

U.S. OFFICE OF
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WASHINGTON, D.C.

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**NATIONAL INSTITUTES OF HEALTH REPORT
TO THE U.S. OFFICE OF SPECIAL COUNSEL
OSC FILE NUMBER DI 13-3318**

October 1, 2014



DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health
Office of the Director,
Office of Intramural Research,
Office of Human Subjects Research Protections
Building 10, Room 2C/146
Bethesda, MD 20892

October 1, 2014

The Honorable Carolyn N. Lerner
The Special Counsel
U.S. Office of Special Counsel
1730 M Street, N.W., Suite 300
Washington, D.C. 20036-4505

Re: Office of Special Counsel File No. DI-13-3318

2014 OCT -8 AM 9:36
U.S. OFFICE OF
SPECIAL COUNSEL
WASHINGTON, D.C.

Dear Ms. Lerner:

On behalf of the National Institutes of Health (NIH), I respectfully submit the attached report regarding the referenced Office of Special Counsel (OSC) file. The Secretary of Health and Human Services has delegated me the authority to sign this report and to take action as necessary under 5 U.S.C. § 1213(d)(5).

The attached report provides additional information requested by OSC in response to a report regarding the referenced file originally submitted by NIH on January 8, 2014. This revised report provides the NIH response to the complaint made by Dr. Nazli McDonnell to the OSC regarding the Baltimore Longitudinal Study on Aging (BLSA), an intramural research study conducted by the NIH National Institute on Aging (NIA). Dr. McDonnell consented to release of her name in the report.

The NIH Office of Human Subjects Research Protections (OHSRP) led a review of the allegations associated with the complaint made by Dr. McDonnell. Specific details, including a summary of the evidence and conclusions for each allegation are provided in the report. Additionally, the report describes corrective action that has occurred or is in progress. I plan to monitor the National Institute of Aging (NIA) corrective action work.

I deeply appreciate your cooperation in providing NIH additional time to complete this work. Our personnel used that time to do a comprehensive assessment of the allegations and the evidence, as explained in the report. If you have any questions, please do not hesitate to contact me.

Sincerely,

Michael M. Gottesman, M.D.
Deputy Director for Intramural Research

Enclosures

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I. SUMMARY OF THE INFORMATION WITH RESPECT TO WHICH THE INVESTIGATION WAS INITIATED

This report is in response to a November 22, 2013 letter from the U.S. Office of Special Counsel (OSC) to the Honorable Kathleen Sebelius, former Secretary of the Department of Health and Human Services (HHS) (OSC Letter). The OSC Letter refers to a whistleblower disclosure regarding allegations of noncompliance with National Institutes of Health (NIH) Standard Operating Procedures (SOPs) and failure to follow good clinical practices in the administration of the Baltimore Longitudinal Study on Aging (BLSA), which may constitute violations of law, rule, or regulation, gross mismanagement, and a substantial and specific danger to public health and safety. The Office of Special Counsel (OSC) received these allegations from Dr. Nazli McDonnell (Complainant), who consented to release of her name in this report.

The Complainant, a Staff Clinician at the National Institute on Aging (NIA) Clinical Research Unit from January 2008 through December 2013¹, alleged that NIA research staff violated NIH SOPs and failed to follow good clinical practices in the administration of the BLSA.

The Complainant has made 15 specific allegations involving activities pertaining to the implementation and operation of the BLSA. For example, as described in the OSC Letter, the Complainant alleged that since February 2012:

- 1) BLSA participants were not timely informed of abnormal medical test results, including the results of electrocardiograms, prostate cancer screening, Dual-energy X-ray absorptiometry (DEXA) bone density scans, and full metabolic panels, some of which indicated that immediate medical treatment was necessary.
- 2) The notifications that patients received were inadequate because they did not include the information required by the BLSA Protocol, such as an explanation of the medical test results.²

In response to Complainant's allegations, OSC requested the Secretary to investigate the matter and prepare a report of findings. The Secretary delegated authority for the investigation and report to Michael M. Gottesman, Deputy Director for Intramural Research, NIH. As described further below, Dr. Gottesman formed a review team for this purpose.

Based on applicable Federal regulations, protocol requirements, and other NIH policies, the NIH review team made conclusions regarding each allegation. These conclusions are explained in the discussion regarding each allegation. The NIH review team found no apparent violation of law or endangerment to public health or safety. However, some of the conclusions concerning specific

¹ The Complainant held other positions of employment with NIA, beginning in 2003.

² OSC Letter, page 1.

allegations require NIA officials to take corrective action, which will be discussed at the end of this report in sections V and VI. Other issues, including possible protocol deviations, will be managed by the applicable Institutional Review Board, which will assess the information to assure that BLSA practices comply with protocol requirements. Details regarding each allegation and NIA's corrective actions are found in sections V and VI of this report.

II. BACKGROUND

On March 19, 2013, the Complainant met with the NIH Deputy Director of the Office of Human Subjects Research Protections (OHSRP)³ and described her initial concerns related to implementation of the BLSA protocol. The Complainant's concerns were similar, but not identical, to the allegations in the OSC Letter:

On April 15, 2013, OHSRP communicated the Complainant's March 2013 concerns to the MedStar IRB.⁴ The IRB leadership recommended that NIA conduct an internal review since many of Complainant's concerns focused on quality of medical care, an issue not within the scope of the IRB's oversight.⁵ Accordingly, NIA engaged an outside contractor to evaluate these concerns. In August 2013, the contractor performed a review of protocol compliance and evaluated whether there were any participant safety issues in the BLSA study. From that review, NIA was able to conclude that no problems were identified that impacted participant safety.

The OSC Letter included allegations and supporting details that the Complainant did not provide to NIH in March and April 2013. The Deputy Director of the NIH Office of Human Subjects Research Protections met with representatives at OSC to clarify what information was being requested to supplement the earlier report that had been submitted by NIH to OSC on February 4, 2014. OSC requested that additional the evidence to support the conclusions from the original report be provided to the OSC by June 23, 2014. On May 7, 2014, NIH requested, and was granted, an extension until August 28, 2014 in order to finalize the review process when it was determined that various interviews needed to be conducted and additional personnel was needed. On June 20, 2014, NIH requested another 4 week extension in order to analyze documentary and testimonial evidence as well to review BLSA participants' medical charts. OSC granted the extension until September 25, 2014. On August 6, NIH requested a final 2 week extension due

³ OHSRP is an NIH Office that provides regulatory oversight for protection of human research subjects within the NIH.

⁴ During 2012 and most of 2013, the NIA protocols were reviewed by the MedStar IRB, affiliated with Harbor Hospital, a MedStar Health Research Institute. Harbor Hospital is the location of the NIA Clinical Unit.

⁵ As explained later in this report, during the course of the 2014 investigation, the NIH review team obtained additional, detailed information about Complainant's allegations, details that were not available when the Complainant contacted the Medstar IRB in 2013. Additionally, the protocol is now being managed by an NIH IRB, following NIH policies. That NIH IRB has started to review issues within the scope of its oversight that were identified through this recent investigation.

to extensive follow-up work that was needed after receiving the report from the independent audit.

Following its discussions with OSC in February and March 2014, NIH formed a review team comprised of staff from OHSRP and the Office of Management Assessment (OMA), and subsequently reviewed the 16 allegations identified in the OSC letter and other allegations identified during interviews with the Complainant and former and present BLSA employees. This investigation included an in-depth review of communications involving the return of test results between NIA/BLSA staff and BLSA participants, inclusion/exclusion criteria for the protocol, and the quality of medical care provided to BLSA participants. The review focused on the period from 2012 to 2013, the period of the actions that formed the basis of the allegations.

III. INVESTIGATIVE METHODOLOGY

Conduct of the Investigation and Preparation of this Report

The NIH review team, comprised of staff from OHSRP and the NIH Office of Management Assessment (OMA) obtained information, analyzed that information according to applicable criteria, and wrote this report. The NIH review team's members have backgrounds in human subjects' protections, law, nursing, and internal controls testing.

The NIH review team engaged two outside contract firms, one with expertise in auditing research records (referred to in this report as the audit group or audit team), and the other with expertise in the testing of internal controls and federal project support services. Three members of the audit group have medical degrees; all have significant experience auditing research protocol records. As needed, the NIH review team consulted with NIH physicians, unaffiliated with the NIA/BLSA study, to obtain medical opinions for specific cases identified in the Complainant's allegations. The physicians that provided information to the NIH review team were all board certified in specialties relevant to the particular allegation.

From April to August 2014, the NIH review team completed the following activities.

- **Document Collection and Analysis:** The NIH review team gathered and reviewed documents from NIA/BLSA staff, including the BLSA protocol and informed consent documents, NIA/BLSA standard operating procedures and policy documents, study participant surveys, and BLSA medical records pertaining to the allegations. Team members visited Harbor Hospital in Baltimore, Maryland, the location of the NIA Clinical Unit (where the BLSA participants are studied), for the purpose of interviews and reviewing documents.
- **Interviews with the Complainant and NIA/BLSA personnel:** The NIH review team conducted four telephone interviews with the Complainant. The purpose of these

interviews was to clarify her allegations and obtain any other relevant information. Additionally, the review team interviewed 19 current and/or former NIA/BLSA staff and contractors in person or by phone. To facilitate these interviews, the NIH review team developed a comprehensive interview procedure regarding each allegation. Development of the procedure included a review of NIA/BLSA policies and BLSA protocol requirements. The 19 interviewees were selected from names provide by BLSA leadership, from the protocol list of personnel and from the Complainant. The NIH review team summarized the interviews and verified the accuracy and completeness of the summaries with each interviewee. Eighteen interviewees confirmed the accuracy and completeness of the information; one did not reply.

- **Internal Controls Auditing:** The NIH review team developed audit questions based on the allegations, and retained an audit group to answer those questions. The audit group drew samples from various populations and executed four audit tests. For each allegation tested by the audit group, the NIH review team selected a random sample of the relevant populations sufficient to meet a 95 percent confidence interval with a plus or minus 3 percent precision and a 1 percent expected error rate to achieve statistically significant results that they could use to measure, analyze, and draw conclusions. There were 766 BLSA study participant visits between January 1, 2012, and December 31, 2013. To test whether notification of routine clinical tests results occurred and to identify participants who may have required urgent medical care, the audit group selected a sample of 40 charts. To evaluate compliance with protocol eligibility criteria, the audit group obtained a list of all 148 participants screened for the study in 2012 and 2013 and selected a sample of 32 charts. To review notifications of abnormal test results, auditors reviewed a sample of 29 letters from a total of 88 letters that NIA/BLSA staff identified. Audit results were analyzed to determine compliance with the applicable criteria.
- **Expert Medical Opinions:** The registered nurse on the NIH review team analyzed participant charts for each specific case that the Complainant cited in the allegations. The nurse then redacted the records and reviewed them with NIH physicians unaffiliated with NIA. As needed, the review team nurse followed up with NIA/BLSA personnel for additional information.

IV. SUMMARY OF BACKGROUND INFORMATION (EVIDENCE)

BLSA Study Overview

The BLSA is a long-term research study that NIA has administered in Baltimore, Maryland since 1958. BLSA activities are primarily performed at the NIA Clinical Research Unit located within the MedStar Harbor Hospital. The study is designed to collect data to address scientific

questions about aging and factors that contribute to healthy aging. This study is subject to HHS requirements for the protection of human subjects, as defined in 45 C.F.R. 46.⁶

Governance and Oversight

BLSA activities are governed by the BLSA protocol, which contains the formal description and design for the study, and requirements for the conduct of the study. The BLSA protocol is reviewed and approved by an IRB, in accordance with 45 C.F.R. 46.⁷ During the period of the review (2012 to 2013), six different IRB-approved versions of the BLSA protocol were sequentially in effect.

The IRB is responsible for oversight of allegations involving deviations from protocol requirements and other issues covered by the Federal regulations involving the protection of human research subjects.⁸ Several NIA/BLSA internal policies and procedures provide guidance on the implementation of the study, consistent with the protocol requirements. Informed consent is an individual's voluntary agreement, based upon adequate knowledge and understanding, to participate in human subjects research. The IRB reviews and approves the BLSA informed consent process and consent documents.⁹ The BLSA Protocol states that "no procedures will begin until the informed consent has been properly obtained."¹⁰

Study Population and Enrollment

The BLSA Protocol recruits healthy volunteers of different ages, referred to as participants, and follows them indefinitely, with evaluations and tests conducted over time. Prior to enrollment in the study, potential participants are screened against eligibility criteria set forth in the protocol. Although participants must be healthy to enroll in the study, they can remain in the study if medical conditions develop after they are enrolled. More than 3,000 participants have entered the study since its inception.

BLSA Procedures

Participants entering the BLSA are provided with information about the study design, their role as participants, the evaluations and tests they will receive, and the potential risks associated with these evaluations and tests. The BLSA protocol requires participants to sign the BLSA informed consent form at each study visit. The tests and evaluations set forth in the protocol are conducted during a three-day study visit at the NIA Clinical Research Unit, located in Harbor Hospital in Baltimore, Maryland.¹¹ A BLSA study visit includes a medical history, a physical examination,

⁶ 45 C.F.R. 46, <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>.

⁷ Ibid.

⁸ MedStar Harbor Hospital (MedStar) served as the IRB for the BLSA from January 1, 2012 to September 30, 2013. NIA transitioned this role from MedStar to an NIH IRB for the period of October 1, 2013 to December 31, 2013.

⁹ Ibid.

¹⁰ Protocol # 2003-076. Longitudinal Studies of Human Physiology, Biochemistry and Psychology (the Baltimore Longitudinal Study of Aging-BLSA v. 11-14-11 approved by the Medstar Health Research Institute IRB on 2-8-12: page 23.

¹¹ Home visits and telephone interviews are also performed as part of the BLSA. However, they are not relevant to the allegations made and were, therefore, not included in the scope of the NIH review team's work.

and a number of tests and questionnaires to collect research data. Follow-up visits are scheduled within one to four years according to the requirements of the protocol. (Visits are more frequent as a participant ages.)

Roles and Responsibilities

The BLSA Principal Investigator (PI) is responsible for assuring that all investigators have the appropriate education, training, and experience to perform their delegated roles for the study. Associate Investigators (AIs), who may include contractors and non-NIH collaborators, also contribute to the BLSA study design and execution. The BLSA Medical Advisory Investigator (MAI) (also referred to as the medically responsible investigator, medically responsible physician, or BLSA Medical Officer) is responsible for medical decision making if the PI is not credentialed to practice medicine at the NIH.

According to NIA/BLSA staff interviews, Clinical Research Coordinators (CRCs) (also referred to as nurse managers) oversee the day-to-day administration of study visits, including coordinating participant scheduling, executing informed consents, and monitoring tests conducted under the protocol. Nurse Practitioners (NPs) work directly with participants to complete the study procedures, including test screening, obtaining medical histories, performing physical exams, administering questionnaires, performing test procedures, communicating test results, and documenting visits in participant charts.

During each BLSA study visit, BLSA staff and contractors are responsible for working with participants to complete the procedures specified by the BLSA protocol.

Testing Conducted with BLSA Participants and the Return of Test Results

Most of the Complainant's allegations involve the return of BLSA test results to participants.¹² The interviews with BLSA medical personnel indicate that the term "abnormal results," although used in the protocol and consent, involves medical decision-making. BLSA staff return only those abnormal results which are "clinically significant" for the particular participant. "Clinical significance" varies by individual, depending on the age and medical history of the participant. Consequently a result may be "abnormal," for one person, but not for another person; and a large number of "abnormal results" usually are not "clinically significant" results.

¹² In December 2013, the Presidential Commission for the Study of Bioethical Issues issued a report titled, *Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts*. This report identifies the significant challenges involving the return of test results to research participants. See the following link to view this Presidential Commission report: http://bioethics.gov/sites/default/files/FINALAnticipateCommunicate_PCSBI_0.pdf (Please refer to Chapter 5, *Ethical Management of Incidental and Secondary Findings in the Research Context*.) The report highlights the fact that there is no Federal law or regulation addressing this issue directly. *Id.* at 81. Instead, ethical issues, based on the Belmont Report (1979), must be evaluated by the IRB for appropriate management of test results in the research context. See the following link to view the Belmont report: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>

The PI provided the NIH review team with the following information regarding the return of test results conducted in the BLSA protocol.

All tests done in the BLSA program are performed only for research purposes, in that they are used to study the mechanisms and effects of aging in humans but not to make diagnoses or to provide medical care. Thus, all tests done in BLSA are considered forms of research tests. Some tests done in BLSA may at times provide information that could be used by a participant's doctor to make diagnoses or plan medical care. Of the tests done in BLSA that may be used by doctors, some are routine and are often done in doctor's offices and other usual clinical settings. We refer to these types of routine tests as "clinical tests." Some other tests done in BLSA that are not routinely done in doctors' offices may, at times, be used by doctors to make diagnoses or to plan care. We call these tests "research tests with possible clinical significance." Many of the tests done in BLSA cannot be used by doctors to make diagnoses or plan care. We call these tests pure "research tests."

Consistent with the above description, the protocol and consent divide BLSA tests into two categories: clinical tests and research tests. Appendix I(A) and I(B) of this report contain the language from these documents. Test results are managed differently depending on their categorization. All clinical tests results are provided to BLSA participants, regardless of whether or not those results are normal. Research test results, however, are only returned to participants if they are "abnormal," which, according to the PI, means that there is possible clinical significance.

Interviews showed that BLSA nurse practitioners meet with, discuss, and provide copies of clinical labs to, the participants prior to the participant's discharge from the NIA clinical unit. Any clinically significant abnormalities are discussed and notes written on the participant's lab copy so that the participant can provide these copies to their doctors. If any lab results require immediate action, the lab values in question are discussed by the BLSA medical staff and a decision made regarding continued visit participation and referral to the participant's primary care physician. Furthermore, the participant visit schedule always includes a thirty minute time slot for the nurse practitioners to discuss test results with participants. In some cases, additional discussion sessions take place at the request of the participant. It is important to note that the protocol makes it clear that the NIA/BLSA staff do not make diagnostic or treatment decisions for participants. If they find "abnormal" results, their role is to inform the participant to seek follow up medical guidance from a primary care physician.

Role of NIA/BLSA Staff Regarding Medical Care of BLSA Participants

Some of the allegations involve the quality of medical care that NIA/BLSA staff provided to participants during protocol visits. The protocol and consent documents make it clear that this

protocol does not provide medical treatment to the participants. Furthermore, protocol visits are only scheduled when participants are in good health or stable condition. However, it is possible for NIA/BLSA staff to identify an urgent medical issue during a protocol visit. NIA/BLSA staff members explain that their responsibility is to ensure that participants obtain proper medical care. Such treatment may require sending the participant to the emergency room or direct admission to Harbor Hospital. This report will explain individual cases that required emergency medical care during a BLSA visit. An NIH physician or the IRB reviewed each case.

V. SUMMARY OF EVIDENCE REGARDING THE 16 SPECIFIC ALLEGATIONS

Categorization

The Complainant made 15 allegations regarding activities pertaining to the BLSA protocol. Some of these allegations were included in the OSC Letter. Additional allegations were raised during subsequent communications with the Complainant and are included in this report. One additional, related allegation was made by a former BLSA contractor during the interview with the NIH review team. Some allegations are very broad while others refer to specific cases. The allegations fall into two distinct groups. The first group pertains to matters covered by the BLSA research protocol or NIH policy. The allegations in this group involve the following themes:

- Return of test results to BLSA participants
- Eligibility requirements for BLSA protocol or procedures
- NIH requirement for a Medical Advisory Investigator

The second group of allegations pertains to matters outside of the BLSA protocol. The allegations in this group involve the following themes:

- The quality of medical care provided to BLSA participants if urgent care was needed
- Activities pertaining to a 2013 protocol audit

We grouped the allegations in the categories set forth above. Below are the number of allegations identified with each theme. We then provide charts which summarize the information for each allegation.

Return of Test Results

This theme contains eight allegations (1-8) and the report contains a document summarizing information pertaining to each of these allegations. Appendix I (A-D) contains the full text of the criteria for the return of test results to BLSA participants (language from the relevant protocol and consent documents, as well as NIA Nursing Policies 076 and 077.)

As indicated in the chart below, Allegation 8 is very broad. To address this issue, the NIH review team asked an outside audit group to review BLSA medical charts. Appendix II(A)

contains a document that summarizes the findings regarding return of results from that audit, as well as NIA comments about the audit findings.

Eligibility Requirements (Inclusion/Exclusion Criteria)

This theme contains two allegations (9 and 10). Allegation 10 was made by a former BLSA contractor during an interview with the NIH review team. Appendix I(E) contains the BLSA inclusion/exclusion criteria, and Appendix I(F) contains the BLSA checklist for the apheresis procedure, a medical procedure performed on some BLSA participants.

Medical Advisory Investigator

This theme contains one allegation (11) that pertains to an NIH policy.

General Allegations about Protocol Deviations

This theme contains one broad allegation (12) that involves protocol and policy noncompliance previously identified.

Quality of Care

This theme contains three allegations (13-15) involving two NIA policies (see Appendix I(G) and (H)). In addressing the broad allegation regarding quality of care, the NIH review team looked at cases other than those four provided by the Complainant. The team engaged an outside audit group to review BLSA medical charts to identify participants who may have required immediate medical care during BLSA visits. Appendix II(B) summarizes the audit group's findings. The NIH review team then obtained those records and asked NIH medical experts not affiliated with NIA to review them and provide an opinion about the adequacy of the care. Additionally, the team reviewed all adverse events reported to the IRB during 2012 and 2013 to determine whether the IRB was satisfied with the management of those matters. Appendix II(C) summarizes all cases reviewed by the IRBs during that period.

Activities Pertaining to a 2013 Audit of the BLSA protocol

This theme contains one allegation (16), which involves NIA preparations for a BLSA audit by an outside auditing group. The Complainant made this allegation during the interview process.

Charts

The following 16 charts summarize the review of each allegation, including criteria and methodology used to test the validity of each allegation, a summary of the findings (evidence), and conclusions.

ALLEGATION 1: “Baltimore Study participants were not timely informed of abnormal medical test results, including the results of electrocardiograms, prostate cancer screening, DEXA bone density scans, and full metabolic panels, some of which indicated that immediate medical treatment was necessary.”

THEME OF ALLEGATION: RETURN OF TEST RESULTS (OVERALL TIMING)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains (a) BLSA protocol, (b) consent language regarding return of test results, and (c and d) NIA Nursing Policies 076 and 077.</p> <p>BLSA Protocol: Abnormal tests or incidental findings are immediately provided to participants.</p> <p>BLSA Consent: Abnormal results from your tests will be communicated to you for follow up by primary care physician.</p> <p>NIA Nursing Policy 076: During visits, issues of clinical significance are communicated in real time. A clinically significant finding identified after visit ends and not discussed at visit is the subject of a call and noted in the chart, followed by a letter.</p> <p>NIA Nursing Policy 077: Before visit end, nurse provides clinical lab results and any clinically significant abnormal test results are discussed. Significant abnormal test results available after visit, judged to require medical attention, are communicated by phone and results are mailed.</p>	<p>Auditing: The audit team reviewed 29 charts of participants who received letters about abnormal results to determine the date of test, the date of results, and to document how NIA communicated the results.</p> <p>Interviews: The NIH review team interviewed 19 NIA/BLSA current and former staff and asked specifically about NIA policy NP-077.</p> <p>NIA/BLSA Response to Audit: NIA/BLSA personnel indicated that the timeframes for notifications may, in some cases, be attributed to the timeframe in which test results are made available, as some tests may be performed offsite or by contract resources. In addition, NIA personnel noted that participants sometimes receive verbal notifications as well as notification letters. However, there is no requirement for NIA/BLSA personnel to document verbal notifications in the participant chart.</p>	<p>Audit Results: Of the 29 letters and corresponding participant charts that the NIH review team analyzed, the range of days elapsed between when tests were performed and when participants received notification of abnormal results ranged from 1-206 days with a mean of 54 days and a median of 28 days. The range of days from when test results were available to staff and when participants received notification was 0-102 days, with a mean of 35 days and a median of 24 days. See Appendix II(A): Return of Results-Audit Findings and NIA response.</p> <p>Most charts do not contain documentation of verbal communications with participants. Letters are often the only form of documentation in the participant charts</p> <p>Interviews: NIA/BLSA personnel stated that the mailing time for notification letters varied and often depended on availability date of the results. They also stated that verbal communications were common, particularly for results that require immediate attention.</p>	<p>Interviews indicate that NIA/BLSA personnel routinely and promptly communicate test results verbally, particularly results requiring immediate action. However, the audit findings indicate that NIA/BLSA personnel frequently do not document these verbal communications. Moreover, the documentary evidence from the medical records audit shows that NIA/BLSA personnel do not provide abnormal results to BLSA participants immediately. Rather, the first documentation of notification to participants is frequently a letter dated many weeks after the visit.</p>

ALLEGATION 2: “Dr. McDonnell viewed these problems as both poor medical care and poor clinical research because the BLSA protocol states that abnormal results will be immediately provided to the research participants. She states that researchers have an obligation to follow the protocol regarding the collection, analysis and sharing of data with research participants.”

THEME OF ALLEGATION: RETURN OF RESULTS (IMMEDIATELY, BEFORE DISCHARGE OR WITHIN FOUR WEEKS)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains (a) BLSA protocol, (b) consent language regarding return of test results, and (c and d) NIA Nursing Policies 076 and 077.</p> <p>BLSA Protocol: Abnormal tests or incidental findings are immediately provided to participants.</p> <p>BLSA Consent: Abnormal results from your tests will be communicated to you for follow up by primary care physician.</p> <p>NIA Nursing Policy 076: During visits, issues of clinical significance are communicated in real time. A clinically significant finding identified after visit ends and not discussed at visit is the subject of a call and noted in the chart, followed by a letter.</p> <p>NIA Nursing Policy 077: Before visit end, nurse provides clinical lab results and any clinically significant abnormal test results are discussed. Significant abnormal test results available after visit, judged to require medical attention, are communicated by phone and results are mailed.</p>	<p>Interviews: The NIH review team interviewed current and former NIA/BLSA personnel regarding protocol and policy requirements. Specific questions were asked about the language involving return of test results, the protocol, consent, and NIA Nursing Policies 076 and 077.</p> <p>Audit: The NIH review team developed the following three questions based on BLSA protocol criteria. An audit team reviewed 40 participant charts for the first two questions and 29 charts for the third question.</p> <p>Questions reviewed by the audit team:</p> <ol style="list-style-type: none"> 1. Were available clinical test results provided to participants prior to the end of a BLSA visit? 2. Were clinical test results mailed to BLSA participants; and were they mailed within 4 weeks? 3. Were BLSA participants immediately informed about abnormal results? 	<p>Interviews: The NIH review team found that many NIA/BLSA staff members discuss results verbally with BLSA participants. The staff does not routinely document these discussions in participant charts, but indicated that they quickly communicate test results that require immediate action to participants.</p> <p>Audit: Appendix II(A) contains the audit findings relevant to the three questions.</p>	<p>Question 1: The NIH review team concluded that NIA/BLSA staff members follow the practice of providing available clinical test results to participants prior to the end of visit, based on information from interview. However, this communication is frequently not documented in the charts.</p> <p>Question 2: The NIH review team concluded that all participants received copies of their clinical results in a letter sent after their visit; however, in 2012-2013, there were often delays in mailing of the clinical results.</p> <p>Question 3: The NIH review team concluded that NIA/BLSA staff members document abnormal results in charts primarily through letters. While they do not send the letters immediately, they have a practice of communicating these results to participants verbally, if urgent action is required. These communications are frequently not documented in the charts.</p>

ALLEGATION 3: “The notifications that patients received were inadequate because they did not include the information required by the Baltimore Study protocol, such as an explanation of the medical test results.”

THEME OF ALLEGATION: RETURN OF TEST RESULTS (INFORMATION TO PARTICIPANTS REGARDING ABNORMAL RESULTS)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>The protocol, consent, and policies do not require NIA/BLSA personnel to provide specific information to participants when returning test results, other than advising them to follow up with primary care physicians.</p> <p>Appendix I contains (a) BLSA protocol, (b) consent language regarding return of test results, and (c) NIA Nursing Policy 076.</p> <p>BLSA Protocol: Abnormal tests or incidental findings are immediately provided to participants and they are informed to contact their primary care physician for treatment.</p> <p>BLSA Consent: Staff will notify participants and of any abnormal test results and instruct them to seek attention from a primary care physician.</p> <p>NIA Nursing Policy 076: Clinically significant findings obtained after a visit are communicated by phone and documented with a note in the chart.</p>	<p>Interviews: NIH review team interviewed 19 NIA/BLSA current and former staff members and asked specifically about BLSA practices and communications involving the return of BLSA test results.</p> <p>Audit: The audit team reviewed 29 letters that communicated findings of “abnormal results” to participants and corresponding participant charts to determine whether the notifications of abnormal test results also directed participants to contact their primary care physician for treatment related to abnormal test results.</p>	<p>Audit: Of the 29 letters and corresponding participant charts, the auditors found that only 2 letters did not include information specifically directing BLSA participants to contact their primary care physician for treatment. However, the first of these two letters contained language stating that the participant should have a follow up ultrasound scan of the upper thigh, and the second letter included MRI results and stated “I hope that this information is of assistance in your further evaluation.” See Appendix II(A) for a complete summary of the audit findings.</p> <p>Interviews: NIA/BLSA personnel, including the BLSA PI and the NIA Clinical Director and Scientific Director, indicate that they flag test results that require a need for follow up by a primary care physician or other medical professional. NIA/BLSA personnel stated repeatedly that it is not their role to diagnose or treat participants after noting abnormal results, unless urgent intervention is required. They also stated that they do not routinely document verbal communications in participant charts.</p>	<p>The only “information” requirement in the protocol is to inform participants to follow up with their primary care physicians.</p> <p>The audit findings indicate that almost all letters (27 out of 29) to participants regarding abnormal results instructed them to follow up with primary care physicians. Of the two letters that did not contain specific language regarding follow up with a primary care physician, one letter stated that the participant should have a follow up ultrasound scan of the thigh, and the second letter included results to assist with further evaluation of the abnormal finding.</p> <p>Although participant charts do not routinely contain documentation of telephone communications of clinically significant findings, as required by NIA Nursing Policy 076, interviews indicate that BLSA staff members routinely have discussions with participants about abnormal results that require follow up with by a primary care physician.</p>

ALLEGATION 4: “...Dr. McDonnell explained that according to study records, test results were not mailed to participants for approximately 4-6 months after they were available to clinicians administering the study.”

THEME OF ALLEGATION: RETURN OF TEST RESULTS (TIMING OF NOTIFICATION OF CLINICAL AND ABNORMAL TEST RESULTS)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains the full text of (A) the BLSA protocol and (D) NIA Nursing Policy 077.</p> <p>BLSA Protocol: Staff members explain the results of clinical tests to participants and mail copies of the tests to them shortly after their visit, with comments, if required.</p> <p>NIA Nursing Policy 077: Staff members send participants a complete packet that includes copies of results from blood tests, urine tests, oral glucose tolerance tests (OGTTs), electrocardiograms (ECGs), bone density tests (DEXAs), and treadmill tests when all results and interpretations are available.</p>	<p>Interviews: The NIH review team interviewed 19 current and former NIA/BLSA employees, and asked questions about management and mailing of clinical test results. The NIH review team asked NIA/BLSA leaders about target goals for mailing test results.</p> <p>Audit: The audit team reviewed 40 charts specific to the 6 clinical tests (i.e., laboratory blood tests, urine tests, ECGs, OGTTs, treadmill tests, and bone density scans) identified in the BLSA protocol that are routinely sent to all participants. The audit team evaluated whether staff sent the test results to participants and how often staff mailed results within 4 weeks from the date of the test.</p> <p>In a separate test, the audit team evaluated the number of days that it took for staff to send participants the abnormal test results from 1) the time the test was performed, and 2) the time the results were available to staff.</p>	<p>The NIH review team’s interviews indicate that NIA/BLSA staff inconsistently mailed clinical test results to participants between 2012 and 2013.</p> <p>The audit team found letters in all 40 charts containing results for all 6 clinically significant tests indicating that staff notified all participants. The audit team found that staff sent letters containing notifications of specific test results within 4 weeks 4-27% of the time. The mean/median duration between test performance and result mailing was 54/28 days (range 1-206 days), and the interval between result availability and mailing was 35/24 days (range 0-102 days).</p> <p>NIA/BLSA Response: NIA/BLSA leadership expressed a goal to send test results within four weeks after a visit but explained that they sometimes do not receive the results within that period. Some tests are batched and only run after collecting a minimum number of samples. Some of these letters may have been sent to participants who had requested particular research results long after their study visit.</p> <p>Appendix II(A) contains detailed audit findings regarding the timeframe for mailing clinical results.</p>	<p>BLSA participants received copies of their clinical test results, but the time of mailing varied and was often longer than 4 weeks. The BLSA protocol states that staff will mail results “shortly” after the visit. BLSA leadership indicated that their goal is to mail results within 4 weeks.</p>

ALLEGATION 5: “[W]hen test results were mailed to study participants, the mailings did not include any of the information required by the Baltimore Study protocol, such as explanatory notes, comments, and language regarding any abnormalities or indicating participants should consult their primary care physicians....”

THEME OF ALLEGATION: RETURN OF TEST RESULTS (INFORMATION TO PARTICIPANTS REGARDING ABNORMAL RESULTS)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains (A) BLSA protocol and (B) consent language regarding return of test results.</p> <p>BLSA Protocol: Abnormal tests or incidental findings are immediately provided to participants and they are informed to contact their primary care physician for treatment.</p> <p>BLSA Consent: Staff members notify participants of any abnormal test results and instruct them to seek attention from a primary care physician.</p>	<p>Audit: The audit team reviewed 29 letters to participants that NIA/BLSA staff identified as returning abnormal results. The auditors evaluated whether the letter instructed the participant to follow up with a primary care physician.</p> <p>Interviews: The NIH review team asked 19 past and present NIA/BLSA personnel about how they managed communications about abnormal test results.</p>	<p>Of the 29 letters and corresponding participant charts reviewed, only 2 letters did not include information specifically directing participants to contact their primary care physician for treatment. The first of these two letters contained language stating that the participant should have a follow up ultrasound scan of the upper thigh, and the second letter included MRI results and stated “I hope that this information is of assistance in your further evaluation.” See Appendix II section (A) for the complete summary of findings and information provided in Allegation 3 above.</p> <p>Many interviews showed that NIA/BLSA personnel verbally communicated the need for follow up by a primary care physician.</p>	<p>The protocol does not contain specific requirements for the content of letters containing information about test results, other than referring BLSA participants to their primary care physicians. This language is consistent with other protocol language, which states that BLSA staff members do not provide medical treatment. In almost all cases, the audit team found documentation indicating that participants received instructions to follow up with their primary care physicians.</p>

ALLEGATION 6: “The participants do not receive clinical summaries prepared by the nurse practitioner. This summary is used for data research coding purposes only. Findings such as 'myocardial ischemia' are coded for data analysis purposes, but not communicated to the participants in a timely or appropriate manner.”

THEME OF ALLEGATION: RETURN OF RESULTS (IS A CLINICAL SUMMARY NEEDED?)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains (A) BLSA protocol, (B) consent language regarding return of test results, and (C and D) NIA Nursing Policies 076 and 077.</p> <p>BLSA Protocol: Abnormal tests or incidental findings are immediately provided to participants.</p> <p>BLSA Consent: Abnormal results from your tests will be communicated to you for follow up by primary care physician.</p> <p>NIA Nursing Policy 076: During visits, issues of clinical significance are communicated in real time. A clinically significant finding identified after visit ends and not discussed at visit is the subject of a call and noted in the chart, followed by a letter.</p> <p>NIA Nursing Policy 077: Before visit end, nurse provides clinical lab results and any clinically significant abnormal test results are discussed. Significant abnormal test results available after visit, judged to require medical attention, are communicated by phone and results are mailed.</p>	<p>The NIH review team did not obtain information about this allegation because there are no applicable criteria. Instead, the review team audited the return of results requirements, as described in Allegations 1-5 and 7-8.</p>	<p>Not applicable because we did not find criteria for this allegation.</p>	<p>Not applicable because we did not find criteria for this allegation.</p>

ALLEGATION 7: “...the study participant came to the facility on July 18, 2012...the stress treadmill showed myocardial ischemia and the test results were sent without commentary or explanation two months after on September 21, 2012. The DEXA bone density results letter was sent on January 8, 2013, a delay of six months.”

THEME OF ALLEGATION: RETURN OF TEST RESULTS (CARDIOVASCULAR AND DEXA TEST RESULTS FOR ONE PARTICIPANT)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains complete criteria pertaining to the return of results, as described in the (A) protocol, (B) consent language, and (D) NIA Nursing Policy 077.</p> <p>BLSA Protocol: Staff members immediately provide abnormal tests results or incidental findings to participants.</p> <p>BLSA Consent: Staff members communicate abnormal test results to participants for follow-up by primary care physician.</p> <p>NIA Nursing Policy 077: Staff members send participants a complete packet that includes copies of results from blood tests, urine tests, oral glucose tolerance tests (OGTTs), electrocardiogram (ECG), bone density scan (DEXA), and treadmill tests when all results and interpretations are available.</p>	<p>The NIH review team obtained medical records for the participant identified in the allegation. An NIH cardiologist (not affiliated with NIA) reviewed the participant’s records and provided an expert medical opinion for the cardiac issue.</p> <p>The NIH review team did not seek a medical opinion for the bone density issue because the medical records indicated that the results were unchanged since NIA/BLSA staff notified the participant of her condition approximately 10 years earlier.</p>	<p>Medical Record Review: A 78-year-old female subject was followed by her cardiologist since 2000 after having an asymptomatic positive exercise treadmill test (ETT) at BLSA. After the test, a local cardiologist ordered a stress nuclear scan that was “...completely within normal limits.” BLSA ETTs in 2002 and 2004 were again positive but without chest pain. Repeat nuclear stress tests by her local cardiologist were again normal in 2006 and 2008. In 2009, the participant underwent an aortic valve replacement, and her 2010 BLSA ETT again demonstrated asymptomatic ECG findings consistent with myocardial ischemia. A repeat nuclear scan by her local cardiologist in 2012 found “...no definite evidence of infarct or ischemia in this study.” The chart was also reviewed for the bone density issue. The interpretation of the DEXAs had not altered since August 2002, when NIA/BLSA staff first measured the participant’s bone density. The participant’s bone density, while below average for her age, had been stable (i.e., no age or disease-related changes to the density of her bones) over the past 10 years.</p> <p>NIH Cardiologist’s Expert Opinion: “The participant had been followed by her local cardiologist since 2000 with repeated nuclear scans demonstrating no evidence of ischemia confirming that the ECG changes on BLSA ETTs were false positive findings. The participant, having had positive ECG changes on ETT since 2000, had received very close follow-up from her local cardiologist over the prior 12 year period at the time of the 2012 BLSA ETT and she did not need commentary on the results as this had been a repeated finding determined to be false positive test on multiple occasions.”</p>	<p>The participant’s cardiologist was closely following her cardiac issues, so there was no immediate need for NIA to provide additional information to the participant in 2012.</p> <p>Although the letter notifying the participant of the DEXA results was significantly later than the visit date, the participant had been aware of her bone density issues since 2002, and medical records indicated that this condition had been stable for 10 years.</p>

ALLEGATION 8: “Dr. Luigi Ferrucci, the Baltimore Study Medical Investigator, has stated in staff meetings of the Baltimore Study personnel that no follow up of abnormal test results is necessary.”

THEME OF ALLEGATION: RETURN OF TEST RESULTS (STATEMENT REGARDING FOLLOW UP OF ABNORMAL RESULTS)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains (A) BLSA protocol, (B) consent language regarding return of test results, and (C and D) NIA Nursing Policies 076 and 077.</p> <p>BLSA Protocol: Abnormal tests or incidental findings are immediately provided to participants.</p> <p>BLSA Consent: Abnormal results from your tests will be communicated to you for follow up by primary care physician.</p> <p>NIA Nursing Policy 076: During visits, issues of clinical significance are communicated in real time. A clinically significant finding identified after visit ends and not discussed at visit is the subject of a call and noted in the chart, followed by a letter.</p> <p>NIA Nursing Policy 077: Before visit end, nurse provides clinical lab results and any clinically significant abnormal test results are discussed. Significant abnormal test results available after visit, judged to require medical attention, are communicated by phone and results are mailed.</p>	<p>Interviews: The NIH review team questioned 19 current and former NIA/BLSA personnel about the management and return of test results, and asked whether they had issues or concerns related to the allegations. The NIH review team asked specific questions about the requirement for returning abnormal test results, as required by the BLSA protocol and the NIA policy. The NIH review team also asked specific questions about issues discussed during weekly BLSA staff meetings in 2012 and 2013.</p> <p>Production of Documents: The NIH review team requested that NIA produce copies of abnormal test result letters sent to participants during 2012 and 2013.</p>	<p>NIA provided consistent information about compliance with BLSA requirements for the return of abnormal results, particularly about verbal communication of results. However, many personnel stated that during 2012 and 2013, there were problems related to when NIA mailed test results to participants. Personnel also expressed concern that the study’s definition of “abnormal” was insufficient and unclear. For example, abnormal test results for a young person may not be abnormal for an elderly person.</p> <p>Personnel did not confirm that Dr. Ferrucci made the statement noted in the allegation, even when asked about problems and concerns.</p> <p>NIA produced 88 letters to BLSA participants during 2012 and 2013, informing them of abnormal results.</p> <p>NIA did not keep minutes of weekly BLSA staff meetings.</p>	<p>The NIH review team found no evidence that Dr. Ferrucci made statements that NIA/BLSA personnel should not follow up with participants on abnormal test results.</p>

ALLEGATION 9: “There have been patients whose cardiac test results indicated they should not undergo the apheresis procedure who nevertheless were enrolled and underwent the procedure because the individual’s test results from the Baltimore Study were not included in the medical chart.”

THEME OF ALLEGATION: PROTOCOL ELIGIBILITY INCLUSION/EXCLUSION CRITERIA (BLSA APHERESIS PROCEDURE SCREENING)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>The BLSA protocol has specific inclusion/exclusion criteria for a procedure called apheresis. Appendix I(F) contains the full text of the inclusion/exclusion criteria involving cardiac matters.</p> <p>29. Is without a history of severe cardiac arrhythmia?</p> <p>30. Per current history or physical exam there is no indication of active CAD [coronary artery disease]?</p> <p>31. Is without a history of myocardial infarction, episodes of angina or stroke in the last 6 months?</p> <p>32. Is without current history or physical exam indicating active congestive heart failure (NYHA stage III or IV)?</p>	<p>The NIH review team asked the Complainant if she had a specific example of this problem, and she identified the participant discussed in this allegation.</p> <p>The NIH review team analyzed the participant’s medical chart and provided the records to an NIH cardiologist, who is not affiliated with NIA, for an expert opinion.</p>	<p>Medical Chart Review: NIA/BLSA staff saw an 83-year-old male subject for his initial study visit in November 2011. On the medical questionnaire and initial history and physical, he denied all symptoms of cardiovascular disease (e.g., chest pain, SOB [shortness of breath], dyspnea [SOB] on exertion, orthopnea [difficulty breathing while lying down], extra fluid as in the legs or lungs), and his exam was negative, except for a grade two holosystolic [heart] murmur in the right upper sternal border. On 11/14/2011, staff evaluated the subject for possible apheresis (withdrawal of blood from a donor’s body, removal of one or more blood components, and transfusion of remaining blood back to the donor). The nurse practitioner (NP) completed the apheresis checklist, which indicated that the subject had no history or exam findings of cardiovascular disease or congestive heart failure. On 11/15/2011, staff performed apheresis and the progress note indicated, “Apheresis procedure completed without difficulty.” On 11/16/2011, an echocardiogram demonstrated abnormalities: moderately reduced [left ventricular] systolic function, borderline concentric LVH [left ventricular hypertrophy], moderate aortic stenosis, basal lateral and inferior akinesis.” At the 2012 BLSA visit, the NP noted, “On the initial visit, he was told that he had an abnormality on his ECG and needed to see his physician. He did, and his physician sent him to a cardiologist, who told him he had ‘a silent MI in the past’.” Apheresis was not repeated.</p> <p>Expert Opinion: “With regard to the allegation, the echocardiogram was performed the day after the apheresis. The participant had no history of or symptoms to suggest cardiovascular disease and had no known contraindication to apheresis. Soft systolic murmurs along the upper sternal border of the chest and ECG abnormalities reported for this subject are common in older individuals, and in the absence of symptoms or other physical findings generally do not warrant further evaluation. After the echo findings, the participant saw his personal physician for follow-up of the echo findings. The echo results were not in the chart at the time the decision was made to perform apheresis because the initial echo had not yet been performed.”</p>	<p>The NIH review team determined that in 2011, at the time of the apheresis test during a BLSA visit, evidence did not exist that the participant had a cardiac problem; therefore, the participant met eligibility criteria at the time of the 2011 apheresis procedure. The participant’s cardiac findings emerged later during the 2011 visit, when the participant underwent an echocardiogram. After obtaining this cardiac information during a BLSA visit in 2011, the participant did not have the apheresis procedure in 2012. The NIH review team found no violation of the BLSA protocol.</p>

ALLEGATION 10: “The interviewee felt that many participants are cleared (considered eligible) who should not be cleared (i.e. they do not meet protocol eligibility criteria).”

THEME OF ALLEGATION: PROTOCOL ELIGIBILITY INCLUSION/EXCLUSION CRITERIA (BLSA ELIGIBILITY SCREENING)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I(E) contains the full BLSA protocol eligibility criteria.</p>	<p>Audit: The NIH review team requested that NIA provide a list of all BLSA screening visits during the review period. NIA provided a list of 147 BLSA screening visits during 2012 and 2013, which served as the total population for determining the test sample. The review team defined a random sample of 32 screening visits and requested the corresponding participant charts. For each participant, the audit team evaluated whether the potential participant met the screening criteria prior to enrollment.</p> <p>NIA Response: The NIH review team obtained feedback from NIA after the audit report was completed. As a result, some corrections were made.</p> <p>Interviews: The NIH review team asked 19 current and former employees if they knew participants who did not meet eligibility criteria. Several employees identified cases that they disagreed with, but were subject to the judgment of the PI. Staff stated that they discussed these issues at weekly BLSA staff meetings.</p>	<p>Audit: Of the 32 charts reviewed, the audit team found the following.</p> <ul style="list-style-type: none"> • 3 subjects were correctly excluded • 0 met eligibility criteria requiring a statement that subject was “in good health” • 5 did not meet weight criteria; they self-reported weight instead of being weighed prior to visit 1 • 7 charts did not have evidence of negative HIV, hepatitis B and C, and syphilis testing done at screening (prior to visit 1) • 1 did not meet criteria for “no history of severe hormonal dysfunction (requiring supplementation or chronic drug treatment)” • 1 did not have documentation of “no history of active cancer (except locally limited basal cell cancer)” • 6 did not have “no history of metabolic disease.” <p>NIA Response: “In good health” is not specifically an inclusion/exclusion criterion. It is a perception intended to convey that a participant enrolling in the BLSA has fulfilled the eligibility requirements, and thus, is considered to be in good health.</p> <ul style="list-style-type: none"> • Potential subjects who had their screening visits performed at home had confirmation of actual weight (vs. weight they reported) at visit 1. All subjects met the weight criteria. • Subjects who had their screening performed at home had tests for HIV, hepatitis B and C, and syphilis performed at visit 1; this was unknown to the auditors at the time of the chart review. • 0 subjects enrolled had a positive test for HIV, hepatitis B and C, or syphilis. • 1 subject enrolled was taking chronic thyroid replacement hormone despite the criterion that subjects with “severe hormonal dysfunctions (requiring supplementation or chronic drug treatment)” be excluded. NIA responded that chronic hypothyroidism requiring supplementation is not considered a severe hormonal dysfunction. • 0 had “active” cancer; 1 subject had a lobectomy for Stage 1 lung cancer in 1999 and was enrolled in 2012. The subject had a 13-year history of being cancer-free. • 0 had metabolic diseases. NIA did not exclude individuals with hypercholesterolemia as they did not consider it a metabolic disease. 	<p>The IRB has approved PI amendments to the protocol to clarify eligibility criteria issues identified during the audit. This issue is discussed further in Section VI, “Action taken or Planned as a Result of the Investigation.”</p>

ALLEGATION 11: “Dr. McDonnell stated that when Dr. Metter retired as the medically responsible investigator, no one was assigned...his duties.”

THEME OF ALLEGATION: NIH REQUIREMENT FOR A MEDICALLY RESPONSIBLE INVESTIGATOR

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>An NIH intramural SOP, effective during 2012-2013, states that if the PI is not a licensed MD, the protocol must include a medical advisory investigator, who has the lead role for making medical decisions, if needed.</p>	<p>Interviews: The NIH review team asked current and former NIA/BLSA employees whether BLSA had a medical advisory investigator or a medically responsible investigator in 2012-2013. The team also asked questions about the adequacy of medical expertise on the protocol during that period, even if the IRB had not formally appointed such a person.</p> <p>Review of IRB Records: The NIH review team requested IRB records to show the dates of formal appointment for the protocol’s medically responsible investigator.</p> <p>PI Credentialing: The NIH review team requested information from NIA regarding the date on which Dr. Ferrucci received his credentials to practice medicine at NIH.</p>	<p>Interviews: NIA/BLSA personnel indicated that while there was no medically responsible investigator formally appointed to the protocol during the period from March 2012 to January 2013, protocol physicians were continually present to make medical decisions. In addition to the availability of physicians listed on the protocol, there was a physician on-call for emergency medical matters.</p> <p>Review of IRB Records: IRB records showed that NIA did not have a Medical Advisory Investigator formally designated for the BLSA protocol between March 2012, when Dr. Metter retired, and January 2013, when the IRB approved the next Medical Advisory Investigator.</p> <p>Credentialing of the BLSA PI: Dr. Ferrucci, the BLSA PI for most of 2012 -2013, is an international expert on aging, licensed in the State of Maryland, and credentialed at NIH on 4/4/2013.</p>	<p>NIA did not comply with NIH policy for appointing a medically responsible investigator during the period from March 2012 to January 2013. However, NIA/BLSA personnel indicated that protocol physicians were readily available on the NIA Clinical Unit to make medical decisions, as needed. Additionally, there was a physician on-call for emergency medical issues involving BLSA participants. Under that system, a specific MD provided medical coverage for the entire week. Interview evidence showed that a BLSA physician was always present on the NIA Clinical Unit or an on-call physician was available, as needed, after business hours, for any medical issues involving BLSA participants.</p>

ALLEGATION 12: “NIA research staff violated NIH standard operating procedures (SOPs) and failed to follow good clinical practices in the administration of the 'Longitudinal Studies of Human Physiology, Biochemistry, and Psychology' (the Baltimore Longitudinal Study on Aging [Baltimore Study]).”

THEME OF ALLEGATION: GENERAL PROTOCOL DEVIATIONS

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>The term “good clinical practices” has multiple meanings, but the Complainant explained that she views this term as the researcher’s adherence to protocol requirements and ethical principles that apply to research involving human subjects.</p> <p>45 C.F.R. 46, which is based on the ethical principles of the Belmont Report, provides the regulatory requirements for the protection of BLSA participants.</p> <p>45 C.F.R. 46 requires researchers to comply with IRB-approved protocol requirements. These requirements include participant eligibility, visit and test schedules, and protocol information involving the return of test results.</p>	<p>Identification of Protocol Deviations: The NIH review team identified whether NIA/BLSA staff deviated from the requirements of this protocol.</p> <p>Interviews: The NIH review team questioned current and former NIA/BLSA employees about possible protocol deviations, based on the allegations.</p> <p>Audits: The NIH review team designed audits to evaluate whether NIA/BLSA personnel complied with BLSA protocol requirements.</p>	<p>Identification of Protocol Deviations: The NIH review team identified the following areas of possible deviations from protocol requirements and NIH policy.</p> <ol style="list-style-type: none"> 1) Timeliness of the communication of test result to participants 2) Participant eligibility criteria for enrollment 3) Presence of an IRB-approved Medical Advisory Investigator during 2012 and 2013 when the PI was not credentialed to practice medicine at NIH <p>However, the review team found no evidence that participants were harmed as a result of these deviations.</p>	<p>The NIH review team informed the PI that she is required to report the protocol deviations to the IRB and request protocol amendments to reflect the correct BLSA practices that may have changed over time.</p> <p>The IRB will assess whether deviations have occurred, the seriousness of any deviations, and the IRB will determine whether deviations constitute noncompliance. If the IRB finds noncompliance it will determine whether it is serious and/or continuing, and if any corrective action is needed.</p>

ALLEGATION 13: “Dr. McDonnell contends that roughly 80% of the 1,350 study participants had some type of abnormal test result, and in some instances the results indicated that study participants required immediate medical attention.”

THEME OF ALLEGATION: QUALITY OF CARE (OVERALL ASSESSMENT)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains the full text of (G) AP-004 and (H) AP-005, which are policies for managing issues that require immediate medical attention.</p> <p>AP-004 addresses the process for direct admission of a BLSA participant to Harbor Hospital for urgent medical care.</p> <p>AP-005 discusses equipment and procedures on the NIA Clinical Unit for emergency treatment, if needed.</p>	<p>The audit team reviewed 40 participant charts and identified 4 events that appeared to require immediate medical attention. All four events emerged during the audit process, and the NIH team nurse reviewed the four charts. After obtaining copies of redacted chart documents, the NIH team nurse met with NIH physicians not affiliated with NIA, who provided medical opinions regarding the appropriateness of medical attention that NIA provided. Appendix II(B) summarizes this information.</p> <p>The NIH team nurse reviewed all adverse events that were reported to the IRB between 2012 and 2013 and determined that the IRB approved action taken by NIA/BLSA medical staff (see Appendix II(C)). Some of these cases involve issues that emerged during the audit process.</p> <p>The NIH review team reviewed charts of all individual cases cited by the Complainant and obtained NIH medical opinions about each case (see Appendix II). Some cases involved medical issues that emerged during the audit process.</p>	<p>Audit findings: Please refer to the following two sections of Appendix II that summarize evidence and medical opinions pertaining to this broad allegation:</p> <p>Appendix II (B) summarizes events that the auditors identified. During the review of 40 charts, the audit team only identified 4 cases in which participants may have needed immediate medical attention.</p> <p>Appendix II(C) summarizes events identified during a review of adverse events that occurred between 2012 and 2013 and were reported to the IRB.</p> <p>Additionally, this report contains two specific cases, provided by the Complainant, involving the quality of care, and that evidence is summarized as part of those specific allegations.</p> <p>Interviews: The term “abnormal” is not synonymous with “clinically actionable” for a specific participant. Age and medical history of the participant must be assessed to determine what results are returned as “clinically actionable.”</p>	<p>NIA took appropriate medical action in response to incidents involving BLSA participants that may have required immediate medical attention.</p> <p>The identification of 4 out of 40 medical charts in which participants may have needed medical attention is 10%.</p> <p>BLSA staff return only those abnormal results which are “clinically significant” for the particular participant. That group of test results is much smaller than the total group of “all abnormal” results. “Clinical significance” varies by individual, depending on the age and medical history of the participant. Consequently a result may be “abnormal,” for one person, but not for another person; and a large number of “abnormal results” usually are not “clinically significant” results.</p>

ALLEGATION 14: “...[Dr. McDonnell] reported that in Case 1, the study participant was at the NIA Clinical Unit on July 18, 2012, and underwent a number of tests....the stress treadmill test was suspicious for myocardial ischemia, reduced blood flow to the heart...this indicates the need to immediately refer the patient for coronary angiography to rule out/treat coronary artery disease.”

THEME OF ALLEGATION: QUALITY OF CARE (NEED FOR INTERVENTION AFTER ETT?)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>Appendix I contains the full text of (G) AP-004 and (H) AP-005, which are policies for managing issues that require immediate medical attention.</p> <p>AP-004 addresses the process for direct admission of a BLSA participant to Harbor Hospital for urgent medical care.</p> <p>AP-005 discusses equipment and procedures on the NIA Clinical Unit for emergency treatment, if needed.</p> <p>There are no criteria for specific cases regarding quality of care allegations because this issue depends on the circumstances of the allegations and the standards in the medical community.</p>	<p>The NIH review team analyzed the participant’s medical records and obtained an expert medical opinion regarding quality of care from an NIH cardiologist who does not work for NIA.</p>	<p>Medical Record Review: The Complainant cited test results for the Exercise Treadmill Test (ETT) performed during the participant’s prior visit on 6/17/2010. The medical chart indicated that staff sent a letter to the participant with results of the prior ETT on 8/30/2010. The participant had previously had positive treadmill tests without symptoms since 1998. On 7/18/2012, the participant again underwent treadmill testing, which concluded, “Exercise EKG: There were no ischemic EKG changes during exercise. Impressions: Submaximal stress test, Negative for ischemia.” Staff mailed the treadmill test results to the participant on 9/21/2012. The 2010 and 2012 letters both instructed the participant to “...follow up with a doctor for a complete checkup. The doctor can help you understand any abnormal findings and discuss ways to manage them.”</p> <p>Expert Medical Opinion: “The participant, who was 79 years old at the time of her 2012 ETT, had had positive treadmill tests without symptoms since 1998 and was not in need of immediate referral for coronary angiography to rule out/treat coronary artery disease. She had previously been informed of earlier test results and had been encouraged to share this information with her personal physician.”</p>	<p>Based on the expert medical opinion of the NIH cardiologist, NIA managed the issue appropriately.</p> <p>The NIH review team noted that the participant had received earlier notification from NIA pertaining to this matter.</p>

ALLEGATION 15: During the work week that ended July 27, 2012, complainant discharged an “elderly BLSA participant with a urinary tract infection and multiple abnormal tests results ... who needed immediate treatment from a private physician, but this issue involved significant conflict with staff... including Dr. Ferrucci.”

THEME OF ALLEGATION: QUALITY OF CARE (ABNORMAL URINALYSIS)

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>See Appendix I(G) and (H).</p> <p>AP-004 addresses the process for direct admission of a BLSA participant to Harbor Hospital for urgent medical care.</p> <p>AP-005 discusses equipment and procedures on the NIA Clinical Unit for emergency treatment, if needed.</p> <p>There are no specific criteria for this allegation. Appropriate medical decision-making would be determined by standard of care in the medical community.</p>	<p>Medical Record Review: The NIH review team reviewed the medical chart for the participant identified in the allegation.</p> <p>Expert Medical Opinion: The NIH review team obtained expert opinion about the urgency of this matter from an NIH physician who is board certified in infectious diseases (and not affiliated with NIA).</p> <p>Interviews: The NIH review team asked NIA/BLSA personnel if they were aware of a conflict between Dr. Ferrucci and the Complainant. The team also asked BLSA leadership if there was a conflict about this matter at a BLSA staff meeting on 7/27/2012.</p>	<p>Medical Record Review: Although the participant was asymptomatic, his urinalysis noted an elevated white blood cell count, elevated leukocyte esterase [LE, a marker for genital tract inflammation], and presence of Enterococcus and Streptococcus alpha-hemolytic bacteria. The UA was repeated with similar findings. The Complainant, who was the on-call physician at the time, discharged the participant before the end of the visit so that he could see his primary care physician for evaluation of the asymptomatic bacteriuria.</p> <p>Expert Medical Opinion: The NIH physician noted the following.</p> <ul style="list-style-type: none"> • Urinalysis that reveals bacteriuria, pyuria, and red cells as well as a positive LE. • Asymptomatic bacteriuria is not an indication by itself for treatment even if pyuria is present. The presence of two bacteria suggests the possibility of a contaminant rather than true bacteriuria. • While the positive red cells and LE and bacteria seen merit follow up, there is no indication and no urgency to intervene at the time these results were obtained. • A repeat UA would have been prudent but was not urgent. <p>Interviews: Each Friday, the BLSA PI, investigators, and staff meet to discuss the week’s study visit participants. At the 7/27/2012 meeting, the PI indicated that, although the Complainant was within her purview to discharge the participant if she felt that it was in his best interest, the literature does not support treatment of asymptomatic bacteriuria.*</p> <p>NIA/BLSA Response: This case was the topic of a BLSA team meeting on 7/27/2012 during which the PI and the Complainant expressed differing medical opinions. The PI noted journal articles to support his decision to discharge the participant.*</p> <p>*Nicolle LE, Bradley S, Colgan R, et al. <u>Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults.</u> <i>Clin Infect Dis.</i> 2005 Mar 1; 40(5):643-54.</p> <p>*AGS Choosing Wisely Workgroup. <u>American Geriatrics Society identifies five things that healthcare providers and patients should question.</u> <i>J Am Geriatr Soc.</i> 2013 Apr;61(4):622-31</p>	<p>The NIH review team concluded that there was a difference of medical opinion between the Complainant and the PI. The expert medical opinion indicates that the matter was non-urgent. Interviews with staff indicate that the topic was discussed at a weekly staff meeting, where the Complainant and the PI expressed differing views. Staff stated that the PI made it clear that the Complainant had a right to express her opinion regarding the participant’s discharge, but would not have made that decision himself. He provided journal articles to support his opinion.</p>

ALLEGATION 16: “A number of employees complained about charts being doctored prior to them being provided to the auditors.”

THEME OF ALLEGATION: CHANGING INFORMATION IN CHARTS

CRITERIA	METHODOLOGY	SUMMARY OF EVIDENCE	CONCLUSION
<p>The NIH review team did not identify criteria for this allegation. If the team had found evidence to support the allegation, they would have sought guidance from the HHS Office of General Counsel.</p>	<p>Interviews: The NIH review team asked 19 current and former NIA/BLSA employees whether they know of anyone who made improper changes to medical charts in preparation for the 2013 contract audit of the BLSA protocol.</p> <p>Review of 2013 Audit Report: The NIH review team read the 2013 audit report to determine whether the auditors noted concerns about employees making changes to the charts.</p>	<p>Interviews: Interviews indicate that NIA/BLSA personnel spent significant time reviewing charts identified for the audit. However the NIH review team found no evidence that personnel changed the information in the charts. Some employees indicated that certain existing documents may have been missing and there was an effort to organize the charts properly. While employees noted that rumors circulated about the audit preparation, the review team found no evidence to support the allegation.</p> <p>NIA Response to Review of 2013 Audit Report: According to the 2013 audit report, “There are instances of paper data corrections by white wipe, black markers or obscuring the underlying data.” NIA explained that they used this type of deletion on teleforms because the proper correction technique (single line through the error and addition of the correct information with initials of the person making the change and the date of the change) could not be recognized when the teleforms are scanned for data entry.</p>	<p>There is no evidence to support this allegation. NIA adequately explained the white wipe deletions identified by the audit group in 2013. The interviews did not provide evidence that employees made changes to medical charts in preparation for a 2013 contract audit.</p>

VI. ACTION TAKEN OR PLANNED AS A RESULT OF THE INVESTIGATION

Changes in Agency Rules, Regulations, or Practices

- A. The following corrective action began in 2013 and continues through the present.
- 1) In 2013, NIA held many training sessions pertaining to regulations and policies that protect human subjects in research. Significant work was done during 2013 as preparation for a site visit in January 2014 from an outside organization that provides accreditation to institutions that conduct human subjects research. Full accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) was achieved by the NIH in March 2014.
 - 2) The BLSA was transitioned from a MedStar IRB to an NIH IRB in the summer/autumn of 2013. This transfer required meeting NIH IRB standards instead of MedStar requirements. Significant changes were made to the protocol and those changes will continue in response to the information contained in this report.
 - 3) Participants Packets are now mailed 3-4 weeks after the participants' visit. The Packet contains the final results of the Harbor Hospital clinical blood and urine lab tests, ECG and report, exercise treadmill report (if completed), and the DEXA report (if completed). Other test results may be included if deemed by the medical staff to potentially have relevance to the participant and their primary care doctor.
 - 4) The NIA Clinical Director has instructed BLSA research staff to increase the level of documentation regarding the discussion and reporting of results. The preliminary lab discussions with the participants now include a stamp on the progress notes that is signed by the NP and the participant to indicate that the lab results were discussed and provided. Furthermore, the staff has been instructed to utilize the Participant Admission System (PAS) tracking system, an electronic NIA database, for reporting correspondence with the participant, and template letters have been developed that help to more efficiently allow the reporting and mailing of the results to the participants. Discussion among the BLSA medical staff has continued regarding value of tests and, in some instances, forms are being created in different testing areas to indicate a test level of reporting significance.
 - 5) Staffing changes have occurred in the medical records department. The new medical records staff member is making significant improvements. Medical records policies and procedures will be written and internal audits conducted to ensure compliance.
 - 6) The BLSA is currently developing an electronic data system that integrates research and clinical data. Since the amount of data is very large and comes from multiple sources, this work is a long term project. Appendix III sets forth the progress to date and plans for the future.

- 7) BLSA staff received training on the appropriate method for making corrections on paper documents. Staff will now use a line strikeout and initial corrections (as originally stated in December 2013). Note that this method cannot be used for teleforms because it would interfere with the electronic scanning of those documents.
- B.** The NIH review team discussed their findings and conclusions with NIA leadership on July 23, 2014, who decided to take the following additional corrective actions.
- 1) **Participant medical chart policy.** In July 2014, NIA developed, finalized, and implemented a policy that aligns with the unique work of the NIA Intramural Research Program (IRP), focusing on older adults, entitled Medical Records Policy-002, Procedures for Notification, Packets, and Letters for BLSA Participants – Clinical Unit Visits (Implementation date: 7/14/2014 and date of revision: 8/28/2014)). NIA studies are focused on aging and age-related conditions that are not disease-specific, in self-referred older adults.
 - 2) **BLSA visit summary form.** In August 2014, NIA created a draft electronic BLSA visit summary form that standardizes the format for inclusion of key findings, tests completed and not completed (with reasons for non-completion), and key actions, including any problems that required management during the visit and any follow-up actions planned. The draft form will be tested for two months and NIA will then refine the format and implement it within the context of a weekly summary review of all participants seen during that week. The summary will be placed in the participant chart.
 - 3) **Policy on return of test results.** In August 2014, NIA developed, finalized and implemented a policy for classification and return of test results for all NIA intramural human studies. This policy is entitled, Administrative Policy-025- Classification and Return of Test Results on NIA Clinical Research Unit (Implementation date: 8/28/2014). Since BLSA does not treat participants for specific diseases, none of the tests are done for clinical reasons. The tests are all performed for research purposes, although some of them may occasionally show findings that suggest the need for follow up by a primary care physician. NIA’s current plan is to clearly classify tests as “routine” or “research.” BLSA tests classified as routine include clinical labs, such as blood cell count, electrolytes, kidney function, liver function, and ECG. These findings will be provided to the participant by the end of their visit and a note in the participant chart will document that the findings were provided to participants and discussed. All other BLSA tests are for research purposes only. NIA plans to classify these research test results into three groups.
 - i. *Immediate Alert.* These are research findings that require medical action within hours to days. The policy will state that these findings must be

communicated to the participant and their preferred medical provider within hours to days, depending on the clinical appropriateness judgment of BLSA physicians. If the participant is still on the unit, BLSA health professionals will examine the participant, discuss the finding with the participant and possibly their provider, and make a plan for care that might include transfer to a clinical facility or other arrangements, as agreed. In this case, the care plan will be recorded in the progress notes of the participant chart. If the result is received after the participant leaves the unit, communication will be by telephone to the participant and their physician and sent by FedEx within 24 hours.

- ii. *Clinically Significant.* These are results that may have clinical impact, but are not judged by BLSA physicians to require immediate medical attention. If detected during the visit, the findings will be reviewed with the participant in person and a copy of the finding provided to the participant. The participant's chart will contain a progress note confirming that this occurred. If findings are received after the participant leaves the unit, the findings will be mailed to the participant with a cover letter providing a brief explanation and recommendation to bring the issue to the attention of the participant's medical provider. The letter will be mailed within 30 days of receipt of results.
- iii. *Courtesy.* These are research results that are received after the participant leaves the unit that will be provided to the participant as a courtesy due to participant interest. Examples include bone density (DEXA) and possibly Vitamin D levels. These test results will be mailed to the participant, but no specific timeline will be required since the results have no urgent clinical relevance.

All NIA intramural investigators will operationally define their plan to return results to participants based on that policy. NIA's plans for monitoring and communicating test results do not require individual signatures on routine and courtesy results, as those results are not of urgent clinical significance and are provided as formatted letters with attachments. Similarly, NIA will continue to use identification numbers rather than hand written signatures to track the identity of individuals who perform tests. NIA's rationale is that electronic tracking and data entry using teleforms will replace written signatures in the future. Furthermore, in the case of teleforms, handwritten materials interfere with the scanning of the form.

4) **Changes in language for the BLSA protocol and consent to reflect practices.**

NIA/BLSA staff are clarifying language in the protocol and consent form related to return of results and will continue with this work until language is consistent with current practices. After finalizing the NIA policy on return of results, NIA/BLSA

submitted additional protocol amendments to the IRB seeking further modification of language in the protocol and consent.

The BLSA protocol was changed during 2013 to delete the term “in good health” because of the vagueness of this term. The protocol now uses only objective criteria for assessing this issue. On August 4, 2014, the IRB approved proposed amendments to the protocol, which had been previously submitted for review. Approved protocol amendments include the following clarifications (Revised language is reflected by underline below):

- i. Clarification of inclusion requirements to delete metabolic dysfunction as the individual criteria are already listed and clarify verbiage for exclusion regarding severe hormonal dysfunction to now say subjects must “*not have severe hormonal dysfunction (Laboratory values out of range despite supplementation and/or drug treatment)*.”
- ii. Clarification regarding which results are discussed at discharge: “*Results of clinical lab tests are explained to the participant and copies of their available labs are provided at discharge*.”
- iii. Clarification regarding routine return of results to participants via mail to indicate that results of OGTT’s will not be included. Additional/changed language is as follows with new language underlined. “*If medically indicated, but not of an urgent nature, copies of the echocardiogram report, CT scan report, MRI report and/or other results that the research medical staff want to communicate to the participant may also be enclosed. New clinically significant results or incidental findings are reported to the participant (and their PCP if authorized) either in person, (and PCP as authorized) via fax, mail or Fedex.*
- iv. Addition to the section regarding potential benefits of study participation the following language: “*New clinically significant results or incidental findings are reported to the participant (and their PCP if authorized) either in person, by phone, or by a letter. The results are then provided to the participant (and PCP [primary care physician] as authorized) via fax, mail or Fedex.*”

On August 4, 2014, the IRB approved the following proposed amendments to the consent form:

- i. Clarification in the section that addresses “Will I be given results from this study?” updated language is underlined in the following “*In addition, as applicable, you will receive copies of your clinical tests such as the blood tests and EKG. The DEXA and treadmill results will also be provided if completed. However, these tests do not replace tests prescribed by your*

primary care physician. A copy of these tests may be provided to your doctor but only after you have provided written release to us. If the medical staff determines that results from your test(s) are new findings and clinically significant, you will be notified to seek attention from your primary care physician.

- ii. Under the section which addresses “*Who can participate in this Study?*” the consent will delete metabolic dysfunction as the individual criteria are already listed and clarify verbiage for inclusion regarding severe hormonal dysfunction as noted above in the amendments to the protocol.
- iii. Clarification of testing requirements for HIV, Hepatitis B and C, and Syphilis which will occur “*at your Screening Visit. We may test you for these conditions at a Routine Visit if you are scheduled for cytapheresis or your last Routine Visit was prior to 2003.*”

5) **Quality Assurance/Quality Improvement (QA/QI) plans.** In the past, MedStar led QA/QI monitoring, as part of Medstar IRB and contractual oversight services to the NIA Clinical Unit in Baltimore. NIA transitioned to NIH IRBs for review and oversight of their protocols during the winter of 2013,¹³ and NIA is now developing its own QA/QI plans. NIA envisions several components to these plans.

- i. NIA will first develop a list of key indicators of excellent practice such as participant safety, communication with participants and providers, documentation in participant charts and other core functions.
- ii. NIA will then define indicators of compliance and adherence, how they will be sampled and measured, and how frequently they will be assessed. Some indicators may be monitored continuously through ongoing chart reviews and checklists. Some may be summarized and reviewed by the QI team composed of BLSA leadership on a periodic basis.
- iii. NIA plans to have an independent review by an outside agency on an annual basis. The scope of that annual review will be determined each year. NIA has drafted a QA/QI policy which is in process of going through internal review/discussion. NIA plans to have final draft by Oct 15, 2014. At that point, NIA will conduct a 3-month pilot of the policy and evaluate results. Any further changes to policy will be made following the pilot, and final policy adopted. The policy will be reviewed

¹³ In 2013 the NIH Office of Human Subjects Research Protections requested a transfer of all NIA protocols from the Medstar IRB to NIH IRBs to ensure that NIA protocols (as well as other NIH protocols) all have oversight by NIH IRBs. This harmonization was part of a broad NIH effort to ensure consistent application of NIH policies and practices, and was an important part of NIH work to obtain AAHRPP Accreditation of its Human Research Protection Program, which was granted in March 2014.

and updated at least annually based on potential new indicators or the need to refine old indicators.

- 6) **Report deviations to the IRB as needed for final conclusions.** Deviations related to this review involve the timing of mailing clinical results and the application of protocol inclusion/exclusion criteria. NIA has and will continue to work closely with the NIH IRB in identifying whether any of the report findings constitute a reportable protocol deviation. While none of these issues appear to have impacted the safety of participants, the IRB must make final determinations about whether deviations are “serious” or “not serious.”

VII. CONCLUSION

The NIH review team conducted a comprehensive evaluation of all of the allegations made by the Complainant, as explained in the report. The team did not find any apparent violation of law or endangerment to public health or safety. However, some of the conclusions, concerning specific allegations, require NIA officials to take corrective action. The corrective action, including IRB reporting, will adequately address matters that are the subject of the allegations. Michael Gottesman, M.D., the Deputy Director for Intramural Research and the Institutional Official for Human Subjects Research at the NIH, will monitor the corrective action work, obtain annual progress reports from NIA on the improvements proposed in this report, and assure that they are implemented in a timely fashion.

APPENDIX I(A). BLSA PROTOCOL LANGUAGE

APPENDIX I. CRITERIA

A. BLSA Protocol Language

Language	IRB Approval Dates					
	5/19/2011	2/8/2012	6/28/2012	10/11/2012	1/28/2013	6/30/2013
Results of the clinical tests are explained to participants and copies of the tests are mailed to them shortly after their visit, with comments if required. Results of most research tests, including cognitive and neurological tests, are not given to the participant because their clinical value in the context of an epidemiological study is still undefined. Some tests results are provided to participants, but research orientated nature of these tests and their limitations for diagnostic use are clearly stated.	same	same	same	same	same	same
Most results of these studies contain new, unverified information of unclear significance and, therefore, they will not be given to the participants or their doctor.	same	same	same	same	same	same
Subjects are not informed of the results of studies on their genes or genetic make-up.	same	same	same	same	same	same
If any abnormality is detected in the clinical cardiovascular or respiratory tests, they are communicated to the participants and if the participants authorize, to their primary care physicians.	same	same	same	same	same	same
Similarly, they will not receive information about other family members nor will they receive any laboratory results from this type of testing.	same	same	same	same	same	same
Participants will be informed about the information from this or other studies that may affect their health, welfare or willingness to stay in this study.	same	same	same	same	same	same
Subjects are not informed of the results of studies on their genes or genetic make-up.	same	same	same	same	same	same
Participants do receive copies of laboratory tests, urine tests, EKGs, OGTTs, treadmill, and bone density scans (clinically significant tests).	same	same	same	same	same	same
Copies of these tests will only be provided to their physicians after proper written release has been obtained.	same	same	same	same	same	same
Abnormal tests or incidental findings are immediately provided to participants and they are informed to contact their primary care physician for treatment.	same	same	same	same	same	same

A. PENDIX I(B). BLSA PROTOCOL CONSENT LANGUAGE

B. BLSA Protocol Consent Language

Language	2/22/2011	2/8/2012	6/28/2012	10/11/2012	1/28/2013	6/30/2013
If any new information is learned, at any time during the research, which might affect your participation in the study, we will tell you.	same	same	same	same	same	same
No original text				We will do a urine pregnancy test on the first morning of the visit and you will be notified of the results so that tests that may be hazardous during pregnancy can be avoided.	We will do a urine pregnancy test on the first morning of the visit and you will be notified of the results so that tests that may be hazardous during pregnancy can be avoided.	We will do a urine pregnancy test on the first morning of the visit and you will be notified of the results so that tests that may be hazardous during pregnancy can be avoided.
Most results of these studies contain new, unverified information of unclear significance and , therefore, will not be given to you or your doctor.	same	same	same	same	same	same
If you allow future research on your sample and the research provides information important to your health, we will try to contact you.	same	same	same	same	same	same
We will do tests that study the heart, blood vessels, and respiratory system. These tests may show you have an abnormality or disease of the heart and vessels or respiratory system. If any significant clinical abnormality is detected in the cardiovascular and respiratory tests, it will be communicated to you and, if you authorize, to your primary care physician.	same	same	same	same	same	same
(Vision) We will discuss with your any abnormality or disease detected by this test.	same	same	same	same	same	same

A. PENDIX I(B). BLSA PROTOCOL CONSENT LANGUAGE

Language	2/22/2011	2/8/2012	6/28/2012	10/11/2012	1/28/2013	6/30/2013
The clinical significance has not been established; therefore you will not receive results of these tests. If we observe significant memory problems or symptoms of depression during these assessments; we will notify you and your physician that further clinical evaluation may be warranted.	same	same	same	same	same	Language change: All BLSA participants are given some tests to assess memory, problem solving, different types of learning, and information processing skills. These tests take about 10 minutes. You may be scheduled for an additional 90 minutes of testing depending on your age and other characteristics. You will be asked to provide the name and contact information of a family member or close friend who can provide information regarding your daily activities. You may also be contacted by phone between regularly scheduled visits to update us on your cognitive functioning.
If the PSA is abnormal it will be recommended that you consult your primary care doctor and he may suggest further testing, such as a prostate biopsy.	same	same	same	same	No PSA testing language	No PSA testing language

A. PENDIX I(B). BLSA PROTOCOL CONSENT LANGUAGE

Language	2/22/2011	2/8/2012	6/28/2012	10/11/2012	1/28/2013	6/30/2013
Genetic information about you will not be revealed to others, including relatives, without your written permission. Similarly, you will not receive information about other family members. NIA researchers do not plan to provide you with the results of any laboratory investigations involving the use of your samples for genetic testing.	same	same	same	same	same	same
You will receive copies of your clinical tests such as the blood tests, EKG, DEXA and treadmill. A copy of these tests may be provided to your doctor but only after you have provided written release to us. If we find any abnormal results from your tests, you will be notified to seek attention from your primary care physician since this is a research study only and we cannot provide treatment to you. Some results from the research-orientated tests will be provided to you but you need to be aware that the results of these tests have limited diagnosis value. You doctor should decide whether based on the results of these tests you need further medical testing.	same	same	same	same Plus text: The study doctor may recommend that a test be repeated if in their opinion the test result is inconclusive. Because, this is a research study only, we cannot provide more in depth testing for diagnostic purposes nor prescribe treatment for you.	same Plus text: The study doctor may recommend that a test be repeated if in their opinion the test result is inconclusive. Because, this is a research study only, we cannot provide more in depth testing for diagnostic purposes nor prescribe treatment for you.	same Plus text: The study doctor may recommend that a test be repeated if in their opinion the test result is inconclusive. Because, this is a research study only, we cannot provide more in depth testing for diagnostic purposes nor prescribe treatment for you.
Participants will be informed about new information from this or other studies that may affect their health, welfare, or willingness to stay in this study.	same	same	same	same	same	same
We will tell you about new information that may affect your health, welfare, or willingness to be in this study.	same	same	same	same	same	same

APPENDIX I(C). NURSING POLICY 076

C. Nursing Policy 076

Department of Health and Human Services
National Institutes of Health
Clinical Research Branch/Intramural Research Program/
National Institute on Aging (CRB/IRP/NIA)

NURSING POLICY



Policy Title:

Clinical Rounds on the NIA Clinical Research Unit

Policy Number: NP-076

Implementation Date: 04/01/2010

Date Reviewed without Revision: 03/15/2013

Date Reviewed with Revision:

PURPOSE:

- This document describes the clinic flow for participants of the BLSA.

SCOPE OF PRACTICE:

- This SOP applies to the NIA/IRP LCI/Clinical Unit: Principal Investigators, Clinical Research Coordinators, Nurse Practitioners, Research Nurses.

COMPLIANCE:

- 100% compliance is required.

PROCEDURE and RESPONSIBILITY:

The PIs, Clinical Research Coordinators and Nurse Practitioners are responsible for ensuring that these procedures are followed

- Report sheets are prepared by the Nurse Manager twice daily for the 7:00 a.m. and 3:00 p.m. rounds. Rounds are mandatory for the clinic nursing staff, Nurse Practitioners, and Pharmacist. 7:00 am rounds are attended by the Clinical Director (unless out-of-town), and 3:00 pm Rounds are attended by the BLSA Medical Officer, doctor on-call (if different from BLSA medical officer), epidemiologists, and on occasion other medical staff, PIs, and/or post-doctoral fellows.
- A physician is 'on call' at all times for any emergent clinical issues as long as there is a participant in-house. While treadmills are being performed, a doctor is on site.
- Based on the findings reported by nurses and technicians in those twice daily rounds, issues of clinical relevance to the participants and/or that may directly impact the health of participants are discussed and followed up in real time. Issues are communicated to participants and further testing is performed if needed.

APPENDIX I(C). NURSING POLICY 076

Clinical Rounds on the NIA Clinical Research Unit
Page 1 of 2

- Every Friday morning at 9:00 a.m. there is a mandatory BLSA meeting. The BLSA PIs, NPs and physicians who performed H & P, CRCs, testers (gait, echo, PWV, treadmill, strength, cognition), nursing staff, post-doctoral fellows all participate to the meeting. BLSA participants evaluated during the current week are again discussed in great detail by all staff involved in BLSA testing. This includes discussion of pertinent history and physical findings, lab values, cardiovascular findings, imaging findings, cognitive findings, and any relevant health-related information. If a clinically significant finding is felt to require follow-up because it may impact the health of the participant, and has not been earlier taken care of during the week, the NPs call the participant to inform them of the discussion, and writes a note in the chart. The phone call is then followed up with a letter, to include discs and reports, as necessary.
- At the Friday BLSA meeting, known medical history and information on the participants that are scheduled for the following week are discussed by all BLSA staff. Matters of concern that may impact the schedule of testing for the coming week are resolved and appropriate measures to preserve health and safety of participants are implemented, in particular concerning possible risks of falls.

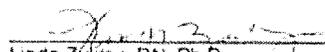
DOCUMENTATION:

- Report results in the protocol specific progress notes and/or on applicable report forms

COMMUNICATION/EDUCATION:

- The policy will be distributed for inclusion into the CRB/IRP/NIA Unit Clinical Practice Manual

APPROVED:



Linda Zukley, RN, PhD
Clinical Nurse Manager, MHR1



Date



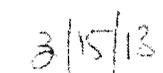
Josephine Egan, MD
Clinical Director, NIA, NIH



Date



Luigi Ferrucci, MD, PhD
Scientific Director, NIA, NIH



Date

APPENDIX I(D). NURSING POLICY 077

D. Nursing Policy 077

Department of Health and Human Services
National Institutes of Health
Clinical Research Branch/Intramural Research Program/
National Institute on Aging (CRB/IRP/NIA)

NURSING POLICY

**Policy Title:**

Planning, Scheduling and Completion of BLSA Participant Study Visit

Policy Number: NP-077

Implementation Date: 04/01/2010

Date Reviewed without Revision: 03/15/2013

Date Reviewed with Revision:

PURPOSE:

- This document describes the planning, scheduling, and completion of BLSA participants' visit.

SCOPE OF PRACTICE:

- This SOP applies to the NIA/IRP LCI/Clinical Unit: Principal Investigator (PI), BLSA Medical Officer, Clinical Research Coordinators (CRC), Nurse Practitioners (NP), Pharmacist, Research Nurses and Certified Nursing Assistants (CNA's), and the Clinical Nurse Manager (CNM).

COMPLIANCE:

- 100% compliance is required.

RESPONSIBILITY:

- The Clinical Director and the CNM are responsible for ensuring that these procedures are followed. Any alteration must also be discussed with the PI of the study.

POLICY & PROCEDURES:

- Scheduling staff identifies and schedules BLSA participants due for their upcoming BLSA visit.
- NPs review the participant's records from previous visits and contact participants for pre-visit telephone screen. Any contraindication to testing procedure(s) or study visit is discussed during the Friday BLSA meeting prior to their actual study visit. (see Policy NP-076)
- BLSA Clinical Research Coordinator reviews the scheduling and inclusion/exclusion criteria for all testing procedures on the Friday before all visits.

APPENDIX I(D). NURSING POLICY 077

BLSA Participant Study Visit
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- During the participant's study visit, the staff/testers always review all relevant information and inclusion and exclusion criteria in real-time before each testing procedure. All testing procedures are done per protocol only in participants who are eligible, have no exclusion criteria, have consented to perform the specific test and are judged to be safe.
- Before discharge from the unit, all BLSA participants have an interview with the NP who evaluated them during which all available clinical laboratory results and any clinically significant abnormal test results are discussed. A copy of all available results is provided to the participants as they leave.
- For significant abnormal test results that become available after the participant has been discharged and are judged to require medical attention (for example, CT reports, testosterone levels, or results that are discussed during the BLSA Friday morning meeting), the participant is contacted by phone and a copy of the test results is mailed to the participant and also to his/her primary provider if authorized to do so by the participant.
- A complete packet that includes copies of results from blood tests, urine tests, oral glucose tolerance test (OGTT), electrocardiogram (EKG), DEXA and treadmill exercise test is sent to participant when all results and interpretations are available.

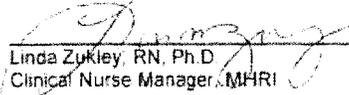
DOCUMENTATION

- Report results in the protocol specific progress notes and/or on applicable report forms

COMMUNICATION/EDUCATION:

- The policy will be distributed for inclusion into the CRB/IRP/NIA Unit Clinical Practice Manual.

APPROVED:



Linda Zukley, RN, Ph.D.
Clinical Nurse Manager, MHR1

1/3

Date



Josephine Egan, MD
Clinical Director, NIA, NIH

3/15/13

Date



Linda Zukley, RN, Ph.D.
Clinical Nurse Manager, MHR1

3/15/13

Date

APPENDIX I (E). PROTOCOL INCLUSION/EXCLUSION CRITERIA

E. Protocol Inclusion/Exclusion Criteria

Test 1 – Protocol Eligibility Screening Test Questions

1 Review Date:

2 Reviewer Name:

3 Supervisory Reviewer Name:

4 Sample Number:

5 Screening Visit Start Date (dd/mm/yyyy):

6 Screening Visit End Date (dd/mm/yyyy):

APPENDIX I (E). PROTOCOL INCLUSION/EXCLUSION CRITERIA

7 Review Results for Protocol Inclusion Criteria

Subjects are enrolled into the study population if they:

	1. Evidence of Screening Activity?		2. Source of Evidence (e.g., test result documentation, nurse's note)	3. Result of Screening Activity?			4. Reviewer Comment Enter supporting details:
	Yes	No		Met	Unmet	N/A	
A. Are at least 20 years old	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
B. Are in good health	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
C. Weigh < 300lbs and/or have a BMI	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
D. Have no established genetic diseases	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
E. Report no difficulties or need for help in performing self-care or instrumental activities of daily living	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
F. Are able to walk independently for at least 400 meters without using assistive devices	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
G. Have no shortness of breath while performing normal activities of daily living, such as walking or climbing stairs	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
H. Have no substantial cognitive impairment based on mental status screening tests	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
I. Have no history of cardiovascular disease (including angina, myocardial infarction, congestive heart failure, cerebrovascular diseases but not controlled hypertension)	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

APPENDIX I (E). PROTOCOL INCLUSION/EXCLUSION CRITERIA

	1. Evidence of Screening Activity?		2. Source of Evidence (e.g., test result documentation, nurse's note)	3. Result of Screening Activity?			4. Reviewer Comment Enter supporting details:
	Yes	No		Met	Unmet	N/A	
J. Have no history of diabetes (requiring any medical treatment other than diet and exercise)	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
K. Have no history of active cancer (except for locally limited basal cell cancer)	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
L. Have no history of metabolic disease	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
M. Have no history of severe hormonal dysfunctions (requiring supplementation or chronic drug treatment)	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
N. Have no history of neurological diseases	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
O. Have no history of birth defects (other than minor anatomical abnormalities which do not affect physical and/or cognitive function)	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
P. Have no history of established genetic diseases	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Q. Have no history of kidney or liver disease (associated with reduced kidney or liver function)	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
R. Have no history of severe gastrointestinal (G.I.) diseases	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
S. Have no history of muscle-skeletal	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

APPENDIX I (E). PROTOCOL INCLUSION/EXCLUSION CRITERIA

	1. Evidence of Screening Activity?		2. Source of Evidence	3. Result of Screening Activity?			4. Reviewer Comment
	Yes	No		Met	Unmet	N/A	
<p>with antibiotics, corticosteroids, immunosuppressors, H2 blockers and/or proton pump inhibitors, or pain medications</p> <p>V. Have no history of important sensory deficits (e.g. legally blind) and/or any condition that precludes them from being tested with standard neuropsychological tests or providing informed consent</p>	<input type="radio"/>	<input type="radio"/>	(e.g., test result documentation, nurse's note)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Enter supporting details:

APPENDIX I (E). PROTOCOL INCLUSION/EXCLUSION CRITERIA

8 Review Results for Protocol Exclusion Criteria

The following criteria are considered as markers of pathological conditions and are used as exclusion criteria for study enrollment:

	1. Evidence of Screening Activity?		2. Source of Evidence (e.g., test result documentation, nurse's note)	3. Result of Screening Activity?			4. Reviewer Comment Enter supporting details:
	Yes	No		Met	Unmet	N/A	
A. HIV virus infection	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
B. Hepatitis B or C	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
C. Syphilis	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
D. WBC > 12,000/mcrL	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
E. Platelets < 100,000 or > 600,000/mcrL	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
F. Hemoglobin < 11 g/dL	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
G. Creatinine > 1.5 mg/dl or calculated creatinine clearance < 50 cc/min	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
H. Bilirubin > 1.5 mg/dl unless higher levels can be ascribed to Gilbert's disease	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
I. SGOT, SGPT or alkaline phosphatase twice the normal serum concentration	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
J. Corrected calcium < 8.5 or > 10.7 mg/dl	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
K. Albumin < 3.4 g/dl	<input type="radio"/>	<input type="radio"/>		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

APPENDIX I (E). PROTOCOL INCLUSION/EXCLUSION CRITERIA

9 TEST CONCLUSION: Does the medical record contain evidence that the participant met all inclusion/exclusion criteria for study enrollment?

- Yes
- No

9a Reviewer Comment:

APPENDIX I(F). APHERESIS ELIGIBILITY CHECKLIST

F. Apheresis Eligibility Checklist

**National Institute on Aging Apheresis Unit
Baltimore Longitudinal Study of Aging (BLSA)
On Study Eligibility Form**

BLSA #	Institution: NIA CREB	Date on BLSA study
Name	Performance Status ECGG	Date On BLSA Apheresis
Initial Contact Date	Today's Date	Date OFF study

	Yes	No	N/A	Comments
1. Has participant ID been verified?				
2. Does participant meet eligibility requirements per Health History Questionnaire?				
3. Is donor weight \geq 110 pounds?				
4. Is temperature \leq 37.5 Celsius?				
5. Is Pulse 45 - 100 BPM? (Note: If Pulse is <45 BPM, may be eligible if otherwise healthy athlete.)				
6. If participant has a pacemaker, is heart rate 50 -100 BPM? (Note: If Pulse is <45 BPM, may be eligible if otherwise healthy athlete.)				
7. Is systolic B/P \leq 180 mm Hg and diastolic B/P \leq 100 mm Hg?				
8. If B/P is normally low, participant has no associated symptoms?				
9. * Hgb. \geq 12.0 *If the Hgb. is 11.5 - 11.9, a Physician's evaluation, order and signature is necessary to proceed with Cytapheresis procedure.				Hgb result _____
10. Hct \geq 36.0				
11. WBC \geq 3.5				
12. Platelet counts \geq 150				
13. Lymphs within the range of 20-40%?				
14. Granulocytes within the range of 40-76%?				
15. Participant is without significant electrolyte, hepatic, or renal abnormality on chemistry profile?				
16. Negative pregnancy test, if pre-menopausal?				
17. Participant confirms that she is not breastfeeding?				
18. The participants medications are currently without any that would affect the immune system.				

APPENDIX I(F). APHERESIS ELIGIBILITY CHECKLIST

BLSA ID #
Date

	Yes	No	N/A	Comments
19. Is without history of allergy to acid-citrate-dextrose (ACD) anticoagulant?				
20. Is without history of active bleeding disorder?				
21. Does the participant confirm no blood donations anywhere in the last 56 days? (Note: Blood component collection intervals are evaluated per AABB guidelines).				
22. Has the participant been free of seizures within the last three months?				
23. Is participant without a history of sickle cell disease or sickle cell trait?				
24. Does participant confirm no recent history of a treatment regimen for TB?				
25. Does participant confirm no history of Lyme disease? (Note: May be eligible if six weeks post-treatment and without new symptoms).				
26. Is participant without a history of Chagas disease, Babesiosis, or Leishmaniasis?				
27. Is without a history of treatment for syphilis or gonorrhea < one year before planned cytapheresis donation?				
28. Is without current symptoms of an active migraine headache?				
29. Is without a history of severe cardiac arrhythmia?				
30. Per current history or physical exam there is no indication of active CAD?				
31. Is without a history of myocardial infarction, episodes of angina or stroke in the last 6 months?				
32. Is without current history or physical exam indicating active congestive heart failure (NYHA stage III or IV)?				

APPENDIX I(F). APHERESIS ELIGIBILITY CHECKLIST

BLSA ID #
Date

	Yes	No	N/A	Comments
33. If participant has diagnosis of COPD, is without current symptoms of respiratory difficulty?				
34. If the participant has received treatment for cancer in the past six weeks or longer, he/she has recovered fully from the treatment? (NOTE: Some low risk cancers including squamous cell or basal cell carcinomas are not cause for exclusion)				
35. Before first cytappheresis procedure, has no history of HIV, Hepatitis B or C?				
36. At the time of the first cytappheresis, is without seropositivity of HIV, Hepatitis B and / or C? (NOTE: If newly diagnosed with Hep B or C at the time of the first cytappheresis procedure, this is cause for exclusion from future cytappheresis procedures. However, if seropositivity occurs during one of the follow up procedures this is not cause for exclusion from the cytappheresis procedure.)				
37. Is without current Rx regimen of oral or subcutaneous anticoagulant or antiplatelet agents (except low-dose aspirin)?				
38. Participant confirms no treatment with insulin or drugs active on the cardiovascular system started < 4 weeks before visit?				
39. Participant confirms no change in insulin or cardiovascular treatment regimen in the last 2 weeks?				
40. Participant is without current illness for which cytappheresis would increase the risk (i.e. allergies, active infection)?				
41. Participant confirms no plans for major surgery within 8 weeks of cytappheresis procedure?				
42. Has history and physical exam without significant physical or mental abnormalities that would otherwise limit ability to tolerate an apheresis procedure?				

APPENDIX I(F). APHERESIS ELIGIBILITY CHECKLIST

**National Institute on Aging Apheresis Unit
Baltimore Longitudinal Study of Aging (BLSA)
On Study Eligibility Form**

BLSA ID # _____
Date _____

	Yes	No	N/A		Comments
43. Participant confirms that he / she has not enrolled in another research study in the past 6 weeks that would be incompatible with the cytapheresis procedure?					
44. Has adequate venous access in both arms for machine based apheresis i.e. 17 gauge needles and ability to withstand flow rates of 50 ml/minute OR has adequate venous access in one arm for manual apheresis using 17 gauge needle?					
45. Has informed consent for BLSA, HIPAA and Cytapheresis been obtained ?					

Form Completed by _____ Date: _____

Comments _____

Eligible? Yes No Temporary Deferral

N.P./P.A. Signature _____ Date _____

Physician Signature _____ Date _____

APPENDIX I(G). DIRECT ADMISSION TO HARBOR HOSPITAL POLICY

G. Direct Admission to Harbor Hospital Policy

Department of Health and Human Services
National Institutes of Health
Clinical Research Branch/Intramural Research Program/
National Institute on Aging (CRB/TRP/NIA)

NURSING POLICY



Policy Title:

Direct Participant Admission to MedStar Harbor Hospital

Policy Number: AP - 0004

Implementation Date: September 15, 2003

Date Reviewed without Revision:

Date Reviewed with Revision: June 15, 2003, July 21, 2008, April 15, 2013

PURPOSE:

- To ensure a process for direct admission of stable research participants to MedStar Harbor Hospital.
- These criteria are intended as guidelines to assist in the delivery of nursing care to participants. They are not intended to replace the professional judgment of the nurse in participant care delivery matters.

DEFINITIONS:

- **Stable Participant** – No immediate change in the participant's condition is expected as determined by the medical staff.

POLICY:

- At the discretion of the medical staff, and in lieu of going to the emergency room for treatment, a stable participant may be admitted directly to a non-critical care unit of MedStar Harbor Hospital.

SCOPE OF PRACTICE:

Research staff caring for participants on the clinical research unit are responsible for monitoring and reporting changes in participants conditions to the medical staff.

COMPLIANCE:

- The Clinical Nurse Manger will monitor compliance.

EQUIPMENT:

- Wheel chair or stretcher.

PROCEDURE and RESPONSIBILITY:

- At the discretion of the National Institute on Aging's (NIA) Medical staff, MedStar Harbor Hospital's Hospitalist will be notified about a possible candidate for direct admission. After conferring with the NIA medical staff, the MedStar medical staff will determine whether to admit the participant to the emergency room for evaluation or directly to a non-critical care hospital bed.

APPENDIX I(G). DIRECT ADMISSION TO HARBOR HOSPITAL POLICY

Direct Participant Admission to MedStar Harbor Hospital
Page 2 of 3

- The NIA medical staff will report the decision to the NIA Clinical Director and the MHRI Clinical Nurse Manager or designee.
- The MHRI Clinical Nurse Manager or designee will call MedStar Harbor Hospital Registration to arrange the registration of the participant.
- Pertinent information in the participants chart will be copied and given to the accepting unit.
- When MedStar Harbor Hospital calls with a floor/bed assignment, the participant is readied to be transported to the room. All of the participant's belongings will be packed and will accompany the participant to the assigned room in either a wheelchair or on a stretcher with a nurse and another staff member as needed.
- Report and copies of the medical record will be given to the assigned nurse on the floor.
- The medical staff will document in the medical record the events/reasons leading to the admission of the participant. If indicated, an incident report and/or an adverse event report will be generated and provided to the Protocol and/or NIA Safety Office as applicable.
- In the event of an admission to the MedStar Harbor Hospital Emergency Room (ER), the participant will be taken to the ER accompanied by medical staff after the NIA medical staff has discussed the case with the ER medical staff. Copies of the medical record and oral report to the MedStar Harbor Hospital ER staff will be provided upon arrival. The ER medical staff will notify the NIA Unit of admission to the hospital or discharge. If the participant is to be admitted, the participant belongings will be transported to the assigned hospital room. If the participant is to be discharged from the ER back to the NIA research unit, the ER staff will accompany the participant and provide oral report to the NIA research staff. Upon arrival, final disposition of the participant will be determined by the NIA medical staff. As applicable, an adverse event report and/or incident report will be generated and sent to the Protocol office and/or the NIA Safety Office.

DOCUMENTATION:

- Medical chart progress notes.

COMMUNICATION/EDUCATION:

- The policy will be distributed for inclusion into the CRB/IRP/NIA Unit Clinical Practice Manual.

ATTACHMENTS/REFERENCES/CROSS REFERENCES:

- Not Applicable

ORIGINATORS:

Eric Westin, MD.

APPENDIX I(G). DIRECT ADMISSION TO HARBOR HOSPITAL POLICY

APPROVED:

Linda Zukley, RN, Ph.D.
Clinical Nurse Manager, MHRl

Date

Jody Gatuso, MBA, CM
Program Manager, MHRl

Date

Neil Weissman, MD
Principal Investigator, MHRl

Date

Josephine Egan, MD
Clinical Director, NIA, NIH

Date

APPENDIX I (H). EMERGENCY CARE POLICY

H. Emergency Care Policy

Department of Health and Human Services
National Institutes of Health
Clinical Research Branch/Intramural Research Program/
National Institute on Aging (CRB/IRP/NIA)

NURSING POLICY



Policy Title:

Emergency Medical Response-Impending Cardiac Arrest or Cardiac Arrest

Policy Number: AP - 0005

Implementation Date: June 16, 2005

Date Reviewed without Revision:

Date Reviewed with Revision: July 21, 2008, March 1, 2013

PURPOSE:

- To provide guidelines for provision of equipment, personnel and processes for expeditious and effective response to all patients/visitors/hospital personnel on the NIA Clinical Research Unit who require emergency medical treatment.
- These criteria are intended as guidelines to assist in the delivery of nursing care to patients. They are not intended to replace the professional judgment of the nurse in patient care delivery matters.

DEFINITIONS:

- **Visitor:** Any person who is not a participant or who is not an employee or contractor of the National Institute on Aging/NIH.
- **Emergency Medical Treatment:** Basic Life Support, Advanced Cardiac Life Support or Emergency Department/Emergency Medical Systems interventions administered for any medical/surgical condition.
- **Basic Life Support (BLS):** Non-invasive assessments and interventions used to treat victims of respiratory and/or cardiac emergencies and stroke. This includes external chest compression and mouth-to-mouth (or mouth to mask) ventilation (CPR) and automatic external defibrillation (AED).
- **Advanced Cardiac Life Support (ACLS):** Medical interventions used to treat victims of respiratory and/or cardiac emergencies and stroke including invasive techniques such as: defibrillation, definitive airway support (ventilation with 100% oxygen via ambu bag and mask and/or intubation), establishment of IV access and administration of medications.
- **Defibrillation/Cardioversion:** Use of a device to deliver a transthoracic electric current to the heart to re-establish a normal cardiac rhythm.
- **Cardiopulmonary Resuscitation (CPR):** An emergency procedure in which the heart and lungs are made to work by manually compressing the chest overlying the heart and forcing air into the lungs.
- **Automated External Defibrillator (AED):** A portable defibrillator designed to be automated such that it can be used by persons without substantial medical training who are responding to a cardiac emergency.

POLICY:

- Clinical unit staff will maintain certification in Basic Life Support to include AED use.
- Medical staff-Nurses and Nurse Practitioners as well as the Exercise Physiologist conducting stress testing, will maintain ACLS certification.

APPENDIX I (H). EMERGENCY CARE POLICY

Emergency Medical Response

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- MedStar Harbor Hospital's Cardiac Arrest or Rapid Response Team consists of:
 - Physicians in the immediate vicinity
 - The Intensive Care Unit (ICU) medical resident and interns on CPR call
 - Respiratory Therapist on CPR call
 - Nursing Supervisor (evenings, nights, and weekends)
 - Emergency Department (ED) charge nurse
 - ICU charge nurse
 - IV therapist assigned to the area
 - An ACLS-certified nurse from the critical care unit will respond to calls for the Alert Team made by inpatient units and act as a resource person for unit staff.
- Clinical Unit staff responsible for the participant:
 - All staff assigned to the participant
 - Clinical Nurse Manager
 - ACLS certified clinical staff
 - Physician of the Day/ On-Call and/or NIA Clinical Director

NIA EQUIPMENT:

- Mouth-to-mask devices are located in each patient room and each emergency evacuation box, and are used for initial ventilation.
- Code Carts
 - Emergency carts (Crash Carts) are located in the hall on South Main (SM)-5 at the nurse's station and in the treadmill room on North Main (NM)-5. The research staff performs quality assurance checks on the cart each day.
 - The carts contain emergency drugs, airway/ventilation/oxygen delivery equipment, a cardiac board, intubation tray, venous access equipment and IV fluids.
 - Emergency cart content standards are reviewed at least annually and revised as changes in practice and the American Heart Association Advanced Cardiac Life Support (ACLS) guidelines dictate.
 - The emergency cart will be locked. The intact tamper evident locks indicate that the MedStar Harbor Hospital (MHH) Pharmacy and Sterile Processing Department (SPD) have properly stocked the cart. The lock may be easily broken for immediate use. Once opened, the cart is to be exchanged promptly by SPD (410-350-3308). If a lock is broken, notify SPD immediately for cart inspection, restocking, and replacement of the lock.
- Defibrillator/Monitor
 - Portable defibrillator/monitors are located with the Crash Carts in the hall on SM-5 and in the treadmill room on NM-5. Only the defibrillator in the treadmill room on NM-5 has AED and external pacing capabilities.
 - An AED is located in the front reception area directly across from the women's bathroom.
 - An AED is located in the MRI suites outer room.
- Suction Equipment
 - Centralized suction is available in each patient room, treadmill room, procedure room, and exam room.
 - Portable suction is stored in SM539.
 - Suction equipment can be found in the control room in the MRI suite.
- Oxygen Equipment
 - Centralized oxygen is available in each patient room, treadmill room, procedure room, and exam room.
 - Portable oxygen tanks (2) are stored in SM539.
 - Oxygen/equipment can be found in the control room in the MRI suite.
- An ambu bag with facemask is stored on each crash cart.
- There are two GE/Marquette EKG machines located in the main hallway on the south side.

APPENDIX I (H). EMERGENCY CARE POLICY

Emergency Medical Response

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PROCEDURE and RESPONSIBILITY:

• **IMPENDING CARDIAC ARREST/CARDIAC ARREST PROCEDURE:**

- o Any person discovering or suspecting a case of unresponsiveness or cardiopulmonary arrest will immediately call for help and initiate resuscitation according to American Heart Association BLS Standards. Research staff will ensure that the Emergency Resuscitation Team is summoned promptly. The AED and the emergency equipment nearest to the victim will be immediately brought to the location by the clinical staff.
- o To alert the MedStar Harbor Hospital Emergency Resuscitation Team, the switchboard operator is contacted by dialing the Code Blue button on any NIA telephone or by calling 410-350-2000. The operator is then given the location (**SM 5 or NM 5 or NIA MRI**).
- o The research staff will drop all locks at NIA doors, stairwells, and elevators by swiping their MHH badge in one of the two lock drop boxes. These are located at the nurse's station and the reception desk. The locks will automatically open with the swipe and remain open for 8 minutes before automatically resetting to a locked position.
- o Upon calling the MHH switchboard, the MHH operator will announce a system wide overhead page to alert the code team. The operator will announce the code and the location of the arrest.
 - **NOTE:** In case of a pediatric arrest (child less than twelve years of age), the operator will overhead page "PEDIATRIC ALERT TEAM" and the location of the pediatric arrest.
- o Once the operators call is heard, the MHH code personnel listed above are to report to the area indicated immediately. This assures the availability of appropriate staff trained and competent to recognize the need for and use of designated equipment in resuscitation efforts.
- o MedStar Harbor Hospital Pharmacy personnel will be informed and will respond to the area if requested.
- o Other Emergency Resuscitation Team personnel, if needed, must be STAT paged overhead by the switchboard operator (410-350-3200)
 - The Surgical, OB/GYN, and Pediatric House Physicians, and Anesthesiologist on CPR call will respond if STAT paged individually.
 - On day shift during the week, the operator will contact the Anesthesiologist on CPR call by also notifying the Operating Room (OR) desk; the Anesthesiologist will then be paged in the OR.
 - The Pediatric House Physician on CPR call is to be STAT paged in case of an arrest involving anyone younger than eighteen (18) years of age.
 - Any other personnel will be STAT paged overhead by the switchboard operator as requested.
- o Once the Emergency Resuscitation Team has been notified, the switchboard operator will call the area of arrest to ensure that all appropriate personnel have arrived.
- o The MedStar Harbor Hospital Team Leader is responsible for directing the cardiac arrest, (unless the attending physician has assumed this responsibility) and for making all pharmacological and electrical therapy decisions. He/she is responsible for the interpretation of ECG's, placement of IV access (if not already available), and for the conduct of the resuscitative effort using standard ACLS guidelines. If IV access cannot be secured, a surgical resident will be STAT paged. The attending physician will make the decision regarding termination of the resuscitative effort. In his/her absence, the Senior Medical Resident will assume this role.
- o The responding ICU/ED charge nurses or ACLS prepared nurse has the responsibility of assisting the Medical Resident, organizing and delegating tasks to other health care workers assisting with the arrest, medication administration and charting, and overall record keeping.
- o The respiratory therapist (RT) is certified to perform adult endotracheal intubation and will intubate the patient upon request of the team leader. The RT is also responsible for obtaining arterial blood gas samples.
- o Upon completion of the resuscitation:
 - The MHH Nursing Supervisor will arrange any necessary bed reallocation for admission of the successfully resuscitated subject to the ICU.

APPENDIX I (H). EMERGENCY CARE POLICY

Emergency Medical Response

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- Deceased subject's bodies will be prepared and wrapped in a shroud by the unit staff and taken to MHH morgue (NM-Ground). Shrouds are obtained from Materials Management.
- The clinical unit will function independently during the initial phase of arrest until staff from MedStar Harbor Hospital's Emergency Response Team arrives. The clinical staff roles are as follows:
 - BLS and AED procedures will be initiated.
 - Research staff will transport the monitor-defibrillator and emergency cart to the location of the incident.
 - Trained medical staff will attach the subject to the monitor-defibrillator for ECG monitoring.
 - IV access will be obtained with a large bore catheter (18g or larger whenever possible) if not already established.
 - The Clinical Nurse Manager (or designee) will act as team leader.
 - He/She will designate a staff member to be the Recorder. This person is the official timekeeper and will accurately document all data identified on the CPR record.
 - At the conclusion of the arrest, the recorder will review all data with the Team Leader. The physician will complete the "comments" section and countersign the report.
 - Additional roles and responsibilities of the research personnel include:
 - Provide emergency code drugs according to physician order.
 - Set up and assist with defibrillation.
 - Assist with intubation.
 - Monitor vital signs.
 - Provide all adjunctive emergency equipment required.
 - Ensure proper care for all other participants on the unit.
 - Remove excess personnel, furniture, and equipment from the environment.
 - Provide support to family and visitors.
 - The Clinical Nurse Manager (or designee) is responsible for ensuring all roles and responsibilities are performed.
 - Provide medical chart for review to team leader.
- Standard precautions will be utilized.
- When the Harbor Hospital Emergency Response Team arrives, they will be given a report by the team leader and will assume the primary role in managing the resuscitation efforts.
- Once stabilized, arrangements will be made to transfer the participant to the appropriate medical unit.
- Medical staff will accompany the participant during transport to the designated medical unit for completion of report.
- The team leader is responsible for notifying the attending physician of the participant's condition.

COMPLETION OF CARDIO-PULMONARY RESUSCITATION FLOW SHEET (located on a clipboard on each crash cart):

- The subject's identification, date, time, and location will be written or stamped into the flow sheet.
- The recording staff will sign his/her name in the appropriate space provided.
- The name of the physician in charge and the nurse giving medications will be printed in the appropriate spaces. (print physician's name below physician's signature in space provided).
- Recording staff will note the time of the start of cardiac arrest and call out time to arrest team every 5 minutes.
- When the patient is connected to the monitor/defibrillator, a 2-second strip will be printed and attached to a progress note to be appended to the flow sheet, and documentation of the rhythm identified will be made in the "Rhythm" column on the flow sheet.

APPENDIX I (H). EMERGENCY CARE POLICY

Emergency Medical Response

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- After each defibrillation attempt, with any rhythm change, and every 5 minutes during the arrest, the recording nurse will ask the physician to identify the rhythm for documentation on the flow sheet.
- The time and any significant actions taken for the patient will be recorded. These actions include: CPR (chest compressions, ventilation of the patient with 100% oxygen), intubation, defibrillation, insertion of IV access, and route and dosage of all medications.
- "Comments" or other documentation will be made in progress note section. When the subject recovers or expires, the end time will be noted and signatures of physician in charge and medication nurse will be obtained. The physician and medication nurse will review documentation on the flow sheet for accuracy prior to signing.
- If a second flow sheet is required for documentation, page numbers will be written in the open space in the upper right hand corner.
- Copies of the completed forms will be filed in the patient's medical record, in MHH pharmacy, and with the MHH Chief of Cardiology. The Clinical Nurse Manager or designee is responsible for delivery of the copies as well as completing the CPR Evaluation Form (attached) to the Chief of Cardiology.

REVIEW PROCESS:

- Each CPR effort will be reviewed to see if it was appropriate, timely and effective. The results will be communicated to nursing and medical staff. Process changes and education will be used to improve future CPR efforts. The review process is not a part of the medical record.
- A CPR evaluation tool will be completed by the recorder and reviewed and signed by the Team Leader.
- MHH Chief of Cardiology will review the NCR copy of the CPR record and forward his report to the respective MHH Medical Department director and MHH Director of Nursing.
 - The department directors will report findings to the Quality Control Committee and department attending's at their departmental meetings.
 - The Nursing Director will review with the NIA Clinical Care Manager and NIA research staff.

SCOPE OF PRACTICE:

These procedures apply to research staff on the Clinical Research Unit.

COMPLIANCE:

- All clinical unit staff are responsible for assisting/aiding in the emergency medical response as outlined in this policy.
- The Clinical Nurse Manager will monitor compliance and staff competency.

DOCUMENTATION:

- Documentation will be completed on the Cardiopulmonary Resuscitation Flow Sheet located on the Crash Cart.
- Documentation will be made in the participants chart as applicable.
- An evaluation of the Cardiac Arrest Process will be completed and documented on the CPR Evaluation Form.

COMMUNICATION/EDUCATION:

- The policy will be distributed for inclusion into the CRB/IRP/NIA Unit Clinical Practice Manual.

APPENDIX I (H). EMERGENCY CARE POLICY

Emergency Medical Response
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ATTACHMENTS/REFERENCES/CROSS REFERENCES:

- MHH CPR Evaluation Form
- BLS for Healthcare Providers
- 2010 AHA Guidelines for CPR & ECC
- 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.

ORIGINATORS:

Julia McKelvey, RN
Linda Zukley, PhD., RN

APPENDIX II. SUMMARIES OF FINDINGS

A. Return of Results-Summary of Independent Audit Findings and NIA comments

1. Audit Findings for Question 1: Were clinical test results available and returned to BLSA participants prior to end of the visit?

The table below shows the percentage of charts with documentation that results were available prior to the end of the visit for 2012, 2013, and totals for 2012 and 2013. Of the tests that were available prior to the end of the visit, it also displays the % of charts with documentation that results were provided to the subjects prior to discharge

<i>Test type</i>	<i>Charts with data available (%) by year</i>			<i>Of available tests, charts showing results provided before discharge (%) by year</i>		
	<i>2012</i>	<i>2013</i>	<i>Both</i>	<i>2012</i>	<i>2013</i>	<i>Both</i>
<i>Blood</i>	32	33	33	75	60	69
<i>Urine</i>	28	13	23	0	100	22
<i>ECG</i>	28	20	25	0	33	10
<i>OGTT</i>	33	40	36	0	50	21
<i>ETT</i>	19	46	29	25	0	10
<i>DEXA</i>	76	79	77	26	27	27

NIA response to the Independent Audit findings for Question 1

- NIA personnel state that they comply with their policies and the language in the protocol and consent regarding providing available clinical tests at the end of visits, but that they do not routinely document in the medical chart that they have provided these results to participants at the end of the visit. There is not a requirement that such a communication is documented in the participant charts.
- NIA personnel state that laboratory blood and urine results from Harbor Hospital are available to the study nurse practitioners (NP's) a few hours after phlebotomy. They are readily available for review with subjects at the time of discharge from the visit when subjects are scheduled for a time slot on their final day of the visit for "Review Lab Results." The NP's review available test results with participants during this time slot, though in the past this discussion was not always documented in the chart.

APPENDIX II(A). RETURN OF RESULTS – SUMMARY OF THE INDEPENDENT AUDIT FINDINGS AND NIA COMMENTS

2. Audit Finding for Question 2: Were clinical test results mailed to BLSA participants?

<i>Test type</i>	<i>Charts showing results (%) mailed to subjects</i>		
	<i>2012</i>	<i>2013</i>	<i>Both</i>
Blood	100%	100%	100%
Urine	100%	100%	100%
ECG	100%	100%	100%
OGTT	100%	100%	100%
ETT	100%	100%	100%
DEXA	100%	100%	100%

2(a) Audit Findings for Question 2 (a) were clinical test results mailed to BLSA participants within four weeks of the visit?

<i>Test type</i>	<i>Charts showing results (%) mailed to subjects within four weeks of discharge, by year</i>		
	<i>2012</i>	<i>2013</i>	<i>Both</i>
Blood	4	13	8
Urine	4	13	8
ECG	8	13	10
OGTT	4	13	8
ETT	5	15	9
DEXA	12	21	15

NIA response to Audit findings for Question 2 and 2 (a)

- OGTT tests are batched – once a week or every other week. The batching impacts the availability of test results.
- NIA is in the process of amending the BLSA protocol and consent. This information will be discussed under the “corrective action” section of this report.

3. Audit Findings for Question 3: What was the duration of time between test performance and return of abnormal results to subjects?

- Time interval between when a test was done and when abnormal results were provided to the subject: The mean/median number of days for 2012 was 46/24 days with a range of 1-

APPENDIX II(A). RETURN OF RESULTS – SUMMARY OF THE INDEPENDENT AUDIT FINDINGS AND NIA COMMENTS

150 days. The mean/median number of days for 2013 was 103/74 with a range of 30-206 days. For the total period for 2012 and 2013 the mean/median number of days was 54/28 days with a range of 1-206 days.

- Number of charts with evidence that subjects were also notified by phone or in person: 10 % of the charts audited contained evidence that the subject was contacted by phone or in person regarding test results, in addition to receiving a letter.

3(a) What was the duration of time between when abnormal test results were available to the staff and when the results were returned to subjects?

- Time interval between when test results were available to staff and when the results were provided to the subject: Not all charts contained the evidence of when the abnormal test results were available to the staff. The mean/median number of days for 2012 was 32/24 with a range of 0-102 days. The mean/median number of days for 2013 was 45/45 with a range of 16-74 days. For the total period for 2012 and 2013 the mean/median number of days was 35/24 with a range of 0-102 days.

NIA Response to audit findings, Questions 3 and 3(a)

- NIA states that if abnormal results require prompt follow up by a primary care physician, they communicate that information to a participant during a visit, or they call the person at home. These communications, however, are not always documented in the medical charts of the individuals. Consequently the first documentation in the charts is often a letter to the participant, which is sent out at a later date.
- NIA states that feedback from participants, over time, indicates that BLSA activities, involving the return of results, are congruent with participant expectations.
- NIA clarified that some of the letters sent from the staff for non-routine tests test of the 29 samples letters may have been in response to a request from a participant who called to request a specific test result weeks or months after their visit.
- NIA provided additional information explaining some of the delays in returning certain results. For example, samples for measurement of testosterone are “batched” and sent for evaluation when they have enough samples to process. The results are then returned to the Clinical unit. The return of the results from the lab depends on the batch cycle.
- Prostate specific antigen (PSA) levels performed by a research Lab at Johns Hopkins Hospital (JHH) were performed purely for research reasons and are not clinical or screening labs. The return of the results from the lab depended on the batch cycle and may be greater than 1 month. Results were reviewed for level of significance (new or unchanged) and participants notified accordingly (by phone and letter-new clinically significant; or letter - unchanged/previously reported and provided as a courtesy). No prostate cancer screening is done in BLSA—that would require imaging/and biopsy of the prostate.

APPENDIX II(A). RETURN OF RESULTS – SUMMARY OF THE INDEPENDENT AUDIT FINDINGS AND NIA COMMENTS

- During 2012 and 2013, all radiology results were reviewed by a Harbor Hospital radiologist within the first 24 hours of the scan (CT or MRI). However, the average final report time frame for non-urgent reports being received by the clinical unit staff was 7-21 days. (The radiologist called the clinical unit if he felt a finding needed immediate attention and such phone calls resulted in immediate evaluation by BLSA providers prior to getting the written report.) Upon receiving the report, the medical staff reviewed the report and would indicate to the staff if they wanted a letter sent to the participant. At the discretion of the medical staff, incidental findings are reported to the participant. Results were reviewed for level of significance (new or unchanged) and participants were notified accordingly (by phone and letter with or without discussion for new clinically significant; or by letter if results were unchanged or previously reported and provided).
- The NIH IRB currently providing oversight has approved an amendment to the protocol to clarify plans for return of test results.

APPENDIX II(B). QUALITY OF CARE – EVENTS IDENTIFIED IN THE INDEPENDENT AUDIT [SEE COMMENT ABOVE] NEEDING POSSIBLE MEDICAL INTERVENTION

B. Quality of Care – Events Identified in the Independent Audit Needing Possible Medical Intervention

Case#	Incident identified	BLSA chart review by OSC report team nurse	Medical Opinion (MDs are not affiliated with NIA)	Comments
1	A letter from the BLSA cardiologist to the subject in follow-up to the exercise tolerance test (ETT) done on 11-15-12 stated, “During the test you developed a supraventricular tachycardia at peak exercise (214 bpm, regular). In spite of this you demonstrated good exercise capacity and there were no signs of ischemia, but I would recommend that you inform your physician of these findings.” [Supraventricular tachycardia (SVT) is heart rhythm disorder resulting in an abnormally elevated heart rate]	Chart review indicated the participant was observed on a monitor until the tachycardia ceased less than 2 minutes after stopping exercise. Serial ECG’s were reviewed and demonstrated that subject went into a rapid abnormal heart rhythm at approximately 14 minutes of exercise which returned to normal by 2 minutes after exercise.	NIH Physician Board Certified in Cardiovascular Disease: Although there is no written documentation in the chart regarding how the SVT occurring during the ETT was managed, the ECG’s document that the subject continued to be monitored and had spontaneous conversion to normal sinus rhythm by 2 minutes post exercise.	Incident was appropriately managed but a progress note would have explained that the ECG’s demonstrated that the SVT returned to a normal rhythm.
2	A letter from the BLSA cardiologist to the subject in follow-up the 10-17-12, “You had an episode of asymptomatic tachycardia following cessation of testing procedure. While you were sitting, your heart rate remained elevated for several minutes in what appeared to be a largely narrow complex tachycardia (despite your basal bundle branch block). Following several vagal maneuvers, your heart rate slowed and there were no further notable incidents. Tachycardia is an abnormally elevated heart rate.”	Chart review indicated that subject was asymptomatic and was observed continuously on an ECG monitor until the tachycardia ceased. Notation on the ECG’s indicates that vagal maneuvers were employed. Progress note says, “ <i>Treadmill test completed. [BLSA cardiologist] evaluated participant during recovery phase for persistent HR at 110-115 bpm. Participant was asymptomatic with stable blood pressures of 90/62 mmHg. After approximately 23 minutes of recovery time participant’s HR returned to 80 bpm.</i> ”	NIH Physician Board Certified in Cardiovascular Disease: Review of ETT ECG’s demonstrated that the participant’s heart rate increased from approximately 83 bpm at 2 minutes in recovery to approximately 136 bpm. By 23 minutes post exercise, his heart rate had returned to 84 bpm.	Incident was appropriately managed
3	On 2-29-12, the subject had a blood test value for HbA1c (measure of blood sugar control) of 7.9 % which is higher than the normal range of 4.2-5.6.	Chart indicates a nurse practitioner note written 2-29-12 which says, “Since the participant is on insulin, this is not acceptable amount of control” and the printed lab panel results contain the written remark for the circled result of Hgb A1C Glycosylated stating, “F/U c [follow-up with] doctor”.	NIH Physician Certified in Diabetes, Metabolism & Endocrinology Giving this information to the subject (the printed lab panel) with instructions to follow-up with his/her doctor was appropriate.	Incident was managed appropriately
4	A note in the subject’s chart on 5-21-13 indicated that the subject had bradycardia (slow heart rate), and that the subject had experienced an abnormal heart rhythm at the time the treadmill test was done at the prior visit. BLSA staff decided the subject should not undergo treadmill testing at the current visit.	Review of ECG from 4-16-12: Sinus bradycardia Possible Left atrial enlargement ST abnormality, possible digitalis effect Abnormal ECG	NIH Physician Certified in Internal Medicine <i>I agree that the decision not to perform the treadmill test was appropriate.</i>	Incident was managed appropriately

APPENDIX II(C). QUALITY OF CARE – REVIEW OF ADVERSE EVENT REPORTS AND RELATED MEDICAL CHARTS SUBMITTED TO THE IRB FOR REVIEW

C. Quality of Care – Review of Adverse Event Reports and Related Medical Charts Submitted to the IRB for Review

Case#	Incident	Information provided to the IRB in the Event Report and Review of BLSA Charts by OSC Report Team Nurse	IRB determination	Comments
1	Hamstring strain during study test	<p>On 2-27-13, a 73 year old male subject developed left hamstring pain during eccentric strength testing. The staff physician examined the subject and his assessment was hamstring muscle strain. The participant was treated with bed rest for the night with standing/walking as tolerated, ibuprofen 400 mg by mouth every 6 hours as needed, and ice packs locally. He was able to ambulate with a walker without difficulty.</p> <p><u>2/28/13</u>: The subject was seen by the NP and was also seen again by the staff MD who was in agreement that the subject should not undergo treadmill testing. The participant was discharged home.</p> <p><u>3/18/13</u>: Phone call follow-up: The participant stated he was 90-95% better and was ambulating with no problems and an occasional “twinge” in his leg. The <u>3/19/13</u> cover letter accompanying the AE report also indicated the participant said that the prior injury did not limit his ability to move about or complete any daily activities. He did not feel a need to seek further medical attention and anticipated that his leg would be “100%” in the following week or two.</p>	8-7-14 NIH IRB meeting: The report was discussed and accepted by the Board. The event was determined to be an adverse event and no additional action was required.	In late 2013, the BLSA was transitioned from the MedStar IRB to the NIH IRB. BLSA staff mistakenly thought this report had been submitted to the NIH IRB at the time of continuing review in January 2014. Upon realizing it had been omitted, it was submitted for review at the 8-7-14 meeting.
2	Syncopal episode (fainting) during study test	<p>On 1/24/12, a 92 year old male was performing gait test and was instructed to “stand still” to capture a static trial. After 10 seconds he fell on to his left side. The tester checked his pulse and the participant was breathing though not responsive. A code was called and doctors and nurses responded very quickly. The cardiologist noted the participant was minimally responsive with barely audible responses to questions and was breathing normally with a palpable pulse. He had reportedly fallen without hitting his head. Within 5 minutes the participant was speaking and joking and denied pain. The participant was evaluated in ER and admitted to Harbor Hospital telemetry unit for observation.</p>	<p>The MedStar IRB reviewed this event at the time of continuing review on 12-18-12 and, since the report indicated the BLSA staff had been unable to follow-up with the subject (house phone no answers; email messages returned undeliverable; family members cell phones no responses), the IRB asked the staff to verify if contact was ever made.</p> <p>The study investigators responded that the participant contacted the coordinator on March 13, 2012. The participant stated that he was discharged from the hospital the day after the incident and that the doctors “didn’t find anything.” He stated that he is followed by his PCP.</p> <p>The IRB subsequently accepted the investigator’s response to the stipulation.</p>	

APPENDIX II(C). QUALITY OF CARE – REVIEW OF ADVERSE EVENT REPORTS AND RELATED MEDICAL CHARTS SUBMITTED TO THE IRB FOR REVIEW

Case#	Incident	Information provided to the IRB in the Event Report and Review of BLSA Charts by OSC Report Team Nurse	IRB determination	Comments
3	Knee injury during study test	<p>On 1/22/13, the BLSA staff clinician was called evaluate an 86 year old man who tripped during the 400 meter walk. The participant claimed he caught his shoe on the waxed floor, stumbled, and caught himself by extending his right arm against the wall. He did not injure any limbs and did not hit his head. The plan then was to recheck vital signs in 1 hour and escort him to dinner as a precaution. The following morning, the participant completed a DEXA [bone density] scan, body measurements and echo/carotid ultrasound. He then reported stiffness and pain in his right knee and was examined by the on-call MD who noted medial and lateral knee tenderness without joint laxity. He was subsequently evaluated in the hospital ER where X-rays demonstrated a right tibial plateau fracture which was subsequently determined by Orthopedic Service to be a “contusion to the anterior aspect of the right knee, specifically involving the distal quadriceps tendon” and not a fracture. He was also noted to have nonspecific tachycardia [increased heart rate]. The participant returned to the BLSA unit with a right leg immobilizer. The following day, the participant was admitted to the hospital so further assistance could be provided as he lived alone and was unable to care for himself (given the leg injury). He was discharged to a rehab facility on 1/28/13. The participant was called on 2-19-13 and stated that he had been at the assistive care facility for rehab for 2 weeks and had been home for the prior 2 weeks. He denied any knee discomfort from the fall. The BLSA staff subsequently removed all wax from the BLSA floor.</p>	8-7-14 NIH IRB meeting: The report was discussed and the event was determined to be a serious adverse event accepted by the Board and no additional action was required.	In late 2013, the BLSA was transitioned from the MedStar IRB to the NIH IRB. BLSA staff mistakenly thought this report had been submitted to the NIH IRB at the time of continuing review in January 2014. Upon realizing it had been omitted, it was submitted for review at the 8-7-14 meeting.

APPENDIX II(C). QUALITY OF CARE – REVIEW OF ADVERSE EVENT REPORTS AND RELATED MEDICAL CHARTS SUBMITTED TO THE IRB FOR REVIEW

Case#	Incident	Information provided to the IRB in the Event Report and Review of BLSA Charts by OSC Report Team Nurse	IRB determination	Comments
4	Neck pain after a study test	<p>The subject, an 88 year old male, performed Video-Oculography (VOG) on 2-20-13 [which requires rapid turning of the head]. The investigators asked all the appropriate questions prior to the test (i.e. prior h/o neck or spine problems, limited ability to move head from side to side, etc.) and the subject did not have any exclusion to the test. The participant later reported neck pain to the night shift in the early morning on 2/21/13. He was provided with a warm pack but declined non-steroidal anti-inflammatory medication. The participant reported neck pain rated as 6-7 on a scale of 1-10. He refused to take any medication for pain as he did not like to “mask pain.” He was told him about the importance of taking anti-inflammatory medication and one of the NP’s also talked to him about this. He continued to refuse further treatment. He had full range of motion and some discomfort at the time of discharge per the progress note. He called the next morning to report that his neck pain was 8/10, and the NP instructed him to see his PCP, and the participant said he planned to do so later that same day. The participant called on 2/27/13 on an unrelated matter and reported no problems with his neck at that time.</p>	<p>8-7-14 NIH IRB meeting: The report was discussed and accepted by the Board. The event was determined to be an adverse event and no additional action was required.</p>	<p>In late 2013, the BLSA was transitioned from the MedStar IRB to the NIH IRB. BLSA staff mistakenly thought this report had been submitted to the NIH IRB at the time of continuing review in January 2014. Upon realizing it had been omitted, it was submitted for review at the 8-7-14 meeting. Subsequent changes were made to the VOG protocol and the number of head turning maneuvers was reduced to reduce risk of participant discomfort. There have been no subsequent reports of significant neck pain.</p>

Appendix II(C). QUALITY OF CARE – REVIEW OF ADVERSE EVENT REPORTS AND RELATED MEDICAL CHARTS SUBMITTED TO THE IRB FOR REVIEW

Case#	Incident	Information provided to the IRB in the Event Report and Review of BLSA Charts by OSC Report Team Nurse	IRB determination	Comments
5	Abnormal heart rhythm and back pain during a study exercise test	<p>The subject, a 61 year old female, underwent treadmill testing on 9/27/12 and developed a wide complex tachycardia [abnormal fast heart rhythm] at peak exercise which persisted for 4 minutes and then spontaneously returned to normal sinus rhythm. She also reported that she had 1-2 minutes of back pain at maximal exertion. The on-call MD evaluated the participant and his assessment was that the episode was suggestive of stable angina, but acute coronary syndrome (ACS) needed to be ruled out. A set of cardiac enzymes was drawn and repeated in 2 hours. A repeat echo was done with no wall motion abnormalities. Both troponin and CK-MB remained low and she had no recurrence of chest pain. Later that afternoon the MD reviewed the results of the blood tests with the participant. The participant wanted to go home and was going to stay with friends, one of whom was an ER physician. She was cautioned to not disregard any symptoms of chest/back pain and call 911 if such pain occurs. She was advised to see a cardiologist as soon as possible to undergo a diagnostic work-up for coronary disease. She was given copies of her lab results and discharged from the unit. The BLSA cardiologist sent a follow-up letter with the treadmill ECG tracings to the participant and told her to review the data with her PCP for a final opinion. On 10-24-12 the participant was contacted on 10-24-12 for follow-up. She stated that she had not had any additional problems (chest pain, dizziness, shortness of breath or palpitations) since her BLSA visit. She had received her test results and was in contact with her PCP.</p>	<p>The MedStar IRB reviewed this event at the time of continuing review on 12-18-12 and the report was accepted by the Board with no additional action was required.</p>	

APPENDIX II(C). QUALITY OF CARE – REVIEW OF ADVERSE EVENT REPORTS AND RELATED MEDICAL CHARTS SUBMITTED TO THE IRB FOR REVIEW

Case#	Incident	Information provided to the IRB in the Event Report and Review of BLSA Charts by OSC Report Team Nurse	IRB determination	Comments
6	Syncopal episode (fainting) during evaluation	<p>The participant, a 94 year old female, had blood drawn (18 tubes per ER note) at 1130, completed the oral glucose tolerance test, and ate lunch. In the afternoon, the NP was performing the participant's history and physical exam and was assisting the subject to a standing position to measure orthostatic blood pressure [BP] when the participant complained of severe leg cramping and nausea and her skin was very clammy. She sat in a chair with her head against the wall and then became unresponsive to questions.</p> <p>She was evaluated by a BLSA MD and found to be hypotensive [low BP]. She was given IV fluids and became more responsive and answered questions. She was transported to the ER. The ER MD noted that the participant's BP had increased with a small bolus of normal saline and indicated the event was likely vasovagal dehydration. The participant was admitted for overnight observation. The hospital medical progress indicates the plan to "D/C home; vasovagal syncope secondary to blood draw." She was instructed to follow-up with her PCP in one week and was discharged back to the BLSA unit and then transported home. She subsequently saw her PCP and returned to the BLSA on 8/1/12 through 8/3/12 to complete her visit # 20 without difficulty.</p>	The MedStar IRB reviewed this event at the time of continuing review on 12-18-12 and the report was accepted by the Board with no additional action was required.	

APPENDIX II(C). QUALITY OF CARE – REVIEW OF ADVERSE EVENT REPORTS AND RELATED MEDICAL CHARTS SUBMITTED TO THE IRB FOR REVIEW

Case#	Incident	Information provided to the IRB in the Event Report and Review of BLSA Charts by OSC Report Team Nurse	IRB determination	Comments
7		<p>An 80 year old male with a past history of atrial fibrillation which converted without medical intervention had an exercise treadmill test (ETT) on 11/18/11. After approximately 8 minutes of exercise, the subject went into atrial fibrillation/flutter at a rate of approximately 150 bpm. The test was terminated and the participant sat down and denied chest pain but reported he felt “fatigued” and short of breath at the time the test was terminated. After 1 minute his heart rate had decreased to 110 bpm and he was taken off the monitor at 12 minutes post-test with a BP of 132/70 and still in atrial.</p> <p>The NP was notified and indicated that the participant’s discharge should be held up until he was seen by the BLSA cardiologist. The NP directed the participant to go to the ER if he experiences any dizziness, faintness or chest pain. He was discharged that afternoon, and while no repeat ECG was done prior to discharge, a progress note from the NP indicates the subject’s pulse was 80 and regular prior to discharge. The cardiologist sent a subsequent letter to the participant which explained the treadmill test results and indicated he had spoken with the participant’s PCP who said he would schedule the participant for follow-up. The cardiologist advised the participant to follow-up with his PCP to determine if further testing would be warranted and he was provided with copies of his EKG to take to his PCP.</p> <p><u>12/22/2011</u> (Per AE report) Subject returned for visit for the “unexplained anemia” study and an ECG done that day showed sinus bradycardia. The participant stated that he had not followed up with his physician as instructed but he did have an appointment with his doctor in about a month. He was given a copy of the ECG done at this visit as well as previous ECG’s and instructed to follow-up with his doctor. The participant agreed to take the records to his doctor for follow-up.</p>	<ul style="list-style-type: none"> • The MedStar IRB reviewed this event at the time of continuing review on 12-18-12 and stipulated that the PI “clarify the relationship of the SAE [serious adverse event] to the protocol and if not related indicate the cause of the event.” • The study investigators responded “The participant has a history of an irregular heart rhythm (afib) that he can go into or out of at any time for any number of unknown reasons. The fact that the rhythm occurred during the stress test is coincidental and not specifically related to the testing that occurs during their BLSA visit. The cause of the event cannot be determined.” • The IRB subsequently accepted the investigator’s response to the stipulation. 	<p>While the subject’s pulse was normal prior to discharge, it might have been helpful to repeat the ECG to confirm that he had converted to a normal rhythm prior to discharge</p>

APPENDIX III. NIA CORRECTIVE ACTION PROGRESS ON THE ELECTRONIC DATABASE

Project Action - Description	Project Activity Status
Project Requirements	
Met with Principal Investigators to understand research study, data captured and data analysis needs	Completed
Reviewed requirements for NIH system development, data security and system assessment and accreditation	Completed
Assemble infrastructure and resource requirements	Completed
Determine Continuity Of Business requirements	Completed
Establish platform testing and change control requirements	Completed
Establish Project Goals	
Reduce the number of disparate data sources into a central data warehouse repository	Under Development
Migrate and organize existing research study data into the central data warehouse repository	Phase 1 completed
Provide an intuitive secure user friendly web-based geographically independent Graphical User Interface (GUI) to the central data warehouse repository	Phase 1 completed
Incorporate data feeds from the scientific instruments and equipment to acquire testing data	Under Development
User application data entry/update auditing review and control	Completed
Separation of Participant personally identifiable information (PII) from participant research study data repository	Completed
Integrate NIH Single Sign-On (active directory) logon capabilities	Completed
Analyses Build verses Existing Product	
Determine if there are existing applications that match project requirements	Completed
Estimate cost and time to in-house build application matching project requirement	Activity Canceled
Review Return on Investment (ROI) with project stakeholder to determine path forward	Activity Canceled
Analyses Build verses Existing Product	
Stage and evaluate the list of possible existing applications against project requirements	Completed

Set up prototype for researcher evaluations	Completed
Set up engineering evaluations	Completed
Demo Prototype Evaluations with Investigators	Completed
Select Application to move forward	Completed
Build Engineering Proof Of Concept	
Stage infrastructure against project requirements	Completed
Load, assemble and validate concept application platform	Completed
Create the "Snap Shot" environment for experimentation recovery	Completed
Create study Case Report Forms (CRF) and database fields to test research data migration	Completed
Analyze database schema and application CRF mechanisms to determine migration path forward	Completed
Develop data migration Extraction, Transformation and Loading (ETL) logic for each study CRF	Completed
Run and refine test migration ETL logic	Completed
Validate data migration success against source data reposition	Completed
Set up backup and recovery for Proof Of Concept environment	Completed
Investigator and CRC User Validation of Migration	
Create user documentation for testing the Proof Of Concept	Completed
Grant access to Investigator and CRC to evaluate data migration	Completed
Establish stakeholders project update and review	Completed
Schedule hands on training classes for concept validator / testers	Completed
Resolve issues and/or concerns from validator / testers trials	Completed
Check source code into revision control system	Completed
Stage Semi-Production Quality Assurance Trials	
First round trial of entering production research data the current way and a second or mirror entry into the new semi-production central data repository	Completed
Address Tester issues, problems or concerns accordingly	Completed
Set up backup and recovery for semi-production QA environment	Completed

Contact NIA ISSO to start security assessment	Completed
Create Standup Production infrastructure	
Build out Production environment to NIA server / application specs	Completed
Stage Production environment to project requirements	Phase 1 Complete
Contact NIA ISSO to start security assessment and system accreditation review	Completed
BLSA Cytapheresis Study data Migration ETL to Production environment	Completed
Set up backup and recovery for Production environment	Completed
Engineer Continuity Of Business environment	Completed
Import Lab data via HL7 feed from Harbor Hospital	Completed
Dual system production data user entry begins	Completed
New System is in full Production - Phase 1 - BLSA Cytapheresis and Apheresis of Normal Donors	Completed
Develop Heath History Questionnaire printout from Production data system	Completed
Develop Apheresis and BLSA Cytaheresis Accrual reports	Completed
Acquire MAC 5500 HD ECG data directly from the network	Completed
Develop participant info scan-able barcoded worksheets for medical instrument staff	Completed
Created BLSA Neuro imaging Web Service and report synchronizing data sources	Completed
Created BLSA Home Visit Web Service and report synchronizing data sources	Completed
Rewrite BLSA Diagnosis database report removing SAS server dependency	Completed
Rewrite BLSA Medications database report removing SAS server dependency	Completed
Rewrite BLSA TeleForms Print removing SAS server dependency	Completed
Build all BLSA TeleForm CRFs for the new Study Data system	Under Development
Design and develop Clinical Staff Tablet real-time data entry replacing Teleforms	Pending Network & security development resources
Construct enterprise Service Data Bus used to acquire Medical and Instrument data	Pending resources
Migration of BLSA TeleForms data into new data system	Pending resources
Migration of BLSA data from Oracle Clinical database into new data system	Pending resources

Migration of BLSA pre 2000 data into the new data system	Pending resources
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This project is being developed in quantitative deliverable phases. Each phase of development allows for the release of a product replacement.

- Started in mid-2013, Phase I was completed within six months and replaced two studies in Oracle Clinical with the studies migrating to and introduction of OpenClinica.
- The larger Phase II is underway with wireless tablets replacing the Teleforms system.
- Phase III Migrating the remaining BLSA data replaces Oracle Clinical.
- Phase IV Instrument/equipment Data Aggregator (also currently underway).
- Phase V PAS Electronic Medical Records (replaces paper charts).
- Phase VI PAS – OpenClinica API integration (enterprise service bus).

As shown, each project phase will complete and roll-out to production moving us closer to our full integration goal.

APPENDIX IV. LIST OF ACRONYMS

The following is a list of acronyms included throughout the Report of Investigation.

AI	Associate Investigator
BLSA	Baltimore Longitudinal Study on Aging
CAD	Coronary Artery Disease
CFR	Code of Federal Regulations
CRC	Clinical Research Coordinator
DEXA	Dual-Energy X-ray Absorptiometry
ECG	Echocardiogram
EKG	Electrocardiogram
ETT	Exercise Treadmill Test
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
HHS	Department of Health and Human Services
IRB	Institutional Review Board
IRP	Intramural Research Program
MAI	Medical Advisory Investigator
NIH	National Institutes of Health
NIA	National Institute on Aging
NP	Nurse Practitioner
NYHA	New York Heart Association
OGTT	Oral Glucose Tolerance Test
OHSRP	Office of Human Subjects Research Protections
OMA	Office of Management Assessment
OSC	Office of Special Counsel
PI	Principal Investigator
QA/QI	Quality Assurance/Quality Improvement
SOB	Shortness of Breath
SOP	Standard Operating Procedure