UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

JAN - 4 2016

The Honorable John McCain
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

This letter is in response to House Report 111-230, page 312, accompanying the Defense Appropriations Act for Fiscal Year 2010, requesting the Department of Defense (DoD) provide status of implementation of recommendations made to modernize the Armed Forces Institute of Pathology (AFIP) Tissue Repository. DoD sent interim responses to Congressional Defense Committees on April 22, 2010, March 29, 2011, August 7, 2012, and September 16, 2013. This letter provides a final report of the Department's efforts.

From October 2013 through February 2014, the Tissue Repository Working Group (TRWG) reviewed the recommendations of the Institute of Medicine (IOM) regarding the future use of the tissue repository. The working group concurred with 13 of the IOM recommendations and non-concurred with one recommendation. Enclosed is a list of the IOM recommendations with details on actions the Department has taken to address each.

Following the TRWG's review of IOM recommendations and the development of a Concept of Operations for the Repository drafted in June 2014, a number of initiatives were put in place to support the continuous maintenance and modernization of the tissue repository. Among them are the transfer of over 10 million case records to a new tracking system; the complete inventory, database entry, and electronic tracking of all frozen samples; the scanning, digitization, and electronic tracking of all paper case folders, approximately 80,000, collected since the closing of the AFIP. In addition, there are plans to assess the viability of the wet tissue collection to remove contaminated or desiccated specimens deemed irretrievably degraded.

Regarding the implementation of best practices for repositories, a number of standard operating procedures were implemented. Results from a recently taken self-assessment tool provided by the International Society for Biological and Environmental Repositories showed a few areas that may need attention. Those areas are currently being addressed.

There are over 40 research projects using material from the repository including projects on Traumatic Brain Injury and the pulmonary effects of environmental exposures during contingency operations. Current collaborations include National Institutes of Health, Veterans Affairs, and civilian hospitals and universities. I expect the number of research projects to increase. As recommended by the IOM, the legal, regulatory, and ethical policies are in place to address human research protection concerns.

A number of additional initiatives are in the planning stages and will be implemented within the next fiscal year. A current assessment is taking place to estimate what additional financial resources will be needed to support the continued modernization of the largest pathology tissue repository in the world.

Thank you for your interest in the health and well-being of our service members, veterans, and their families. A similar letter has been sent to the other congressional defense committees.

Sincerely,

Brad Carson
Acting

Enclosure:
As stated

cc:
The Honorable Jack Reed
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

JAN - 4 2016

The Honorable William M. "Mac" Thornberry
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

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Sincerely,

Brad Carson
Acting

Enclosure:
As stated

cc:
The Honorable Adam Smith
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

JAN - 4 2016

The Honorable Thad Cochran
Chairman
Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

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Sincerely,

Brad Carson
Acting

Enclosure:
As stated

cc:
The Honorable Richard J. Durbin
Vice Chairman

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

JAN - 4 2016

The Honorable Rodney P. Frelinghuysen
Chairman
Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

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Sincerely,

Brad Carson
Acting

Enclosure:
As stated

cc:
The Honorable Peter J. Visclosky
Ranking Member

The Institute of Medicine Committee Recommendations Regarding Use of the Joint Pathology Center Tissue Repository with Actions Taken as of November 2015

Members of the Joint Pathology Center (JPC) Tissue Repository Work Group (TRWG) reviewed the recommendations of the Institute of Medicine (IOM) regarding the future use of the JPC tissue repository. The TRWG was composed of representatives from National Capital Region Medical Directorate, Murtha Cancer Center, VA Central Research Office, Uniformed Services University, Armed Forces Medical Examiner System, Department of Pathology at Walter Reed National Military Medical Center (WRNMMC), and a number of Senior JPC Pathologists. It was chaired by the JPC Director, and co-chaired by the Director for Research, Education, and Tissue Repository Operations of the Joint Pathology Center.

The following is a list of each of the (14) IOM recommendations with details of actions taken for each.

1. The committee recommends that the JPC, as part of its plan for improving the use of repository materials in research, evaluate the strengths and limitations of the collection to the extent permitted by its resources and current science and technology, consider how to enhance the repository's value given the JPC's organizational and budgetary constraints, and formulate its retention policy and dissemination management and marketing strategies accordingly.

The TRWG agreed that this recommendation is self-evident and not controversial. The challenge is to achieve these objectives on the entire collection with organizational and budget constraints and with a repository containing over 31 million tissue blocks, 55 million slides, and over 750K wet tissue specimens. However, in support of this recommendation there is a policy in place that requires the evaluation of repository material and associated data by one of the JPC pathologists when the specimen is retrieved from the repository for consultative, research, or educational purposes. In addition, efforts are currently in place to link legacy tracking systems going back to 1917 with the current repository IT system. The linking of tracking systems should result in a much more efficient process when disseminating repository information to authorized users. In addition, there has been a transfer of over 10 million entire case records to a new system. The complete inventory, database entry, and electronic tracking of all frozen samples is ongoing as well as the scanning, digitization, and electronic tracking of all paper case folders (approximately 80K) collected since the closing of the Armed Forces Institute of Pathology.

The committee agreed to keep current repository material indefinitely keeping in mind the rapidly changing technologies expanding the use of formalin fixed and paraffin embedded material for future studies. Only if a subject matter knowledgeable pathologist makes the decision that material cannot be utilized will the specimen be discarded. As recommended by the IOM, the JPC has implemented an "Honest Broker" system through a now established Research Program Management Office (RPMO). This system replaces protected health information (PHI) and identifying information with codes before making the material and data available to researchers.

2. The committee recommends that the JPC immediately determine whether it has the statutory ability to recover the costs of providing specimens and data for approved research projects. If it does not, the JPC should work with Department of Defense (DoD) leadership to determine the best way to establish such an ability.

Cost recovery is consistent with the general DoD policy to fully burden research projects with their true costs. The US Army Medical Research and Materiel Command has operated under this policy when collaborating with non-federal and federal partners on research projects for years. DoD policies governing technology transfer, such as DoD Directive 5535.3 and DoD Instruction 5535.8, are relevant and provided guidance. Federal tech transfer laws encourage partnerships with private industry, state and local governments, and provide authorities for receiving funds, in addition to sharing equipment, supplies and personnel. The JPC is already designated as a federal laboratory.

3. The committee recommends that the JPC develop protocols for determining when to retain potentially useful materials and when to dispose of specimens that have no special research or educational value and are past the point of required retention for clinical use.

The TRWG agreed that the issue of separating what is useable from useless is complicated with a repository of this size. In addition, recovery technologies are evolving, and so are topics of interest. The committee agreed that we should not exclude even seemingly routine specimens from populations of interest such as military cohorts from recent conflicts. Advances in retrieval of nucleic acid and proteomic information from tissue blocks is likely to lead to new uses for specimens that may have formerly been considered for discard. As stated under recommendation one, we have a policy in place that requires the evaluation of repository material and associated data by one of the JPC pathologists when the specimen is pulled from the repository for consultative, research, or educational purposes. We are also coordinating a pilot study that will assess the condition and suitability of old "wet" specimens that may be completely desiccated.

4. The committee recommends that as long as it is less expensive to retain specimens than it is to assess their condition comprehensively, specimens be evaluated only when they are retrieved for clinical, education, or research purposes. If a specimen is found to satisfy the disposal criteria, it should be removed from the collection. If and when the cost of retaining specimens exceeds the estimated cost of auditing the collection, a procedure for setting priorities for review and systematically removing specimens that are not usable for clinical, education, or research purposes from the collection should be implemented.

It is currently less expensive to retain specimens than to assess the condition of every one of the millions of specimens in the repository. As recommended by the IOM, we are assessing specimens as they are retrieved for clinical, education, or research purposes. At the same time, we are coordinating a pilot study that will assess the condition and suitability of old "wet" specimens that may be completely desiccated or severely degraded.

5. The committee recommends that the JPC seek the advice of the Office of the General Counsel of the DoD regarding the procedures it should have in place to conform to the laws in force when implementing disposal policies.

Since the repository is a clinical collection created as a result of submission of cases for secondary consultation, we follow the rules of the College of American Pathologists (CAP), our accrediting agency, as well as DoD's Clinical Laboratory Improvement Program guidelines for disposal.

6. The committee recommends that the JPC retain materials in the Base Closure and Realignment (BRAC) Collection for potential clinical consultation only for as long as required by CAP or Clinical Laboratory Improvement Program- Clinical Laboratory Improvement Amendments guidelines and requirements, whichever specifies the longer period.

The TRWG did not agree with this recommendation**.** The committee felt the IOM recommendation did not fully recognize the unique military nature of the BRAC collection. There may be future possible uses of the collection for research purposes that are not immediately evident at this point in time. The BRAC collection has characteristics that conceivably make it distinct from routine community hospital collections. As long as adequate storage capacity is available without undue burden on JPC operations, it makes sense to retain the collection. There is value in military pathology specimens from the time period covered which may soon be unavailable at other institutions. In addition, some of the BRAC material may serve as controls for potential research projects.

7. The committee recommends that the JPC develop a policy for evaluating clinical care and education requests and, when it is appropriate, fulfill them in a manner that protects the privacy of persons from whom the specimens were obtained. The policy should include consideration of whether the material can be provided in a de-identified manner, whether access is necessary to address a medical need that cannot be equally well met by another available means, and applicable legal constraints.

JPC's policy is to de-identify any repository material unless PHI is needed for specific reasons. The HIPAA/Privacy Act attorney and a number of other attorneys at Walter Reed are consulted for specific requests as needed.

8. The committee recommends that dissemination of bio-specimens by the JPC for educational purposes should be subject to strict compliance with rules and procedures to protect source identity.

JPC's policy is to de-identify any repository material for educational purposes.

9. The committee recommends that the JPC adopt a policy regarding research use of tissues originally submitted for clinical consultation that places transparency and respect for source individuals and populations at its core. The procedures adopted should remain flexible enough to adapt to the changing legal, regulatory, and ethics landscape.

In 2013, in following with this IOM recommendation, the JPC leadership hired research management personnel and established the JPC RPMO. Since then, RPMO personnel have established JPC Research Program policies that are in compliance with DoD and WRNMMC Institutional Review Board (IRB) guidelines. Every use of repository material to include data for research purposes requires approval by the IRB and Privacy Board at WRNMMC. All research protocols are reviewed by a Scientific Review Committee and by RPMO personnel to ensure compliance with regulatory guidelines before submission to the IRB. To the maximum extent possible, repository material is de-identified before it is used for research purposes.

10. The committee recommends that the JPC adopt a set of best practices for the collection, processing, and storage of all incoming specimens, either by developing its own standards or by using one developed by another entity—for example, National Cancer Institute's (NCI) Best Practices for Bio-specimen Resources (NCI, 2011).

In support of this recommendation, the JPC became an institutional member of the International Society for Biological and Environmental Repositories (ISBER) which resulted in access to the ISBER Best Practices for Repositories manual and the Self-Assessment Tool for Repositories. Long-term storage conditions, retrieval, and distribution of specimens policies have been assessed and edited as needed to comply with ISBER Best Practices. However, the TRWG agreed that the JPC it is not in a position to dictate collection practices to contributing clinicians and pathologists who usually do not know whether a specimen will be sent to the JPC until days after a procedure.

The results (89%) of the Self-Assessment Tool Survey, a measure to determine how well repositories follow Best Practices, showed a few areas for improvement. Those areas are currently been addressed.

11. The committee recommends that the following considerations be taken in account in evaluating whether any given specimen should be made available for research:

The age of the specimen.
The disease state that it represents.
The specimen's medical, scientific, and historical significance.
The condition of the specimen and its fitness for the proposed use.
Whether a proposed use would exhaust the research potential of the specimen.
Whether the same research need might be met by another, less rare specimen or another source of specimens.
The importance of the public-health or military need the proposed use aims to meet.

The TRWG agreed that all these items should be taken into consideration before releasing tissue/specimens for research use. This recommendation provides a policy framework to ensure that specimens are used appropriately and the supply is sustained. The RPMO and JPC Scientific Review Committee personnel working closely with JPC pathologists from different sub-specialties and tissue repository personnel take these considerations into account. Only then is a request form completed and approved to release any repository material or data in support of research. JPC policy does not allow a tissue block to leave the facility for research purposes. Slides are made from the block, de-identified, and used for research purposes.

12. The committee recommends that the JPC establish criteria for deciding whether to deplete a specimen to exhaustion. The criteria should be determined in close consultation with pathology subspecialty experts in and outside the JPC.

The RPMO and JPC Scientific Review Committee personnel working closely with JPC pathologists from different sub-specialties and tissue repository personnel will take specimen depletion into consideration and make a recommendation through the Director, Research and Tissue Repository Operations to the JPC Director for final decision. As of now, there have been no cases of specimen depletion.

13. The committee recommends that there be no a priori restrictions on which applicants may apply for access to the repository's specimens and data.

The TRWG agreed with this recommendation. It is understood that a priori does not imply that restrictions cannot be imposed and the application will be approved. All applicants would have to submit protocols that meet criteria for release. Also, as stated previously, at least one JPC pathologist will need to be involved to assess the considerations on recommendation eleven (11), a scientific review is conducted, the research is of value to DoD efforts, and there is an IRB approval that meets the guidelines of our IRB of record.

14. The committee recommends that the JPC condition its provision of repository materials to researchers outside of the federal government on:

- **Approval of a Data Access Committee that develops and applies criteria for determining whether the interests of specimen and data sources, the repository, and the federal government are being met.**

- **Participation of a DoD-affiliated monitor trained in and assigned the responsibility of ensuring the appropriate use of repository specimens and data and safeguarding the interests of its sources, the repository, and the federal government.**

- **Implementation of data-use agreements and material-transfer agreements, as appropriate, to help to protect the identified interests.**

In concert with this IOM recommendation, the JPC currently has a number of conditions in place before repository material is provided to researchers outside the federal government. First, all conditions outlined above under recommendation thirteen (13), are applicable to this recommendation. Second, JPC personnel involved in recommendation eleven (11), provide the basis for the Data Access Committee. Third, the Director, Research and Tissue Repository Operations serves as the DoD-affiliated monitor. Four, data use agreements, Cooperative Research and Development Agreements, material-transfer agreements, Memoranda of Agreement, etc. are already in place to help protect the repository holdings. Lastly, all repository material and data provided was de-identified.