFIOH and ViroMed specimens are being transported.

Strategy 13: Increase the frequency of specimen shipment to the repository

Increasing the frequency of specimen shipment, e.g., from the current two-monthly schedule to monthly, could be achieved through modification of the current AMSA contract or purchase of a vehicle for this purpose. While we understand that a vehicle was recently purchased for this purpose, we are not sure if this is actually the case and that specimen shipments are now more frequent; we therefore decided to include this strategy. Either option, i.e., more frequent transport by the contractor or purchase of a truck for specimen transport, increases

the cost to the military, either one-time or recurring. However, timelier archiving of specimens can potentially render the repository more relevant for real-time support of serosurveillance, investigations, and clinical management. AMSA should consider the most desirable timing and efficient mechanism for transport of specimens to the repository. In lieu of more frequent shipments, another option would be to develop a policy to allow expedited shipment of specimens from the testing laboratories for special circumstances when specimens are needed quickly.

Strategy 14: Reduce the number of routine freeze-thaw cycles

The measurement of biomarkers in blood specimens has become an integral component of many epidemiologic studies. As noted above, freezing and thawing biological specimens can impact the measurement of many components of the specimen, including biomarkers and genetic material. (Mitchella et al., 2005) Most repositories and researchers minimize the number of times a specimen is frozen and thawed. In addition, NHANES takes part of their specimens and freezes aliquots in liquid nitrogen to save as a pristine specimen. DoDSR procedures could change to provide for aliquoting the specimens before they are frozen and shipped to the storage facility. This would increase costs associated with storage and shipping.

Strategy 15: Reduce the size/volume of serum aliquots released for testing

With current testing methods, the volume of specimens required for testing has been reduced, although it varies by analyte and test protocol. Currently DoDSR sends all requestors a 0.5cc aliquot. For many tests, a smaller volume would be sufficient. For instance, aliquots of 0.25cc would double the number of specimens available from an individual specimen. For rare cases that 0.5cc aliquots are actually required, 2 vials could be sent. However, the issue of running out of specimens has not been a problem with the repository to date, and will only be an issue if DoDSR significantly increases the number of specimens that are provided to researchers and other users. However, increasing the number

of aliquots by decreasing their size may require additional storage space.

Strategy 16: Perform a standard set of tests on serum specimens

If AMSA wants to be more proactive in performing surveillance with the specimens in the DoDSR, a set of predetermined tests could be performed on all, or subsets of, the specimens as they are collected. This would allow AMSA personnel to perform more immediate surveillance activities. Other repositories, such as NHANES, perform a standard set of biological tests on the blood specimens they collect and the results of these tests are then made available to researchers who request data and specimens. In addition, those researchers are often required to submit the results of their tests back to the repository, which then become part of the data available to other researchers. This strategy would require new laboratory and/or financial resources to support a new routine panel of tests. It is not clear that all potentially worthwhile routine tests could be identified in advance, and if these would remain constant over time. The advantages of this strategy would be the availability of more routine test results from each specimen (or selected specimens) from which to perform routine surveillance and a reduction in the freeze-thaw cycles before having such results. The disadvantages relate mostly to resources – financial, human and laboratory. Nonetheless, it may be worthwhile to ask an appropriately constituted military body to consider this question in more detail, to identify potentially useful tests and specific advantages and disadvantages, and then to weigh these carefully and offer recommendations.

Strategy 17: Collect and archive blood fractions that permit a wider range of testing

Other repositories collect and store a wider range of specimens including whole blood, plasma, serum, white blood cells (often as buffy coat), and purified DNA specimens. While there are a wide range of tests that can be performed on serum, some tests require the use of whole blood or plasma. The type of material stored is determined, in most

cases, by the types of tests required. The DoDSR has a mission to engage in medical surveillance and support the prevention and control of diseases relevant to the military. Using avian influenza surveillance and related research as an example, studies could be conducted on military service members who have been deployed to countries that have experienced avian influenza outbreaks to determine if any service members have been exposed. Serum stored in DoDSR could be tested to determine exposure by determining whether any service members had developed an antibody response to avian influenza. This information could then be matched with their medical records to see if they had an influenza-like illness during their deployment. Testing for human influenza subtypes is already being undertaken in a similar manner. If the DoD considers this testing fully sufficient for medical surveillance and disease prevention and control purposes, then serum specimens as currently collected and stored most likely are adequate.

However, should the DoD feel that more in-depth study of factors potentially predisposing or protecting service members from infectious diseases such as influenza, or that other biological and chemical threats are worthy of surveillance, then it might consider the addition of specimens which contain DNA and RNA. Serum and plasma are not good sources of genetic material for either DNA or RNA testing. For example, if the DoDSR stored genetic material, it could be used to help determine if some people have a genotype that makes them more or less susceptible to infection or is a predictor of more severe illness caused by avian influenza. Knowledge of a service member's susceptibility to avian influenza would be useful in multiple ways. A genetic screening tool could be developed to screen service members before deployment to areas susceptible to avian influenza. Susceptible service members could either receive prophylactic treatment to prevent infection or reassigned to not include deployment to high risk areas. The knowledge of genotypes could lead to the development of different vaccines for different people. In all of these cases, access to genetic material would be necessary.

Purifying and then storing DNA from all specimens would be cost-prohibitive. However, collecting and storing buffy coat or whole blood are both options, and allow for the later purification/isolation of DNA

and RNA. Buffy coat and plasma can both be obtained from the same tube of blood. In this case, a separate tube of blood would be required to be collected from the person if serum were still required. However, HIV testing is possible on plasma, and the resulting plasma could be stored for follow on testing, instead of serum. If whole blood is stored, it can be collected and stored in two ways, either in liquid form from venipuncture, or as a blood spot, collected on filter paper. For both buffy coat and whole blood in liquid form, the specimens would need to be stored at -80°C or colder to be useful for a range of testing, including purifying genetic material. According to a review by the UK BioBank Sample Handle and Storage Subgroup, dried blood spots (DBS) offer the most stable storage format for DNA in blood. Studies have also shown that RNA can be isolated and assayed from DBS (Zhang and McCabe, May 1992; Uttayamakul et al, September 2005; Baumann et al, June 2005). DBS are commonly stored on filter paper at -20°C with a desiccant to minimize humidity, although they can be stored at 4°C, as well (Mei et al, May 2001).

Strategy 18: Change the storage temperature of the DoDSR

While the current storage temperature of -30°C is adequate for many analytes, it does not adequately maintain the integrity of all of the analytes available for testing in serum. (Rai AJ, et al.HUPO Plasma Proteome Project specimen collection and handling: towards the standardization of parameters for plasma proteome specimens. Proteomics. 2005 Aug;5(13):3262-77) Proper specimen storage is critical to maintaining specimen integrity, and to be able to perform a broader range of tests. To be more confident in the results of those tests, the serum specimens should be stored at -80°C or colder. As noted in strategy 17, if other fractions are collected and stored, especially for analysis of DNA and/or RNA, at a minimum, -80°C is required to maintain their integrity. DBS are the exception and can be stored at -20/-30°C with a desiccant without loss of information.

Data

Current Status. DMSS is AMSA's data hub and the sole data link to the DoDSR. DMSS is also the sole custodian of deployment health forms. DMSS is a strictly unclassified database that draws different types of data from several sources, as described in detail in chapter 4 and summarized below. DMSS draws data from several sources and retains such data permanently. According to AMSA interviewees, some of the original data sources do not retain data permanently. DMSS data are de-identified and made available as the Defense Medical Epidemiology Database (DMED) to users outside of AMSA. DMSS includes data related to demographic and administrative details, HIV testing, pre- and post-deployment health assessments, immunizations, and inpatient and outpatient encounters from garrison settings.

Issues Identified.

Some interviewees cited data quality and connection issues. Several interviewees commented on the inaccuracy and hence lack of reliability of military data, with one characterizing the problem as "leviathan." Such problems cascade into all military data systems, including DMSS. Solutions to such problems must be recognized by AMSA and others, but remediation is beyond the purview of AMSA alone. Interviewees from AMSA and ASD(HA) commented on data missing from DMSS. AMSA is slowly completing the data entry from paper records for early specimens in the archive. AMSA is also currently incorporating more data into DMSS from routine inpatient and outpatient medical encounters, including diagnoses and pharmacy actions. Incorporation of laboratory data is vexed by the lack of standardization of laboratory testing and reporting across the department.

Deployment-related health data are lacking. The lack of deployment-related data from theater settings represents a gap of particular concern in DMSS at present. Data of interest include health data, (e.g., from the Disease and Non-Battle Injury [DNBI] database, timely tri-service medical event reporting), clinical encounters as recorded in the AHLTA-T platform, and detailed location data.

DMSS links to classified data pose problems. While both the accuracy and availability of personnel location data are problematic, high-resolution person-specific location data during active theater operations (through the Defense Theater Accountability System, DTAS) is generally classified for at least several months. In fact, all data from the field arrive via the classified system, but according to sources in ASD(HA), only the specific location data fields are actually classified. This may be one obstacle to the availability of unclassified location data and timely broader deployment-related data feeds into DMSS. Data classification may also be an obstacle for connecting Mortality Surveillance data into DMSS. We understand that the Theater Medical Data Store is an unclassified data system which may currently or soon contain deployment surveillance data that could be linked into DMSS.

There are opportunities for additional linkages to other military biological specimen collections. Our interviews uncovered and explored potential linkages into DMSS of specimens collected for other purposes and archived elsewhere within the military (that could, through DMSS, be linked to both data and serum repository specimens for specific service members if/as needed). Examples include NHRC's collection of isolates and original throat swab specimens from its Febrile Respiratory Illness surveillance program, the Armed Forces Institute of Pathology (AFIP) Mortality Surveillance Division's necropsy specimens, and AFIP's pathology specimens. At least one of these sources expressed interest in pursuing the potential linkage of such specimens through DMSS and even their availability to complement serum specimens archived by AMSA. There are probably other relevant specimen archives elsewhere within the military services, not uncovered through the RAND team's document review and interviews. In contrast to the generally perceived desirability of DMSS data links for specimens archived elsewhere, there were somewhat divergent views among interviewees regarding storage in the repository of specimens collected for other purposes, e.g., related to specific studies. For example, some expressed interest in collecting and storing specimens from the military's current Millennium Cohort Study overseen

by NHRC (involves 1500 active duty members, to be followed over 20 years),[15] from which specimens are not being collected. However, another military scientist noted that as the source of repository specimens widens, the nature of the specimens -- and hence the standardization of collection and processing procedures – may be compromised, potentially reducing the comparability of specimens that may be selected for subsequent testing.

Data on behavioral risk factors are not available. One interviewee suggested linking behavioral risk factors that may be of interest to acute and/or chronic diseases. Such data are not available through systems currently feeding into DMSS, such as periodic health assessments or pre- and post-deployment assessments, although we learned that DoD does collect such data. The Survey of Health-Related Behaviors Among Military Personnel has collected behavioral risk data from active duty members in several cycles since 1980. The survey was extended in 2005 to include reserve component personnel. However, these data are collected anonymously and as such could not be linked to member-specific records in DMSS. It would be important to ascertain whether survey data could be collected in such a way that data could be linked to individual service member records, or whether selected questions could be added to non-anonymous data collection tools such as pre- and post-deployment health assessment forms.

Access to DMSS is limited. Several interviewees commented that they do not use DMSS. Some expressed discontent that the identified data they send to DMSS is not accessible to them via DMED (which is de-identified and the only database made accessible outside AMSA). Their workaround is to directly obtain the broad range of needed data from such sources as the Defense Management Data Center (DMDC) and other channels.

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[15] Source: accessed 24 January 2008 at: http://www.millenniumcohort.org/endorsements.php

Potential Improvement Strategies. Based on the issues discussed, the key actionable questions related to DMSS data concern lack of connections to certain relevant data sources (especially deployment-related data from theater settings) and data links to other DoD biological specimen archives, the desirability and ability to capture relevant behavioral risk information, potential obstacles associated with classified information, and access by military health users outside AMSA to sufficiently detailed data through DMSS.

- What other data sources should be fed into DMSS?
- Should behavioral risk factor data be captured by DMSS, and if so, how?
- How important are classified data elements, and how can desirable classified data be handled within DMSS?
- Can and should access to DMSS be enhanced?

The strategies described below address these questions.

Strategy 19: Link additional relevant data sources into DMSS in a reliable and timely manner

A first step in this strategy would be establishment of criteria to guide decisions regarding new connections to DMSS. Such criteria should begin with meeting requirements specified throughout relevant military policy, especially deployment health data from theater settings. Other criteria could include potential benefits – e.g., the relevance of specific new data elements to meet the (potentially redefined) mission and range of uses of DoDSR and DMSS in support of Force Health Protection – weighed against potential challenges – e.g., data classification, delays in data availability, interoperability of data systems. An alternative to this systematic process is simply to identify desired new data (several examples are mentioned above) and then proceed to determine how to feed such data into DMSS. It will then be important to review a current inventory of all military databases and their data content and wiring diagrams to determine the best sources of needed data.

Strategy 20: Connect other military specimen collections into DMSS

This strategy first involves a canvassing or inventory of potentially relevant specimen collections currently stored across DoD and then assessing the desirability and feasibility of linking them to DMSS (so that analyses based on these specimens could use the DMSS database) or even making those other specimens available for further testing in conjunction with testing of serum from the same service members. Criteria for such assessments could include size and retrievability of specimens, and the nature and degree of incremental benefit that the new specimens themselves, or at least linkages to DMSS, might provide.

Strategy 21: Capture behavioral risk factor information in DMSS

The first question is the extent to which such information would add relevant value, weighed against the obstacles in obtaining such information. The second question would then be how to do so. Two potential options include changing the longstanding and comprehensive military survey mentioned above from anonymous to non-anonymous status or collection of selected data elements via current non-anonymous tools such as the pre- and post-deployment health and periodic health assessment forms. The first option may not be practical, since the survey's procedures and guarantees of anonymity are well established. Addition of selected questions to current forms is feasible but would take considerable administrative effort, including required approval from Washington Headquarters Services/Directorate for Information Operations and Reports for changing the content of any of these forms. Considerations should include the types of behavioral risk data most relevant to surveillance, epidemiological investigation, clinical support and military health research, the volume of current and projected demand for such data, and the likelihood that information would be truthfully reported (e.g., may be an issue for reporting alcohol or drug use but perhaps less an issue for tobacco use, diet, or physical activity). An appropriately constituted military body should consider the questions related to behavioral risk factor data in greater

detail and weigh potential benefits against administrative and other drawbacks before recommending for or against new data collection that might subsequently be linked into DMSS.

Strategy 22: Overcome obstacles to inclusion of classified data elements

If all relevant data can be obtained from the Theater Medical Data Store, that would be the easiest solution to overcome current limitations ascribed to housing of such data exclusively within classified systems. However, if data are indeed needed from classified systems, there are at least three possible approaches to implementation of this strategy. First, the entire DMSS database could reside and operate within the classified environment and be accessible by others via the SIPRNET. This would require new policy/doctrine and new secure communication facilities, at least for the central AMSA database. The advantages would be access to a broader range of data, most specifically timely, detailed and person-specific location data during deployments. However, all current DMSS data – and the overwhelming majority of any future DMSS data -- are currently unclassified. Permanent residence and operation of DMSS within the classified environment may limit the number of otherwise relevant military users.

A second approach to implementation is a modular one, in which the main DMSS database is maintained within the current unclassified environment but is mirrored into the classified system and linked to classified data elements, on either an as-needed or systematic basis, to permit analyses involving protected data fields. This is particularly relevant to deployment health – to track health in a timely way during ongoing deployments. DMSS is already required to house such information, but currently does not. To fully meet this requirement, AMSA will require a secure communications facility. Similar arrangements would be needed if the full DMSS database were available outside of AMSA. It is important for the broader range of DMSS data – including classified data -- to be available to relevant users when needed, and for AMSA to retain oversight of the DMSS database. It is also important to maintain routine

operations and access within the unclassified environment. Thus, unclassified and classified versions of DMSS, both maintained by AMSA, will likely optimize the number and range of military users.

A third option would be to maintain a strictly unclassified DMSS system which incorporates personnel location information once it becomes declassified. While a logistically simpler approach toward the goal of capturing this information, the disadvantages are the delays until sensitive theater information is declassified and made available to unclassified data systems such as DMSS. Such delays would jeopardize time-sensitive clinical management and epidemiological investigation needs.

Strategy 23: Expand access to DMSS

Expanding access to DMSS beyond AMSA staff can be accomplished in different ways. AMSA already hosts "affiliated analysts" who perform targeted analyses of special interest, e.g., mental health (WRAIR) and deployment health (Deployment Health Support Directorate, under Force Health Protection and Readiness within OSD). If DMSS is made available to remote users, privacy protections must be extended beyond the current central DMSS site to any other sites where DMSS resides or is accessed. This is not a critical factor for the more readily available online DMED database, which includes aggregated and de-identified data.

A first option would be to expand the number of service liaisons and "affiliated analysts" working out of AMSA and directly accessing DMSS. This would enhance AMSA's tri-service visibility and operations while also broadening the AMSA-based staff using the central DMSS database to perform a broad range of relevant analyses needed both by individual services as well as DoD-wide. A second option would be to mirror the DMSS database into each service's surveillance hub (or other designated site), with appropriate privacy protections and procedures as specified and followed by AMSA itself. This would permit direct access by a single site from each service's own location. A third, and related, option would be to broaden DMSS access even further, similar to the

range of access now available online for DMED, by web enabling the data and query systems and controlling its use via password protections. A last approach, and the main one in current practice, is for all analyses requiring identifiable data to be performed by AMSA staff upon request. Because several interviewees expressed concerns about their access to DMSS itself, this last option is probably the least desirable because it poses greatest pressure on the small AMSA staff, resulting in less timely and/or a less robust range of analyses from DMSS, and does not fully satisfy external users who prefer to undertake their own analyses.

Use

Current Status. AMSA and a small number of liaison and periodic "affliliated analyst" staff working out of AMSA's offices are the sole users of the central DMSS database, which has data with individual identifiers (mostly for linking to specimens and for clinical and other support). AMSA converts DMSS into a de-identified database – DMED – for other users. DMED provides aggregated data, mostly from outpatient, inpatient and immunization databases. The full range of users of DMSS and DMED has included AMSA (internal research, e.g., seroepidemiology), military researchers (Uniformed Services University for the Health Sciences, WRAIR, US Army Medical Research Institute for Infectious Diseases, Walter Reed Army Medical Center), clinicians (DMSS data only, for individual patient management), the Military Vaccine Agency, Armed Forces Epidemiology Board (now Defense Health Board), and health surveillance hubs (AFIOH, NHRC, GEIS). Serum specimens are available for use by military researchers. Civilian researchers must partner with military counterparts to access the specimen repository. In addition, patients can request their specimens for medical purposes, but the request must come through their physician. If it is a civilian physician, the request needs to go through a military physician to gain access to the specimen and informed consent must be obtained from the patient.

DMSS data and DoDSR specimens have been used for surveillance, outbreak investigation, clinical management and military research.

Typically, single specimens are requested, e.g. for clinical support or to compare with specimens from ongoing investigations. Longitudinal specimens are much less frequently requested. Moreover, requests for AMSA analyses from DMSS data far exceed the number of requests for serum specimens. Over 175 serum studies were approved by AMSA through early February 2008, mostly for research (and mostly including civilian researchers) and occasionally from policy making components such as the Defense Health Board and Surgeon Generals' offices.

Issues Identified.

Numerous interviewees, both within AMSA and across services, commented that the repository is a "national treasure" that is seriously under-utilized and whose value has not yet been fully realized. Interestingly, several interviewees had personally used the serum repository for research studies or investigations, including studies on chronic diseases. All of them reported good experiences and high value of the repository.

Interviewees commented directly and indirectly about the limited volume of demand for serum specimens stored in DoDSR and the potential for greater use. Data from AMSA indicate that they received approximately 180 different requests for specimens between 2001 and January 2008, or an average of about 25 requests per year.

Underutilization of DoDSR could derive from several potential causes. Interviewees suggested several possible reasons for under-utilization of the repository. First, some commented that military health personnel, especially clinicians, are largely unaware of the repository. Countering this, others expressed concern about managing or accommodating a greatly increased demand. Second, utilization of the repository may be due in part to a perceived mismatch between range of missions for DoDSR as defined in policy (and perceived areas of value as expressed by interviewees) and the surveillance mission of AMSA, which oversees DoDSR. For example, some interviewees commented that the serum repository has no role in surveillance or situational awareness, based on a perception of surveillance within a real-time time frame. In

contrast, AMSA staff consider comparison of pre- and post-deployment specimens a surveillance function.

Some interviewees also commented that the repository is not valuable for (real time) deployment health, and that systematic testing of pre-and post-deployment specimens is not carried out. However, another interviewee countered that infectious diseases, for which the serum specimens are most relevant, are not proving to be a major health problem in current theater operations. Even chronic disease research studies most often have examined infectious disease markers (antibodies) from serum specimens, looking at potential infectious disease precursors to selected chronic diseases.

Nearly all interviewees consider the repository valuable for both outbreak investigations and research. Indeed, one military group commented that the repository is not very valuable because DoD's main focus is operational support, whereas the repository is well suited to support research to improve Force Health Protection, which may not be viewed as operational support, thus limiting -- either by perception or in reality – the use of the DoDSR for research. Indeed, several interviewees commented on the great value – and largely untapped potential – of the longitudinal specimens available through the repository. Finally, there were differing views regarding the utility of the repository for clinical support.

Interviewees expressed mixed views on whether repository specimens should be made more accessible for civilian research. More than one interviewee raised the possibility of making repository specimens more readily available to civilian researchers, including more active use by the Veterans Health Administration (VA). However, others expressed potential concerns with broadening access -- other than potentially to the VA-- e.g., because of the limited number of aliquots per specimen, risk of deviating from military mission or interests, and complications introduced if any funding for additional repository support (in exchanges for increased repository access) might come from non-military sources as a result of opening access beyond the military.

Potential Improvement Strategies. Based on the issues discussed, the key questions related to use of the repository and DMSS data concern under-utilization of specimens, for a variety of potential reasons including lack of awareness, lack of consensus regarding appropriate uses of serum specimens (which may be associated in part with the mismatch between AMSA's stated surveillance mission and limited staff size versus potential research uses), and lack of value or use in support of deployment health. Another key question concerns the under-utilization of multiple/longitudinal serial specimens from the repository.

- Should efforts be made to raise awareness of the repository, especially among military health personnel; similarly among civilian researchers?
- How can the repository be more useful to deployment health?
- How can longitudinal nature of the serum specimens be used to greatest advantage?

The strategies described below address these questions.

Strategy 24: Raise awareness of DoDSR and DMSS

Information campaigns to raise awareness of DoDSR and DMSS can broaden the user base and increase the use of these resources. Communications efforts can selectively target groups relevant to specific uses, e.g., clinicians for clinical support uses; alternatively, they can take a broader approach to educate the entire military health community and others regarding the availability and full range of uses of these specimen and data resources. Once the mission and full range of appropriate uses of the repository and DMSS database are clarified or redefined, information about the availability of and procedures for accessing these resources can be widely disseminated. AMSA can take the lead for such efforts, including renewed encouragement to their service surveillance hub counterparts to enhance their use of the repository and DMSS resources. Other appropriate entities can also help raise awareness, e.g., the Joint Preventive Medicine Policy Group (for surveillance, investigation and research uses), Tricare Management Activity, service Surgeon Generals' offices, and the VA (for clinical

support uses), the Uniformed Services University of the Health Sciences and potentially others for research uses, and/or relevant officials within the Office of the Secretary of Defense such as the Assistant Secretary of Defense for Health Affairs or the Under Secretary of Defense for Personnel and Readiness. The Deployment Health Centers – NHRC (research) and Walter Reed Army Medical Center (clinical) can also contribute to raising awareness across a broader range of relevant military users. The advantages of this strategy include more robust use of what has been widely acknowledged as a valuable but under-utilized military resource. However, increased demand for specimens may lead to more rapid draw-down of available serum aliquots and further burden AMSA's current small staff. Such disadvantages could be mitigated by other improvement strategies, such as release of smaller aliquots and more robust staffing of AMSA, including military staff from other services, if/as required to meet an expanded mission or level of demand.

Strategy 25: Coordinate actions to increase the utility of the repository and DMSS for deployment health

Because military policy (e.g., DoDD 6490.03, DoDD 6490.02E, USD(P&R) Memorandum of April 2003, MCM-0006-02 JCS Memorandum of February 2002) emphasizes the importance of deployment health and requires timely submission of data to DMSS and specimens to the repository, enhancing the use and perceived value of these resources in support of deployment health should be a particular priority, especially acquisition of relevant data from deployed settings. Based on our analyses and comments from interviewees, implementation of this strategy could involve a number of potential specific actions:

- Fully implement current requirements for timely feeds of relevant deployment health data into DMSS, e.g., DNBI, tri-service medical event reports, data from medical encounters as recorded on DD Form 2766 and via the AHLTA-T platform, and person-specific location information (declassified, with a 60+ day delay, or more timely classified location data requiring a classified version of DMSS, as described in Strategies #19 and #22 above).

- Reinforce communications to the other Deployment Health Centers and to other relevant users (including the VA) regarding the availability and utility of the DoDSR and DMSS in support of deployment health --especially if relevant new data are fed into DMSS and on a more timely basis.
- Increase the systematic analysis and reporting on trends specifically linked to deployments, especially based on the new data linkages from theater environments as noted above. A more resource-intensive strategy would be proactive and systematic testing of, pre- and post-deployment serum specimens (all or a relevant specimen) for infectious disease surveillance purposes. This could be done by AMSA, other service surveillance hubs, other Deployment Health centers, the VA, or other relevant military health personnel.

Strategy 26: Broaden civilian access to the specimen repository, including VA and other researchers

There are both incremental and broad approaches to implementing this strategy. For example, a first priority might be to raise awareness and use of DMSS and/or the repository among the VA medical/health community, either selectively, e.g., for clinical support to individuals, or more broadly, e.g., for the full range of uses of the data or serum specimens – individual medical management, public health investigation, or research for health or clinical management policy for service members on active duty or separated. This incremental approach maintains the strong military focus of the specimen and data resources, while extending access beyond the DoD itself. While AMSA provides deployment health form data to the VA for separating service members, more of the VA health community, including its leadership, should be made aware of their access to DMSS and DoDSR resources.

A broader approach to this strategy would be to make the data and/or specimen resources more available to civilian researchers, either

passively (make aware but do not actively advertise) or actively (advertise availability). Further, civilian researchers could still be required to partner with a military co-Principal Investigator or not, and the proposed research could be required to demonstrate relevance to the military or not. Combinations of these various options could result in narrow to broad expansion of non-DoD users of DMSS data and/or specimens. However, human subjects protection becomes an increasing issue and challenge if/as use expands beyond surveillance and investigation purposes and beyond military users. Purely civilian research not directly tied to military priorities may prove to be an obstacle for ethical reasons, unless human subjects protection issues can be resolved. (Strategy #6 proposes ways to address human subject protections.) Military leadership may wish to consider this issue more comprehensively by asking an appropriately constituted group to review the different options and their associated implications and offer more specific policy recommendations.

Strategy 27: Increase use of serial specimens from the repository

Since serial specimens (beyond strictly paired specimens) are of greatest value for longitudinal research, and because both the DoDSR and DMSS are longitudinal in nature, these resources provide unique opportunities for surveillance and research drawing upon a longitudinal population sampling design. Assuming the continued legitimacy of research use for the specimens, the awareness raising efforts described in Strategy #24 would be appropriate. Military health leadership and appropriately constituted groups could help raise awareness across the military and VA health/medical research community, with a particular focus on the unique large and serial nature of the serum repository. The Uniformed Services University of the Health Sciences could also play a key role in both promoting and using specimens for appropriate longitudinal studies.

CHAPTER HIGHLIGHTS

The DoDSR and DMSS have already demonstrated their value to military health surveillance and to military health more broadly. Nonetheless, this systematic review has led to the identification of potential ways to further improve the use and hence value of these resources. Several of the improvement strategies described above are interdependent, so they should not be considered purely independently. Based on the review in this chapter alone, a "package" of improvement strategies could include the following:

- Explicit clarification of the mission and authorized uses of the DoDSR and DMSS to include surveillance, clinical support, investigation, and research in support of Force Health Protection, deployment health and the health of separated service members;
- Communications to promote a common understanding of the meaning of such terms as "surveillance" and "research" as they relate to the DoDSR and DMSS in particular, and to promote use of these resources;
- More timely availability of specimens from DoDSR;
- Establishment of clear criteria and procedures for accessing DoDSR specimens;
- Linkages of new data sources to DMSS, particularly health and other data from ongoing deployments;
- Expanded access to DMSS;
- Ongoing collection of specimens, on a voluntary basis, from separated service members followed at MTF's or through the VA health system;
- Archiving of new blood-derived specimens that reliably retain genetic material for future testing, including biomarkers and tests yet to be identified and developed;
- Final determination of location, space and other requirements for the new repository.

The discussion and recommendations in the following chapter aim to consolidate and suggest priorities for consideration by military authorities.

Figure 6.2.
Summary of Current DoDSR/DMSS System Elements and Characteristics

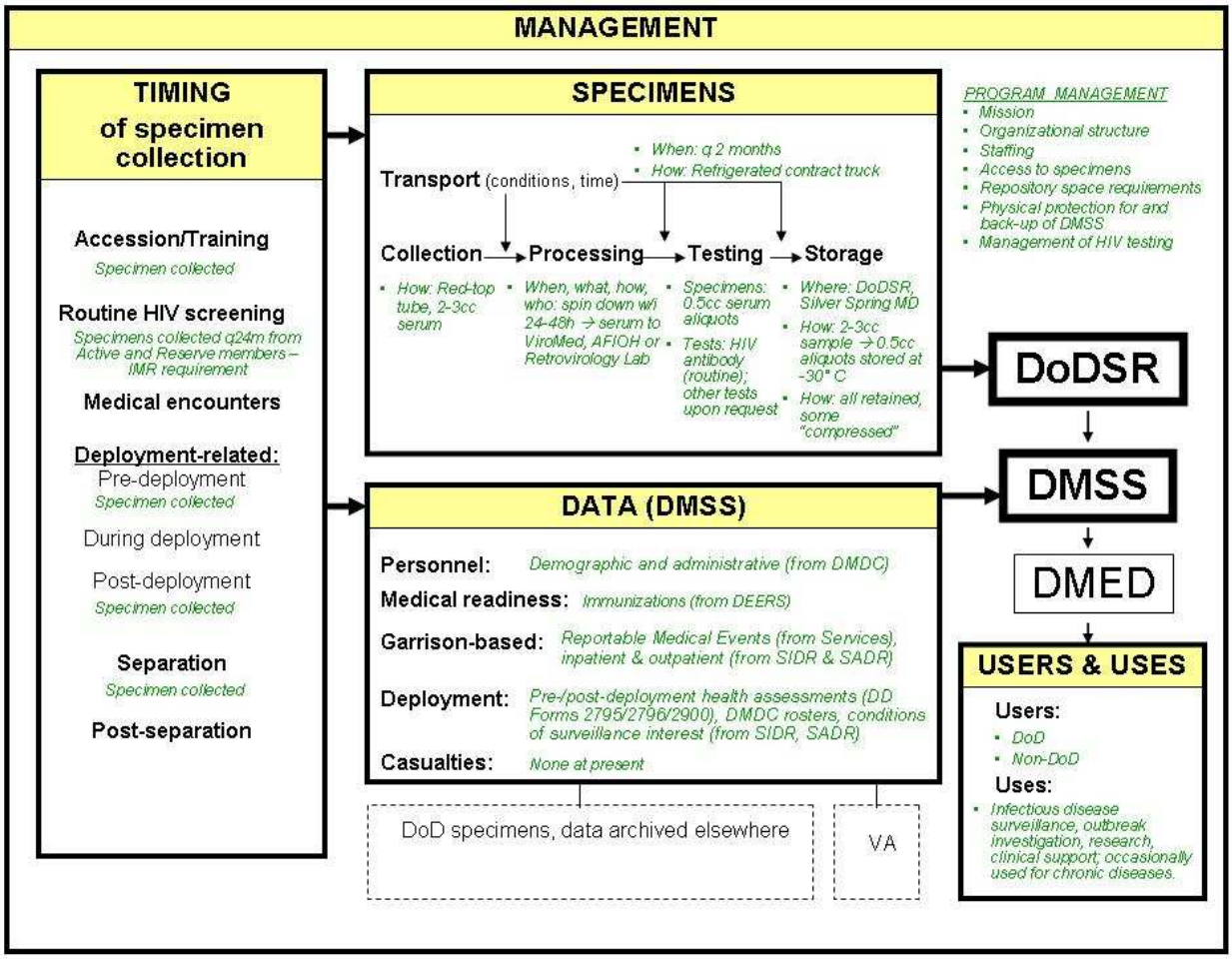
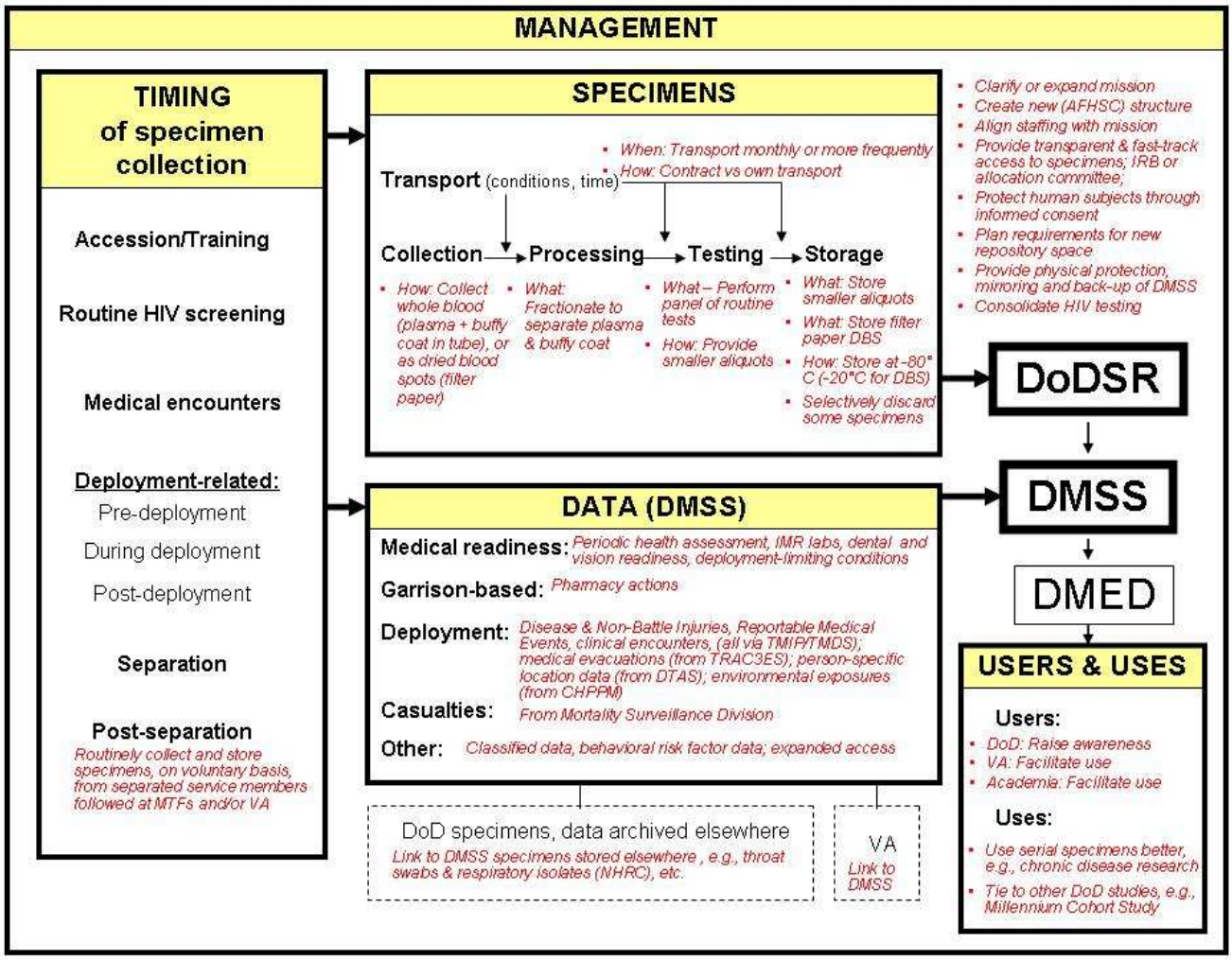


Figure 6.3.
Summary of Potential Improvements in DoDSR/DMSS System Elements and Characteristics



CHAPTER 7. SYNTHESIS AND RECOMMENDATIONS

It is clear from document review and interviews with a broad range of staff throughout DoD that AMSA has been a good steward of the DoDSR and DMSS resources and has used them well in support of military medical surveillance in particular. However, the goal of this study was to help identify opportunities to make even better use of these resources in addressing military health needs now and into the future.

Our analyses have uncovered specific opportunities to better fulfill current requirements, especially to close gaps in the content and efficiency of medical surveillance. The largest gap relates to data from deployed settings, which figures prominently within the strategies described in the previous chapter and the recommendations presented here. Our report also describes the larger context for DoD surveillance, which is important to consider as potential improvements in the DoDSR and DMSS components are contemplated, i.e., medical surveillance together with occupational and environmental health surveillance constituting "health surveillance," and these all within the even larger context of "comprehensive health surveillance," which encompasses the entire career of service across all locations. Beyond surveillance, we have also identified specific ways to position the DoDSR and DMSS resources to better serve the military of the future -- planning now for changes that will permit a wider range of uses to improve not only surveillance but also clinical management and research in support of Force Health Protection. Taken as a whole, the recommendations we offer below suggest that the DoDSR and DMSS could benefit from improved oversight and management to ensure they function within the strategic goals of the Military Health System, and have access to the needed data systems as well as other resources needed on an ongoing basis. This chapter draws from the preceding chapter and synthesizes our findings into six main recommendations. There are key decisions that need to be made at the Undersecretary of Defense level which will cascade across the recommendations we offer here, affecting the direction of the decisions as well as the magnitude of change.

1. CLARIFY AND COMMUNICATE THE MISSIONS OF DODSR, DMSS AND AMSA BOTH WITHIN AND BEYOND DOD

There is a mismatch between Congressional direction for the use of the DoDSR and the DMSS data system as articulated in several enactments of the National Defense Authorization Act and the articulation of the mission and use of the DoDSR and DMSS by AMSA. Clear articulation by military policy makers and a common understanding by AMSA managers and DoDSR and DMSS users of the full range of uses for these resources – including surveillance, epidemiologic investigation, clinical management, and research related to both infectious and non-communicable diseases - should lead to their more efficient use within DoD. Further, the mission of DoDSR and DMSS to collect specimens and data could also extend beyond DoD active or reserve populations to include continuation of data and specimen collection on a voluntary basis from service members followed in Military Treatment Facilities and/or the Veterans Administration health system. To harness the full potential of the DoDSR and DMSS resources, the full range of mission areas for these resources and their organizational oversight must be made explicit and communicated widely across DoD and into related research and epidemiologic communities.

2. EMPOWER, STRUCTURE, AND RESOURCE THE ORGANIZATIONAL OVERSIGHT OF DODSR AND DMSS SO THAT THEY CAN FULFILL THE FULL RANGE OF MISSIONS

In Chapter 2 we describe how DoD's own policy envisioned a tri-service surveillance center, and we believe the vision and guidance to be relevant and timely today. Specifically, a 1999 ASD(HA) Memorandum described the migration of DMSS toward a "DoD Medical Surveillance Agency" collecting all theater medical surveillance and treatment data collected by the services, unified and specified commands, and individual commands within the services. Further DMSS was directed to provide access to personnel and health surveillance data to other agencies involved in medical surveillance and health research. (ASD(HA), September 30, 1999).

As we describe in the preamble to our report, DoD officially established the Armed Forces Health Surveillance Center in late February

2008. We learned from our interviews that the intent for this organization is to encompass DoD-wide *medical surveillance* activities within one organization, by combining AMSA, GEIS and the Deployment Health Support Directorate of OSD(HA). Review of the AFHSC Concept of Operations indicated that the new organization will also encompass the broader range of *health surveillance* components and activities, i.e., including occupational and environmental health in garrison and deployment settings (although details of these were largely beyond the focus of this study). We assume that the name of the new organization, i.e., specifically referring to "Health Surveillance", will not create limitations or confusion in the full range of missions served by the organizational components it oversees, most notably DoDSR. The organization is envisioned to be a tri-service surveillance agency, although we understand that there are serious concerns among the services about how to staff such an agency and what the appropriate oversight of the agency should be.

We recommend that the AFHSC be situated organizationally, empowered, and resourced to connect the various experts, contracts, and systems that are required not only for its primary surveillance mission but also for the full range of uses for the DoDSR and DMSS resources it manages through its Executive Agency function, including surveillance, epidemiologic investigation, clinical management and research. The chain of command and oversight for this organization should be such that it can receive guidance and resources from policy makers responsible for all of these functions, e.g., the ASD(HA), Surgeons General and Army Medical Research and Materiel command, in order to ensure proper alignment with current Military Health System strategy and resources. The AFHSC should be configured and staffed to provide the support needed by all users, and especially those within DoD, in support of its various missions. In Chapter 6 we describe approaches to leveraging new staff resources if needed.

3. CREATE AN INTEGRATIVE DATA PLAN FOR COMPREHENSIVE HEALTH SURVEILLANCE

Ideally, AFHSC should develop a construct wherein all the various data required for medical surveillance and broader health surveillance

would be linked and would reflect the underlying tenets of comprehensive health surveillance. Currently, as we describe in Chapter 3, there are many data systems within the services and COCOMs that are being used for various medical and other health surveillance functions. There are issues related to data classification and connections which impede DMSS from being a fully functional deployment medical surveillance tool, although the capabilities that are not resident in DMSS are being conducted at other sites and with other systems. However, there seems to be no overarching and comprehensive data plan prescribing integration of all relevant heath surveillance data. Such a plan should address issues such as connectivity to occupational and environmental health surveillance systems, both within the garrison and deployed settings, increasing data collection along the service member's period of service and beyond, and fully realizing policy efforts to facilitate access to surveillance and other data by the VA.

Regarding DMSS specifically, over the past several years AMSA has effectively increased the number of data feeds into DMSS and has expanded the breadth of its surveillance reporting accordingly. However, several relevant data sets remain unconnected to DMSS, thus limiting the ability of AMSA to fully execute its surveillance mission and for DoD more broadly to take advantage of the full range of value offered by DMSS. The highest priorities for new data linkages into DMSS relate to deployment health, serving primarily but not exclusively a deployment health surveillance mission. These data sources include theater-based reportable medical events, clinical encounters (via AHLTA-T) and disease and non-battle injury (DNBI) data, all available via the Theater Medical Information Program, TMIP. Ideally, all relevant health surveillance data can be made available to DMSS via the unclassified Theater Medical Data Store. Member-specific deployment location information is also important and available through the Deployment Theater Accountability System, though the data in this system are classified. The main options for linking such data into DMSS include time-delayed incorporation of declassified location data or near-real time incorporation of classified data. The latter imposes potentially new requirements on AMSA, i.e., for

a secure communications facility to house either the original or a mirrored version of the DMSS database. Other relevant linkages to consider are to existing DoD biological specimen archives such as isolates and original nasal swab specimens maintained by NHRC from its Febrile Respiratory Illness surveillance system and pathology and necropsy specimens maintained by AFIP. Consideration should also be given to collecting and archiving specimens from the recently initiated Millennium Cohort Study, overseen by NHRC. More robust linkages in both directions between DMSS and the VA health system should also be considered, to the extent that the mission of DoDSR and DMSS are expanded beyond strictly active duty and reserve populations. Also, consideration should be given to whether and how behavioral risk factor data should be collected and fed into DMSS, as discussed in Chapters 4 and 6. Finally, as technology develops new ways of testing for the presence and use of chemical or biologic weapons, DMSS might be tailored to contribute to surveillance or research for these potential threats. Because there are many current data sources which might be tapped for deployment health surveillance, and there may be more in the future, the new AFHSC would be better positions to fully execute its mission if it were included in the Military Health System information requirements process currently managed at the Tricare Management Agency.

Better protection of DMSS's physical infrastructure and the integrity of the data(i.e., to resist physical or cyber threats to the DMSS database) is also needed. We recommend that strong consideration be given not only to assuring adequate housing of the data system, but also to systematic and frequent off-site back up and even parallel mirroring of the DMSS database, to assure its integrity in response to any threat that may arise, as occurred in late January 2008.

4. ENHANCE THE UTILITY OF SPECIMENS

The DoDSR serum specimens continue to serve well their original purpose of HIV serosurveillance. However as we discussed in Chapter 2, as early as 1997, the DoD made a decision to use serum as the tissue of convenience for deployment health surveillance. The sera permit

examination of deployment-related exposures to and investigations of infectious agents; they are not particularly useful for time-sensitive environmental exposures for which biomarkers are only fleetingly present. And, as military health research becomes broader and more technologically sophisticated, the limitations of current serum specimens become more apparent: Researchers increasingly recognize the importance of genetic material for current and future research into a range of acute and chronic conditions. Serum specimens as presently stored in the DoDSR at -30°C do not reliably preserve genetic material. Therefore, it is timely at this juncture, as the current repository lease expires and AMSA looks toward serving the longer-term needs of the military health system, to consider ways to enhance the utility of the DoDSR specimens.

There may be some incremental value in storing future serum specimens at -80°C (note that storage of current specimens at colder temperatures would not change the availability of analytes for future testing). Even greater value would be derived from whole blood specimens, e.g., stored in liquid form or as dried blood spots, or storage of buffy coat fractions in which the quantity of genetic material is substantially greater (see description in Chapter 5). Storage requirements for dried blood spots are modest and incrementally the easiest. Alternatively, archiving of plasma and buffy coat could be accomplished through collection of blood specimens in a tube that allows fractionation into plasma and buffy coat; plasma can be used in place of serum for routine HIV testing and for essentially all other tests currently performed on DoDSR serum specimens. Storage of both plasma and buffy coat at -80°C reflects current best industry practices for preservation of genetic material and other relevant blood-derived analytes. However, adoption of this alternative would mean costly new repository requirements for future specimens, i.e., walk-in freezers would not be possible for storage at -80°C. Nonetheless, the near-term expiration of the current repository lease and potential relocation provides a timely opportunity for military leadership to think carefully about the needs of the military health system into future and determine

whether new kinds of specimens should be archived, to better serve a broader range of mission areas for this valuable military resource.

5. RAISE AWARENESS OF AND EXPAND ACCESS TO DODSR AND DMSS

A number of interviewees commented that use of the DoDSR and DMSS resources may be limited because of limited awareness across DoD. For example, one military medical officer noted that military clinicians are largely unaware of these resources in support of clinical management. Likewise, a senior health official within the VA system was largely unaware of the rich specimen and data resources managed by AMSA. Several interviewees suggested broad or targeted "educational campaigns" to raise awareness and use of DoDSR and DMSS.

Some interviewees suggested that access has been limited because of what they perceive as lack of fully transparent criteria for release of specimens. A remedy for this could include development and dissemination of updated and transparent criteria and procedures for accessing DoDSR specimens and DMSS data. The cost associated with obtaining specimens from the repository, $20 per specimen, has also been cited as a barrier for civilians wanting to tap into the DODSR for the purposes of research.

In terms of expanding use, the first priority should probably be for military health users within DoD, followed by more robust use by the VA. DoD should carefully consider whether and how to expand use to civilian researchers, while protecting individual privacy, the overall military health mission, and availability of remaining specimens as more users draw down the number aliquots from a given specimen. Finally, efforts should be made to take better advantage of the longitudinal nature of the DoDSR inventory, e.g., through clarifying the legitimate use of DoDSR for research and sensitizing military health researchers to the availability of these serial specimens and linked data.

6. PLAN FOR THE NEXT REPOSITORY FACILITY

Finally, depending on decisions related to the strategies described in Chapter 6 and the recommendations above, DoD should begin

already to define the requirements for the next repository, following expiration of the current lease in 2010. Factors to take into consideration include the time horizon for the next repository (e.g., 20 years or more), the annual rate of specimen acquisition (which would increase if specimens are to be collected from members following separation), the types of specimen to be archived (e.g., serum or plasma, buffy coat, whole blood in liquid form or as dried blood spots), and desired storage temperature (e.g., -30°C or -80°C). All of these influence the size and configuration of the future repository and hence the requirements for future repository space.

CONCLUSIONS

The goal of this study was to help identify opportunities to make even better use of DoDSR and DMSS resources in addressing military health needs now and into the future. Our analyses uncovered specific opportunities to better fulfill current requirements, especially to close gaps in the content and efficiency of medical surveillance. The largest gap relates to data from deployed settings, which figures prominently within the strategies we describe in the report and our recommendations. Beyond surveillance, we have also identified specific ways to position the DoDSR and DMSS resources to better serve the military of the future -- planning now for changes that will permit a wider range of uses to improve not only surveillance but also clinical management and research in support of Force Health Protection. Taken as a whole, our recommendations suggest that the DoDSR and DMSS could benefit from improved oversight and management to ensure they function within the strategic goals of the Military Health System, and have access to the needed data systems as well as other resources they need to fulfill their mission. There are key decisions that need to be made at the Undersecretary of Defense level which will cascade across the recommendations we offer here, affecting the direction of the decisions as well as the magnitude of change.

AMSA has been a responsible custodian for the DoDSR and DMSS, characterized by multiple interviewees as "national treasures" whose

full potential has yet to be fully harnessed. Creation of the new AFHSC and relocation of the repository offer the opportunity to consider how the DoDSR and DMSS resources can be used to even greater advantage to support military health now and into the future. This study took a systematic approach to analysis of current characteristics and opportunities for improvement. Some of our recommendations are relatively easy, while others are more ambitious. Nonetheless, we feel that implementation of all of these recommendations will allow the AFHSC to better fulfill its current requirements, serve a broader range of legitimate mission areas, and position the DoDSR and DMSS resources for valuable service well into the future.

APPENDIX 1.
SUMMARY OF LEGISLATION AND POLICY ESTABLISHING REQUIREMENTS FOR DODSR AND DMSS

Source and Date	Key provisions
ASD(HA) Memorandum December 5, 1985 (Superseded by DoDD 6485.1, March 19, 1991)	***The DoD HTLV-III Testing Program***
DoDD 6485.1 (Originally issued March 19, 1991, Reissued August 10, 1992). Superseded by DODI 6485.01 (October 17, 2006. Not included here)	***Human Immunodeficiency Virus-1 (HIV-1)*** ➢ Establishes DoD's HIV program ➢ Does not mention serum repository
DoDI 6490.3(August 7, 1997) (Superseded by DoDI 6490.03, August 11, 2006. See below.)	***Implementation & Application of Joint Medical Surveillance for Deployments*** ➢ Mandates joint comprehensive medical surveillance for active service, including reserve component, before/during/after deployments ➢ Medical surveillance includes Armed Forces Serum Repository & data ➢ CHPPM charged with operation of repository & data system ➢ Specifies use of specimens exclusively in relation to military operations ➢ Charters establishment of Joint Preventive Medicine Policy Group
DoDD 6490.2 (August 30, 1997) (Superseded by DoDD 6490.02E, October 21, 2004. See below.)	***Joint Medical Surveillance*** ➢ Designates Army as Executive Agent for deployment medical surveillance and serum repository ➢ Requires that medical and personnel data systems be compatible with military medical surveillance ➢ Charges CHPPM to perform periodic (not routine) epidemiologic studies of data derived from the serum repository
Public Law 105-85 (November 18, 1997)	***National Defense Authorization Act, FY98*** ➢ Requires DoD to draw blood specimens pre- and pos-deployment and maintain a central archive of health records relating to deployments

Source and Date	Key provisions
ASD(HA) Memorandum (October 6, 1998)	***Policy for Pre- and Post-Deployment Health Assessments and Blood Samples*** ➢ Establishes the pre- and post-deployment health assessment for all military members, including collection of blood specimens
Public Law 105-261 (October 17, 1998)	***National Defense Authorization Act, FY99*** ➢ Authorizes establishment of a center for deployment health ➢ Requires the center to collect and study data in order to determine the effect of deployment on health
ASD(HA) Memorandum (November 6, 1998)	***Tri-Service Reportable Events*** ➢ Requires the use of a tri-service reportable events list, established by a joint working group, the Joint Preventive Medicine Policy Group, by all services ➢ Directs reportable events to be integrated into DMSS ➢ Requires DMSS to make data available to all services for further analyses
Joint Chiefs of Staff MCM-251-98 (December 4, 1998)	***Deployment Health Surveillance and Readiness*** ➢ Provides standardized procedures for assessing health readiness for deployment ➢ Establishes deployment health surveillance procedures
ASD(HA) Memorandum (February 3, 1999)	***Policy for DoD Global, Laboratory-Based Influenza Surveillance*** ➢ Designates DMSS as the influenza surveillance data base

Source and Date	Key provisions
ASD(HA) Memorandum (September 30, 1999)	***Establishment of DoD Centers for Deployment Health*** ➢ Continues the use of DMSS for medical surveillance ➢ Describes DMSS migration strategy toward "DoD Medical Surveillance Agency" ➢ Requires all theater medical surveillance and treatment data be forwarded to DMSS ➢ Requires remote access to DMSS be provided to NHRC and others involved in surveillance & military health research ➢ Requires TMA provide unrestricted access to applicable MHS data and support DMSS as appropriate ➢ Defines DMSS as the comprehensive longitudinal, relational, epidemiology database for the study of deployment health ➢ Establishes Deployment Health Working Group
ASD(HA) Memorandum (October 25, 2001)	***Updated Policy for Pre and Post-Deployment Health Assessments and Blood Samples*** ➢ Updates original HA Policy 99-002 (October 1998) to apply all deployment-related health assessments and specimen collections for all reserve component personnel called to active duty for ≥30 days ➢ Stipulates use of DD2795 and DD2796 across all services
Joint Chiefs of Staff MCM-0006-002 (February 1, 2002) (Supersedes MCM-251-98, December 4, 1998 See Above.)	***Updated Procedures for Deployment Health Surveillance and Readiness*** ➢ Justifies comprehensive health surveillance within FHP ➢ Requires all deployment health surveillance data be sent to DMSS ➢ Notes the value of near real-time DNBI data ➢ Alludes to DD Form 2766 (also as deployed medical record) ➢ Requires commanders provide DNBI & reportable medical events data and post-deployment health assessment forms on a timely basis ➢ Requires DNBI data be sent weekly and simultaneously to COCOM Surgeon & to service surveillance centers and DMSS

Source and Date	Key provisions
USD(P&R) Memorandum (April 22, 2003) (Canceled by DoDI 6490.03, Deployment Health, August 11, 2006. See below.)	***Enhanced Post-Deployment Health Assessments*** ➢ Requires face-to-face post-deployment health assessment, using revised DD Form 2796 ➢ Shortens the interval for post-deployment health forms and serum specimens to 30 days following redeployment home
ASD(HA) Memorandum (May 01, 2003)	***Tracking Post-Deployment Health Assessments*** ➢ Requires services to put in place weekly reporting of completion rates of post-deployment health assessments
ASD(HA) Memorandum (January 9, 2004)	***Policy for DoD Deployment Health Quality Assurance Program*** ➢ Requires AMSA send at least monthly reports to OSD/DHSD on deployment health assessment data ➢ Establishes baseline metrics relating to deployment health assessment forms and post-deployment sera ➢ Requires services to establish deployment health QA programs
ASD(HA) Memorandum (May 21, 2004)	***Automation of Pre- and Post-deployment Health Assessment Forms*** ➢ Requires plans for electronic submission of DD Forms 2795 and 2796 and integration into an eventual MHS Central Data Repository
DoDD 6200.04 (October 9, 2004; Certified current as of April 23, 2007)	***Force Health Protection (FHP)*** ➢ Requires "routine annual health, medical, and dental assessments", "annual assessment of IMR," (para 4.3.1.3) pre- and post-deployment and separation health assessments ➢ Specifies DoD maintain a central repository for bio-specimens to be used in clinical care, forensics, and epidemiologic studies ➢ Specifies that DoD "pursue scientific and technological advancements to improve and protect the health of the force through medical research, development, clinical investigations, technology insertion, and appropriate acquisition strategies"(para 4.5)

Source and Date	Key provisions
DoDD 6490.02E (October 21, 2004; Certified current as of April 23, 2007) (Supercedes DoDD 6490.2, August 30, 1997. See above)	***Comprehensive Health Surveillance (CHS)*** ➢ Specifies surveillance across service members' careers, duty locations, and spectrum of health risks, interventions & outcomes ➢ Defines comprehensive, health, medical and occupational and environmental surveillance ➢ Specifies CHS as important to FHP ➢ Requires medical and personnel data systems be designed to be compatible with military health surveillance objectives ➢ Requires surveillance data be transferred to VA upon separation ➢ Broadens scope of DoDSR beyond deployment surveillance ➢ Calls (again) for establishment of Joint Preventive Medicine Policy Group ➢ Reiterates Army as Executive Agent for DoDSR, DMSS
Public Law 108-375 (October 28, 2004)	***National Defense Authorization Act, FY05*** ➢ Reduces time frame for collection of pre-deployment specimens from 12 months to 120 days prior to deployment, as an interim standard to be re-examined by DoD ➢ Requires DoD to maintain a theater health record ➢ Requires DoD to evaluate its deployment medical tracking and health surveillance sytems which included a scientific review of the utility of blood sampling procedures for exposure detection ➢ Requires DoD to prescribe policy relating to classification of in-theater data
DASD(FHP&R) Memorandum 27 January 2005	***Requirements for Blood Samples Before and After Deployments*** ➢ Responds to the NDAA FY05 ➢ Requires compliance with interim blood sampling time frames of no more than 120 days pre-deployment and 30 days post-deployment ➢ Describes request to AFEB and CDC to answer questions posed by Congress in NDAA FY05

Source and Date	Key provisions
ASD(HA) Memorandum (March 10, 2005)	***Post-Deployment Health Reassessment*** ➢ Requires post-deployment reassessment 3-6 months following return to home station (new DD Form 2900) ➢ Requires automated form be submitted to AMSA for DMSS ➢ Defines purpose as proactive identification of health concerns emerging over time following deployments, especially mental health
AFEB 2005-03 (April 28, 2005)	***Response to Questions Pertaining to the Utility of the Requirements to Collect and Store Pre- and Post-Deployment Serum Specimens*** ➢ Recommends serum with WBC as an "acceptable and cost effective specimen for the analysis of most biological and some chemical agents of current and future interest to [DoD]"(para 7) ➢ Recommends widespread awareness and use of DoDSR ➢ Recommends consideration of an "oversight panel to help govern access to the archived specimens"(pg3, question 2) ➢ Supports current pre- and post-deployment windows for specimen collection and continuation of 100% sampling for these
DoDI 6025.19 (January 3, 2006)	***Individual Medical Readiness*** ➢ Establishes a baseline of six elements describing individual medical readiness across all services and applicable to all service members ➢ Requires ASD(HA) to oversee tri-service IMR program and to report data
ASD(HA) Memorandum (March 14, 2006) (Rescinds DASD(FHP&R) Memorandum, 27 January 200. See above.)	***Policy for Pre- and Post-deployment Serum*** ➢ Re-establishes timing of pre-deployment serum specimen collection up to one year prior to deployment, and post-deployment collection within 30 days after deployment

Source and Date	Key provisions
DoDI 6490.03 (August 11, 2006) (Supersedes DoDI 6490.3, August 7, 1997. See above.)	***Deployment Health*** ➢ Reiterates requirements for post-deployment and separation serum specimens & forwarding deployment health assessment forms to DMSS ➢ Requires COCOM commanders provide timely reporting of DNBI and other medical information (Note: reporting destination not specified) ➢ Requires DoDSR/DMSS to make "individual and Service aggregated data" available to military services (5.8.11) ➢ Specifies that DMSS provide periodic trend analysis reports and integrated Reportable Medical Events data to service components ➢ Requires all deployment phase medical encounters be recorded on DD Form 2766 or equivalent ➢ Requires daily review of DNBI data and tri-service reportable medical events reported to COCOM or service component "via currently approved and available electronic data collection and transmission devices"(E4.A2.4) ➢ Requires, to the extent feasible, that deployment health data "be collected and maintained in DoD-approved automated health information management systems" (E4.A2.4) (Note: No system specified.)
DoDD 6490.02E (October 21, 2004; Certified current as of April 23, 2007) (Supersedes DoDD 6490.2, August 30, 1997. See above)	***Comprehensive Health Surveillance (CHS)*** ➢ Specifies surveillance across service members' careers, duty locations, and spectrum of health risks, interventions & outcomes ➢ Defines comprehensive, health, medical and occupational and environmental surveillance ➢ Specifies CHS as important to FHP ➢ Requires medical and personnel data systems be designed to be compatible with military health surveillance objectives ➢ Requires surveillance data be transferred to VA upon separation ➢ Broadens scope of DoDSR beyond deployment surveillance ➢ Calls for establishment of Joint Preventive Medicine Policy Group ➢ Reiterates Army as Executive Agent for DoDSR, DMSS

Source and Date	Key provisions
Joint Chiefs of Staff MCM 0028-07 November 2, 2007	***Updated Procedures for Deployment Health Surveillance and Readiness*** ➢ Focuses particularly on occupational/environmental surveillance and risk assessment ➢ Specifies that disease and injury data be reported on timely basis and electronically where feasible (through Patient Encounter Modules [PEMs] that feed into JMeWS, AHLTA-T or JPTA) ➢ Mentions "Armed Forces Health Surveillance Center" as one of several "upstream authorities", and separately notes USACHPPM, AFIOH and NEHC as service surveillance hubs ➢ Does not explicitly specify DMSS as destination for any deployment health data

APPENDIX 2.
PUBLISHED RESEARCH CONDUCTED FROM SERA AT THE DOD SERUM REPOSITORY OR BASED ON DATA DRAWN FROM THE DMSS

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June 27, 2006

In reply refer to:
ET06-0649.0022

BG Michael Cates
MCHB-CG
U.S. Army Center for Health Promotion and Preventative Medicine
5158 Blackhawk Road
Aberdeen Proving Ground, MD 21010-5403

Subject: RAND Proposal No. 2006-0649
Under Contract No. W74V8H-06-C-0001

Dear Brigadier General Cates:

The RAND Corporation is pleased to submit the enclosed proposal entitled "Optimizing U.S. Armed Forces Biosurveillance for Influenza and Other Strategic Health Threats," with Melinda Moore and John Zambrano as Principal Investigators. The objective of this project is to describe the intended and current capabilities of the current Department of Defense Serum Repository (DoDSR), suggest desired characteristics of an optimal system for use of biospecimens, identify and assess specific opportunities for action, and offer recommendations for a target health surveillance architecture to optimize biospecimens for influenza and other key health threats.

Estimated funding required for FY 2006, to be provided by amendment to the subject contract, is $500,000. The work will be carried out under the auspices of the Arroyo Center, the Army-sponsored Federally Funded Research and Development Center at RAND, with Thomas L. McNaugher, Vice President, Army Research Division, Director, RAND Arroyo Center, providing oversight.

For substantive questions regarding this proposal, please contact Terri Tanielian at (703) 413-1100, extension 5404 (Terri_Tanielian@rand.org). Please address contractual matters to the undersigned at (310) 393-0411, extension 6716, by fax to (310) 451-6973, or ellent@rand.org.

Sincerely,

Ellen Tunkelrott
Contract & Grant Administrator

Cc: Dr. Remington Nevin
Mr. Nathan Parks, DAPR-DPD
Ms. Kathy Dobeck, CCE
Ms. Marilyn Shortle, CCE

Proposal 2006-0649

OPTIMIZING U.S. ARMED FORCES BIOSURVEILLANCE FOR INFLUENZA AND OTHER STRATEGIC HEALTH THREATS

Melinda Moore and John A. Zambrano
Principal Investigators

Submitted to
U.S. Army Center for Health Promotion and Preventive Medicine

Submitted by
RAND Corporation
1776 Main Street
Santa Monica, California 90407-2138

June 2006

TABLE OF CONTENTS

PROJECT DESCRIPTION

Project Description

OPTIMIZING U.S. ARMED FORCES BIOSURVEILLANCE FOR INFLUENZA AND OTHER STRATEGIC HEALTH THREATS

Sponsor:	U.S. Army Center for Health Promotion and Preventive Medicine
Action Officer:	Remington Nevin, MD, MPH, CPT, MC, 202-782-4553; remington.nevin@us.army.mil
Project Duration:	August 2006 – July 2007
Funding	$500,000
Program/Director:	Force Development and Technology (Bruce Held) Center for Military Health Policy Research (Terri Tanielian and Sue Hosek)
Project Leaders:	Melinda Moore and John A. Zambrano

OBJECTIVE

Describe the intended and current capabilities of the current Department of Defense Serum Repository (DoDSR), suggest desired characteristics of an optimal system for use of biospecimens, identify and assess specific opportunities for action, and offer recommendations for a target health surveillance architecture to optimize biospecimens for influenza and other key health threats.

BACKGROUND

The accelerating spread of the novel AH5N1 influenza strain and the threat of an emerging human pandemic have highlighted the importance to force health protection of a comprehensive U.S. Armed Forces health surveillance architecture, i.e., a purposefully organized system to address current needs. Reports from investigations following Operation Desert Storm described the low quality of available demographic, medical and deployment surveillance data and consistently noted the lack of connectedness among the DoD's health surveillance databases. In response, DoD implemented policies requiring the services to maintain centralized records of certain health-related deployment data. Despite these efforts, challenges remain related to policy implementation, quality assurance processes, and integration of health surveillance information.

The current U.S. Armed Forces health surveillance infrastructure has several component parts, including medical, environmental, and deployment surveillance systems, and a targeted global specimen collection network with the world's largest repository of biospecimens collected longitudinally from military service members. While new policies and programs demonstrate DoD's strong commitment to protecting and treating service members, remaining is the effective integration and robust use of the DoDSR within the overall Armed Forces health surveillance system. Optimal

structure and use of biospecimens should serve the needs of (a) enhanced situational awareness needed for force health protection and public health protection against emerging threats such as pandemic influenza, (b) robust epidemiologic investigations, and (c) a resource for military and civilian public health research.

TASKS

Task 1: Identify and describe current health data systems

Task 1 includes several sub-tasks: (a) identify and describe the intended purpose, content, structure and use of U.S. Armed Forces data and biospecimen systems that currently inform health surveillance, and related DoD doctrine; (b) identify desirable features of an Armed Forces health surveillance architecture with the capabilities described above under "Background", focusing on the specific role of biospecimens; (c) examine selected non-DoD biospecimen and data systems, to glean important insights potentially relevant to biospecimen collection, processing and use within the U.S. Armed Forces health surveillance system; (d) identify gaps and opportunities related to enhanced biospecimen collection, processing and use; (e) identify specific potential actions and alternative approaches to achieve the desired characteristics of an optimal biosurveillance architecture.

Task 2: Seek expert consensus on the key elements of an optimal biosurveillance architecture

Convene an expert panel composed of force health protection staff and leadership from all services, as well as civilian public health and other experts in order to present findings from Task 1 and seek their views regarding specific recommended actions to optimize U.S. Armed Forces biospecimen collection, processing and use within its health surveillance system.

Task 3: Synthesize findings and recommend desired characteristics of and specific actions to achieve an optimal system.

Working with results from Tasks 1 and 2, define the desired characteristics of, and evaluate all identified specific actions to achieve, a health surveillance architecture to optimize use of Armed Forces biospecimens.

DELIVERABLES

Briefings:	Interim: As determined with sponsor
	Final: 10 months from project commencement
Draft Report:	Initial: 9 months from project commencement
	Final: 12 months from project commencement

Proposal 2006-0649

PROCEDURES FOR INITIATING A RAND ARROYO CENTER ADD-ON PROJECT

PROCEDURES FOR INITIATING A RAND ARROYO CENTER ADD-ON PROJECT CONTRACT W74V8H-06-C-0001

Based on agreement between the sponsoring government agency and the RAND Arroyo Center (the Army's Federally Funded Research and Development Center [FFRDC] for studies and analysis) on the substance and cost of the work to be undertaken, RAND prepares a proposal that includes,

- A technical section stating period of performance, project objective, brief background of why research is warranted, tasks to be undertaken, and schedule of deliverables; and
- A detailed cost section.

RAND sends the proposal to the sponsoring agency with copies to the Arroyo Center's Contracting Officer's Representative (COR), Defense Contracting Command-Washington (DCC-W), and the Army Studies Program Management Office (ASPMO).

The sponsoring agency, after review and concurrence with the proposed work and cost estimate, registers the study in the ASPMO database (see 3, below) and provides the following documents:

(1) Military Interdepartmental Purchase Request (MIPR), (DD Form 448)

A copy must be provided (preferably by fax) to initiate funding action. Please indicate the proposal number and the title of the project on the cover sheet of the fax. In addition, the hardcopy of the original MIPR must be mailed. Send to:

Mr. Nathan Parks
DAPR-DPD, Room 3E365
G8-PAED
700 Army Pentagon
Washington, D.C. 20310-0700
TEL: 703/695-3959
FAX: 703/695-6697
Parks, Nathan T Mr Army G8 [Nathan.Parks@hqda.army.mil]

IMPORTANT: Fax an information copy of the MIPR to Arroyo's COR,

Mr. Nathan Parks
DAPR-DPD, Room 3E365
G8-PAED
700 Army Pentagon
Washington, D.C. 20310-0700
TEL: 703/695-3959
FAX: 703/695-6697
Parks, Nathan T Mr Army G8 [Nathan.Parks@hqda.army.mil]

Alternatively, a direct fund cite memorandum can be used, copies furnished as noted above. Be sure to include proposal number and project title on the fax cover sheet.

The Element of Resource (EOR) for RAND Arroyo is 2513.

(2) Justification for Using Federally Funded Research and Development Centers

This states the sponsor's rationale for selecting an FFRDC rather than performing the work in-house or competing it with non-FFRDC contractors. In addition, the sponsor should review the proposed costs for the work to be performed and provide a statement addressing the reasonableness of the proposed costs. (See following format–limit to one page). Sponsor inserts name and title of authorizing official, who signs in the signature block (GO/SES signature required).

Fax to: Mr. Nathan Parks
DAPR-DPD, Room 3E365
G8-PAED
700 Army Pentagon
Washington, D.C. 20310-0700
TEL: 703/695-3959
FAX: 703/695-6697
Parks, Nathan T Mr Army G8 [Nathan.Parks@hqda.army.mil]

(3) Database Registration

The organization study sponsor must register the proposed study in the ASPMO database. Upon registration, the sponsor must provide a Project Unique Identifier Code (PUIC). This PUIC must be provided on the Justification for FFRDC use in the second paragraph. For questions on this registration, contact Mr. Robert Claude at 703/692-5354 (Robert.Claude@hqda.army.mil).

JUSTIFICATION FOR USING
FEDERALLY FUNDED RESEARCH AND DEVELOPMENT CENTERS

CONTRACTOR NAME: RAND ARROYO CENTER

TITLE OF STUDY/PROPOSAL NUMBER/PUIC:

RATIONALE FOR WORK NOT PERFORMED IN-HOUSE: (Are there adequate resources/skills in-house? If there are adequate resources in-house, this task should not be going to an FFRDC.)

RATIONALE FOR USING FFRDC INSTEAD OF COMPETITION: (Some possible reasons for using the FFRDCs are: special relationship, conflict of interest, unique capability not available elsewhere, proprietary information, etc. Your particular rationale should be explained in detail.)

COST REASONABLENESS: (When reviewed with the Government Cost Estimate, are the costs proposed reasonable? Are the STEs proposed adequate or overstated?
Sample statement: The proposed costs are comparable to other FFRDCs. Based on the nature of the effort, the technical support required, and the duration of the effort, the cost to the government of $X is reasonable and appropriate.)

_____

Signature Block
(GO or SES Sponsor)

COST DETAIL

Contract Pricing Proposal Cover Sheet

Table 15-2 Information

Cost or pricing data is included as a part of this proposal.

1a. SOLICITATION/CONTRACT/MODIFICATION NUMBER

W74V8H-06-C-0001

1b. RAND PROPOSAL NUMBER

2006-0649

2. NAME AND ADDRESS OF OFFEROR

RAND Corporation
P.O. Box 2138
1776 Main St.
Santa Monica, CA 90407-2138

3. NAME, TITLE, AND TELEPHONE NUMBER OF OFFEROR'S POINT OF CONTACT

Ellen Tunkelrott
Contract & Grant Administrator
(310) 393-0411, extension 6716

4a. NAME OF CONTRACT ADMINISTRATION OFFICE

Defense Contract Management Agency, Los Angeles
P.O. Box 9608
Mission Hills, CA 91346-9608
(310) 900-6612

4b. NAME OF AUDIT OFFICE

Defense Contract Audit Agency
6230 Van Nuys Boulevard
Van Nuys, CA 91401-2781
(818) 756-4330

5. TYPE OF CONTRACT ACTION *(check)*

☐ New Contract	☒ Change Order	☐ Price Revision/Redetermination
☐ Letter Contract	☐ Unpriced Order	☐ Other (Specify)

5b. TYPE OF CONTRACT ACTION *(check)*

☒ CPFF	☐ CPIF	☐ CPAF
☐ FFP	☐ FPI	☐ Other (Specify)

6a. PROPOSED COST *(A + B = C)*

A. COST	B. PROFIT	C. TOTAL
$493,097	$6,903	$500,000

6b. TITLE

OPTIMIZING U.S. ARMED FORCES BIOSURVEILLANCE FOR INFLUENZA AND OTHER STRATEGIC HEALTH THREATS

6c. PERIOD OF PERFORMANCE: 12 months

7. No government property will be required in the performance of this work.

8. COST ACCOUNTING STANDARDS (CASB) DATA

- This contract action is subject to CASB regulations
- We have submitted an adequate CASB disclosure statement
- We have not been notified that we are or may be in non-compliance with our disclosure statement or cost accounting standards.
- No aspect of this proposal is inconsistent with our disclosed practices or applicable cost accounting standards.
- This proposal is consistent with our established estimating and accounting practices and procedures and FAR part 31, cost principles.

9. This proposal reflects our estimating and/or actual costs as of this date and conforms with the instructions in FAR 15.403-5(b)(1), and Table 15-2. By submitting this proposal, we grant the Contracting Officer and authorized representative(s) the right to examine, at any time before the award, those records, which include books, documents, accounting procedures and practices, and other data, regardless of type and form or whether such supporting information is specifically referenced or included in the proposal as the basis for pricing, that will permit an adequate evaluation of the price.

10. DATE OF SUBMISSION: 27 June 2006

11. NAME, TITLE, AND SIGNATURE OF OFFEROR *(Type)*

Joanne B. Shelby
Director, Office of Contract and Grant Services

RAND
USE OR DISCLOSURE OF PROPOSAL DATA IS SUBJECT TO THE RESTRICTION ON THE COVER PAGE OF THIS PROPOSAL

COST SUMMARY REPORT

Salaries and Employee Benefits		205,121
Travel Expenses		26,677
Base Computing Services Costs		21,670
Other Direct Costs		26,438
Subcontract Costs		0
Total Direct Costs		279,906
Total Indirect Costs	(96.4% of Salaries and Employee Benefits)	197,736
Cost of Money	(7.53% of Salaries and Employee Benefits)	15,455
Total Estimated Costs		493,097
Fixed Fee	(1.4% of Total Estimated Costs less Cost of Money)	6,903
Total Cost		500,000

SALARY COST DETAIL REPORT

		Daily Rate	Days	Unadjusted	Adjusted Cost
----- PROFESSIONAL EMPLOYEE SALARIES -----					
CECCHINE,GARY A Natural Sci-No MD, Full		403.85	34	13,731	14,055
EISEMAN,ELISA Natural Sci-No MD, Sr		430.50	46	19,804	20,247
HOSEK,JAMES R Economist, Sr		562.00	5	2,810	2,886
MOORE,MELINDA Natural Sci-MD, Sr		747.12	48	35,862	36,702
OLMSTED,STUART S Natural Sci-No MD, Full		363.46	45	16,356	16,721
RESEARCH REVIEWER, SR RESEARCH REVIEWER, SR		561.56	6	3,369	3,461
RESEARCH REVIEWER, SR 2 RESEARCH REVIEWER, SR		561.56	29	16,285	16,406
ZAMBRANO,JOHN A Research Assistant, II		176.92	90	15,923	16,303
	Subtotal		303	124,140	126,781
----- PROFESSIONAL ADJUNCT STAFF SALARIES -----					
PROF. ADJUNCT STAFF SR TBD ADJUNCT STAFF, SR		797.84	16	12,367	12,654
	Subtotal		16	12,367	12,654
----- SUPPORT EMPLOYEE SALARIES -----					
ADMINISTRATIVE ASSISTANT, III ADMINISTRATIVE ASSISTANT, III		161.59	31	4,929	5,046
	Subtotal		31	4,929	5,046

	Daily Rate	Days	Unadjusted	Adjusted Cost
TOTAL		349.0	141,436	144,481
Employee Benefits				60,640
TOTAL				205,121

TRAVEL COST DETAIL REPORT

----- TRIP DESCRIPTION -----		Rate	Days	Unadjusted	Adjusted Cost
Washington D.C. -> Manchester England & Reykjavic					
Per Trip Costs					
Airfare		5409		5,409	
Lodging		230	4.0	920	
Meals and Incidentals		130	5.0	650	
Other Costs		105	5.0	525	
Per Trip Subtotal				7,504	
TOTAL	2 Trips			15,008	15,261
Washington D.C. -> Norfolk VA					
Per Trip Costs					
Airfare		844		844	
Lodging		101	1.0	101	
Meals and Incidentals		43	2.0	86	
Other Costs		50	2.0	100	
Per Trip Subtotal				1,131	
TOTAL	4 Trips			4,524	4,546
Washington D.C. -> San Antonio TX					
Per Trip Costs					
Airfare		1392		1,392	
Lodging		89	1.0	89	
Meals and Incidentals		54	2.0	108	
Other Costs		50	2.0	100	
Per Trip Subtotal				1,689	
TOTAL	4 Trips			6,756	6,870
TOTAL TRAVEL EXPENSE					26,677

COMPUTING DETAIL

----- COMPUTING SERVICES DESCRIPTION -----	Unadjusted	Adjusted Cost
Collaborative Services	2,287	2,320
Computer Backups	1,572	1,594
Computer Hardware	2,429	2,464
Computer Hardware Maint.	1,143	1,159
Computer Software	429	435
Computing Support	2,572	2,609
Network Services Allocation	7,078	7,174
Shared Computing Services	3,859	3,915
TOTAL COMPUTING SERVICES COST		21,670

OTHER DIRECT COST DETAIL

----- OTHER DIRECT COST DESCRIPTION -----	Unadjusted	Adjusted Cost
Food for Conference	1,000	1,017
Honorariums	5,000	5,084
Letter Agreements 1	2,000	2,034
Library/Research Materials	1,000	1,017
Publications	7,000	7,118
Travel reimbursement for Honorariums	10,000	10,168
TOTAL ODC COST		26,438

OTHER ADMINISTRATIVE DATA

SUBMITTED BY:	RAND CORPORATION 1776 Main Street Santa Monica, CA 90401
PLACE OF PERFORMANCE:	RAND CORPORATION 1776 Main Street Santa Monica, CA 90401
RAND CORP. PROPOSAL NUMBER:	2005-0649
TYPE OF CONTRACT:	Cost Plus Fixed Fee
AUTHORIZED NEGOTIATORS:	Ellen Tunkelrott Contract & Grant Administrator Telephone: (310)393-0411, ext. 6716 Joanne B. Shelby, Director of Contract and Grant Services Telephone: (310) 393-0411, ext. 6517 Kenneth M. Krug, Treasurer Telephone: (310) 451-6904 Richard Fallon, Vice President Chief Financial Officer Telephone: (310) 451-6942
COGNIZANT GOVERNMENT AUDIT AGENCY:	Glenn K. Fujikuni, Branch Manager Defense Contract Audit Agency 6230 Van Nuys Boulevard Van Nuys, CA 91401-2781 Telephone: (818) 756-4330
PERSONS AUTHORIZED TO BIND RAND CORPORATION:	Joanne B. Shelby, Director of Contract and Grant Services Telephone: (310) 393-0411, ext. 6517 Kenneth M. Krug, Treasurer Richard Fallon, Vice President Chief Financial Officer
VALIDITY PERIOD:	Proposal is valid for a period of 90 days from receipt by the Client.

NOTE ON ADJUSTED COSTS

Cost increases resulting from inflation and other factors estimated in this proposal, and reflected in the Adjusted Costs columns, have been submitted to the Defense Contract Audit Agency for review and approval.

Period/Fiscal Year	Percent Change
08/02/99 and thereafter until amended	4.0 (Salaries & Adjunct Staff Salaries)
03/31/97 and thereafter until amended	2.5 (Travel, Computing, and Other Direct Costs)

To determine the amount of increase for the proposal, RAND's Online Pricing Utilities System calculates a ratio taking into consideration when the proposal was priced and the end date of the effort. The Unadjusted Cost is then multiplied by this ratio is to yield the Adjusted Cost.

PROPOSAL COST ESTIMATE DEVELOPMENT DESCRIPTION

SALARIES

1. Salary rates for employees and adjunct staff, with the exception of those generic categories described below, represent actual rates paid to the personnel that will work on this project. For personnel with more than one year of service who are exempt from the provisions of the Fair Labor Act, i.e. professionals, the rates include five (5) percent for sabbatical pay.

2. Generic categories (for example, administrative support, research reviewer, or communications analyst) are used when the specific individual who will be working on the proposed project cannot be identified at the proposal stage. The generic daily rate represents a corporate-wide average for the category.

3. Direct salaries are not duplicated in the indirect costs or in any way presented to the Sponsor so that such items are reimbursed more than once.

4. RAND Corporation's salary structure is reviewed biannually by a compensation review team of the Defense Contract Administration Services Management Area, El Segundo.

EMPLOYEE FRINGE BENEFITS

Fringe benefits provide the employee's holidays, vacation, sick leave, retirement plan, payroll taxes, etc. These costs are distributed on the basis of employee salary dollars, and the rates used in the proposal have been reviewed and accepted by the Defense Contract Audit Agency.

INDIRECT (OVERHEAD) EXPENSES

Indirect costs cannot specifically be identified with a project and are distributed to a base consisting of salaries, employee fringe, and adjunct staff salaries. The rate used has been approved by the Defense Contract Audit Agency for forward pricing and billing purposes.

TRAVEL EXPENSES

The travel costs incurred by personnel while in project travel status include transportation, per diem, reasonable lodging, taxis, and other directly associated expenses. The following components are priced for each trip:

Airfare

Airfare is generally estimated using fully refundable coach rates.

Daily Per Diem

Priced at $51 per day for all destinations in the continental United States. For international trips, the applicable per diem rate from the GSA Foreign Rate Table is used. The Per Diem cost is multiplied by the number of nights lodging plus one.

Lodging

Lodging is estimated using the GSA maximum per diem rate for the destination minus the $51 daily per diem. For international trips projected Lodging Daily Cost is the per diem allowance prescribed by Federal Travel Regulations (FTR) intended to cover the cost of lodging and meals and related incidental expenses.

Other Daily Costs

Priced at $50 per day for all destinations in the continental United States and $42 per day for international destinations. This is intended to cover the costs of lodging taxes, ground transportation, business communications, and other reimbursable miscellaneous expenses. The "other daily costs" is multiplied times the number of nights lodging plus one.

COMPUTER SERVICES

The computing estimate includes three elements:

Network Services (Head Tax)

The costs of self-service distributed printing and copying are allocated at $22.56 per day ($2.82 per hour).

Hardware Services and Service Agreements

The costs of hardware services and service agreements are estimated by the Project Leader based on his/her knowledge of the specific computing needs and staffing requirements of the proposed project. This element of the computing estimate is determined primarily by the hardware and service options chosen by the staff that will work on the project and the portion of the staff members' time to be charged to the project. If needed, an estimate for analytic software support, custom support agreement, and/or dedicated printer or copier is also included.

Usage-Based Services

If necessary, an estimate is included for certain other computer costs which, if incurred, will be a direct charge to the project. Examples of these direct charged usage-based costs are: dedicated data circuits, conference room computing support, software purchase, and small direct charged computer supplies.

GOVERNMENT AUDIT

A continuous Government auditing policy is in effect at RAND Corporation by the following agency:

Glenn K. Fujikuni, Branch Manager
Defense Contract Audit Agency
6230 Van Nuys Boulevard
Van Nuys, CA 91401-2781

RAND's in-house auditor may be contacted at:

Anne Morikawa, Resident Auditor
DCAA
RAND Corporation
1776 Main St.
Santa Monica, CA 90401
Telephone: 310-393-0411, ext. 7834

* * *

❖ JUSTIFICATION FOR USING FEDERALLY FUNDED RESEARCH AND DEVELOPMENT CENTERS

CONTRACTOR NAME: RAND ARROYO CENTER

TITLE OF STUDY/PROPOSAL NUMBER: OPTIMIZING U.S. ARMED FORCES BIOSURVEILLANCE FOR INFLUENZA AND OTHER STRATEGIC HEALTH THREATS/PROPOSAL 2006-0649. PUIC CHPPM07260.

RATIONALE FOR WORK NOT PERFORMED IN-HOUSE: Adequate resources are not available in-house to perform this research in a timely manner. Available in-house staff are not able to devote full-time effort to this project.

RATIONALE FOR USING FFRDC INSTEAD OF COMPETITION: Use of an FFRDC is necessary to capitalize on existing strengths, specific knowledge and expertise available within the FFRDC; and to ensure timely completion of this project.

COST REASONABLENESS: The proposed costs are comparable to other FFRDCs. Based on the nature of the effort, the technical support and travel required, and the duration of the effort, the cost to the government of $500,000 is reasonable and appropriate.

Michael B. Cates

MICHAEL B. CATES
Brigadier General, VC
Commanding

Local Tracking Number: CHPPM-HQ-C-0728-00068

US Army Medical Command

REQUEST FOR (select 1): SERVICES CONTRACT APPROVAL
Action Type (select 1): Continuation of ongoing contract (Add-On)
GWOT: No

A. Requesting Activity: CHPPM

B. Unit Identification Code: W03HAA

C. Project Name (contract): Optimizing U.S. Armed Forces Biosurveillance for Influenza and Other Strategic Health Threats

D. Contract Number: Contract W74V8H-06-C-001

E. Position Series/Grade/Step or Contract Manpower Equivalents (CME) and cost:
(1) PP/Series/Grade (civilian):
(2) CMEs (contract; @1,920hrs per):
(3) Cost ($): 500,000
(4a) Funding Source (select 1): Reimbursable Order (GEIS-Provided Pandemic Influenza)
(4b) Funding Limitation (select 1): O&M

F. Justification for contract (do not exceed space provided):

The purpose of the contract is to describe the current and future capabilities of the Department of Defense Serum Repository to assist with the early identification and response to an influenza pandemic. Adequate resources are not available in-house to perform these analyses in sufficient time to prepare for a pandemic. The chosen contractor (Rand Arroyo Center) is a Federally Funded Research and Development Center with the needed expertise, knowledge and skills to complete this assessment within the allowable timeframe.

G. Requesting Commander:
Authorized High-Cost Endorsement Date: 7/26/2006
MICHAEL B. CATES
Brigadier General, VC
Commanding

Requesting Activity POC: Dana Dowell Phone: Comm-410-436-6065, DSN-584

High-Cost Endorsement (if required):
MSC/RMC Commander, Date

H. MEDCOM Commander: ✓ Approve ____ Disapprove Date: 04 AUG 2006
KEVIN C. KILEY
Lieutenant General, MC
Commanding

MEDCOM USE
CCH CHPPM OSTOW DSK
Tracking Number
e-mail completed form to "MEDCOM Hire/Contract Request" in MEDCOM GAL or hire.contract.medcom@amedd.army.mil
Form Version 3, 3 June 2006

US Army Medical Command

REQUEST FOR (select 1): SERVICES CONTRACT APPROVAL
Action Type *(select 1)*: Continuation of ongoing contract (Add-On)
GWOT: No

COPY

A. Requesting Activity: CHPPM

B. Unit Identification Code: W03HAA

C. Project Name (contract): Optimizing U.S. Armed Forces Biosurveillance for Influenza and Other Strategic Health Threats

D. Contract Number: Contract W74V8H-06-C-001

E. Position Series/Grade/Step or Contract Manpower Equivalents (CME) and cost:
(1) **PP/Series/Grade** (civilian):
(2) **CMEs** (contract; @1,920hrs per):
(3) **Cost** ($): 500,000
(4a) **Funding Source** (select 1): Reimbursable Order (GEIS-Provided Pandemic Influenza)
(4b) **Funding Limitation** (select 1): O&M

F. Justification for contract (do not exceed space provided):

The purpose of the contract is to describe the current and future capabilities of the Department of Defense Serum Repository to assist with the early identification and response to an influenza pandemic. Adequate resources are not available in-house to perform these analyses in sufficient time to prepare for a pandemic. The chosen contractor (Rand Arroyo Center) is a Federally Funded Research and Development Center with the needed expertise, knowledge and skills to complete this assessment within the allowable timeframe.

G. Requesting Commander:

Michael B. Cates Date: 7/26/2006
MICHAEL B. CATES
Brigadier General, VC
Commanding

Requesting Activity POC: Dana Dowell Phone: Comm-410-436-6065, DSN-584

High-Cost Endorsement (if required):
MSC/RMC Commander, Date

H. MEDCOM Commander:
_____ Approve _____ Disapprove Date:_____

KEVIN C. KILEY
Lieutenant General, MC
Commanding

MEDCOM USE

Tracking Number
e-mail completed form to "MEDCOM Hire/Contract Request" in MEDCOM GAL or hire.contract.medcom@amedd.army.mil

Form Version 3, 3 June 2006