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| **SPECIAL PARTICIPANT INSTITUTIONAL MEMBERSHIP APPLICATION CHECKLIST** |

**Background and purpose:** TheAMC recognizes that given the diversity of cancers in people living with HIV (PLWH), not all sites will have the breadth of patient resources or scientific expertise necessary to support their role as an AMC core site. The SP application mechanism has been developed for sites that do not have sufficient resources to support their role as an AMC core site but do have sufficient patient resources and adequate infrastructure to make a substantive contribution to selected individual AMC trials. Special participant (SP) sites are expected to contribute at least 4 participants to each AMC trial, or 5% of the total accrual goal, whichever is greater. Approved SP sites will receive trial-specific start-up funding, and per-case reimbursements. SP sites are expected to adhere to AMC policies and procedures relevant to their participation in the AMC trial.

**Study number and title of AMC trial:**

**Your complete application package must include the following documents:**

Completed Special Participant Application, including Trial-Specific Feasibility Questionnaire

Federalwide Assurance (FWA) Number and Expiration Date

Curriculum Vitae (CV) (for Principal Investigator only)

**Submit this completed checklist and the requested documentation to:**

AMC Operations and Data Management Center  
Attn: AMC Regulatory Coordinator  
The Emmes Company, LLC  
401 N. Washington Street, Suite 700  
Rockville, MD 20850

**If approved for AMC Membership, you must then provide the following documents prior to activating any studies:**

Laboratory Certifications (CLIA, CAP, or equivalent certificate)

Curriculum Vitae (CV) (required for all investigators)

Site Staff Information Form (required for all participating staff)

Signed Adherence Statement (original copy required for Principal Investigator)

**Additional documentation for site contracting will be requested by the AMC financial office following approval from the Executive Committee. The documents required to execute a site contract with the AMC will include but are not limited to: AMC Statement of Financial, Equity, and Intellectual Property Interests (for all investigators).**

**Email application requests and questions can be sent to:** [**amcpm@emmes.com**](mailto:amcpm@emmes.com)

**SPECIAL PARTICIPANT (SP) SITE DEFINITION**

AMC SP Sites are defined as those clinical sites that wish to participate in the scientific activities of the AMC and register participants to an AMC study. Sites should consist of a single institution or a consortium of institutions under the administrative authority of a single institution.

PIs and other designated investigators at AMC SP Sites may perform the following functions for the AMC:

***Sites must attain a minimum of 4 accrual credits per grant year to each AMC study in which they are participating.*** Payment for enrolled participants will be based on a per capita basis and prorated based on key milestones in the protocol, e.g., entry on the trial, completion of half of the study visits, completion of end of study visit, etc. Accrual payment and accrual credit will vary for each protocol depending on the intensity of the study as determined by the appropriate Executive Committee subcommittee. Cost reimbursement for procedures not covered by insurance will be made on a per protocol basis.

The local site PI for an AMC trial activated via the SP mechanism, and other designated investigators participating in *the* trial at the SP site, may perform the following functions for the AMC:

* Be appointed to serve as Working Group Chairs or Vice-Chairs
* Serve as Protocol Chairs/Co-Chair or protocol development team members
* Participate as a member of AMC Working Groups
* Serve as an elected member of the Concept Review Committee
* PI must attend at least one group meeting per year

Acceptance as a SP site is determined by vote of the Executive Committee (EC) and will be based on the qualifications and demonstrated capabilities of the site’s PI and the site’s experience and infrastructure for conducting clinical trials, particularly in the area of cancers in HIV, and also based on the needs of the group as determined by the EC. Acceptance as a SP is also contingent upon the availability of funding for the additional site. All newly accepted sites will be required to familiarize themselves with the policies and procedures of the AMC relevant to the specific trial and meet all performance guidelines for their site status as specified by the Site Evaluation Subcommittee.

**MEMBERSHIP APPLICATION**

Complete this application in *proposal* format where applicable to be reviewed by the AMC Executive Committee. We prefer concise and convincing replies over length. Responses that address the questions by presenting tabular information are encouraged. Do not refer the reviewer to documentation not included in this application.

**Institution Information**

City:       State:       Zip + 4:

1. Legal name of Institution:

*(Confirm the legal name with an institutional official)*

1. Legal Address of Institution:
2. Are there any additional street addresses where you would intend to conduct research and enroll participants for AMC studies:

*(Please note for CTEP requirements that* ***all*** *addresses must be listed, even if all locations are located within the same campus, institution, block, etc.)*

Yes **🡪** If “Yes” please provide all street addresses. For each address listed, please name one investigator that can be responsible for overseeing activities at this location. Any Investigator listed for oversight must have a CV submitted as part of the Membership Application Packet:

No

1. Name of Academic Affiliation, if any:
2. Name of Proposed Principal Investigator:
3. Is the Proposed Principal Investigator registered with CTEP?

*(Check one)*

Yes **🡪** If “Yes” please provide current CTEP Investigator ID:

No **🡪** If “No”, please complete the required steps necessary in order to complete an Investigator (IVR) or non-physician Investigator (NPIVR) registration. Information on completing CTEP registration requirements can be located at the following link: <https://ctep.cancer.gov/investigatorResources/default.htm>

1. CTEP Institution Code:
2. Name of Lead Clinical Research Coordinator or Research Manager:
3. Does your Institution currently partner with a local Community Advisory Board (CAB)?

*(Check one)*

Yes**🡪** If “Yes”, please provide the name of your site’s CAB representative and complete a site staff information form for the purpose of collecting contact information:

Briefly describe your site’s interactions and relationship with the CAB:

No**🡪** If “No”, please be advised that a component of AMC member site evaluation includes affiliation and communication with a CAB and that your site will need to establish a relationship with a local CAB if approved as an AMC member institution.

**IRB Information**

1. Specify IRB Name and Location:

IRB registration number:

Expiration date:

1. Does your institution have a current Federalwide Assurance (FWA)?

*(Check one)*

Yes**🡪** If “Yes”, provide your current Assurance number and its expiration date.

Assurance number:

Expiration date:

No**🡪** If “No”, please obtain a Federalwide Assurance from OHRP prior to submitting this application. *This form can be found on the OHRP website at:* [*http://www.hhs.gov/ohrp/assurances/assurances\_index.html*](http://www.hhs.gov/ohrp/assurances/assurances_index.html)

*Applications will be delayed until this information is provided. It is an NIH requirement.*

**Radiation Oncology Information**

1. Will patients entered at this facility have access to radiation therapy?  
   *(Check one)*

Yes**🡪** If “Yes”, list below the name and street address of each RT facility that will be used:

No

**Membership Proposal**

1. Describe the support resources available to assure timely compliance with AMC administrative and data requirements, e.g., oncology nurses, clinical research associates, administrative support for IRB requirements:

1. Describe your pharmacy resources and how you plan to handle investigational drugs that are part of AMC research.

1. Describe your IRB review structure (i.e. central versus local, timing of review, etc., including whether your site participates in the NCI CIRB.

1. Document adequate patient resources available for entry into clinical trials. List your annual caseload of AIDS-related malignancies or pre-malignancies relevant to the trial and cite the source of the data (tumor registry, etc.). Please include data for the past 5 years if available.

1. Indicate accrual target for this specific study.

1. Discuss any preclinical or other special resources which could benefit the AMC’s current scientific directions.

1. Describe your current cancer research programs and your HIV research programs. Describe your accruals to clinical trials for the past three years and cite accessibility rates of patients entered onto studies. Any audit reports or monitoring reviews by outside reviewers could be attached as an appendix.

1. Describe any prior or current cancer research cooperative group experience of your institution.

1. Provide any other information that you feel is important to the review of this application.

**Application submitted by/on:**

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| --- | --- | --- |
|  |  | Click or tap to enter a date. |
| Signature of Proposed PI |  | Date |

**Return Completed Application to:**

AMC Operations and Data Management Center  
Attn: AMC Regulatory Coordinator  
via email to: amcpm@emmes.com  
by standard mail to: The Emmes Company, LLC  
401 N. Washington Street, Suite 700  
Rockville, MD 20850

**ADHERENCE STATEMENT**(Version 2.0 • September 24, 2019)

The AMC is comprised of individuals whose ethical standards build the foundation for the research conducted. The highest standards of integrity are expected among all members of the Group. The AMC Data Safety and Monitoring Plan follows the NCI Data Safety Monitoring Guidelines for Clinical Trials (available on the agency’s web page [[www.nci.nih.gov](http://www.nci.nih.gov)]). To gain the utmost quality of scientific research, the AMC and its members are committed to the prevention and detection of research misconduct in clinical trials. All data are audited internally for data inconsistencies and are periodically audited by AMC monitors during external site visits. Furthermore, all members are obliged to communicate concerns about research misconduct to the Group. The primary purpose of monitoring a clinical trial is to ensure the safety and well-being of the specific patients entered on the trial. All members of the AMC are dedicated to this purpose. Submission of falsified data by member sites will not be tolerated and will be reported according to Federal guidelines.

The AMC Operations and Data Management Center (ODMC) oversees the development of all clinical protocols, including protocol activation and the production of all protocol documents, and is responsible for the data management and database activities involved in all AMC clinical protocols. Their duty is to ensure that the Group, consisting of all AMC institutions, investigators, and operations personnel are in compliance with the Office for Human Research Protections (OHRP) regulations, FDA regulatory requirements, and GCP guidelines. For the AMC to be successful in its mission, the participating sites must be committed to the consortium and must perform at an effective level in accordance to these regulations and guidelines.

By completing the registration materials to become an AMC site, you are agreeing to:

* Abide by the AMC Data and Safety Monitoring policy.
* Adhere to FDA regulatory requirements and GCP guidelines.
* Supply a copy of the Investigator’s most recent curriculum vitae to the AMC ODMC, stating whether you are board certified.
* Provide new information regarding personnel at the AMC institution to the AMC ODMC in a timely manner, including laboratory certifications, licensure of site personnel, and changes occurring to the status/role of any personnel involved in an AMC-sponsored clinical trial (via the Site Staff Information Form).
* To notify the AMC ODMC of lapses in required certifications and/or scientific misconduct.

By signing below, you are stating that you have read the AMC Data and Safety Monitoring Policy and agree to adhere to the policies outlined by the AMC to become one of its members.

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|  |  | Click or tap to enter a date. |
| Signature of Principal Investigator |  | Date |
|  |  |  |
|  |  |  |
| Printed Name of Principal Investigator |  |  |

**AMC DATA SAFETY MONITORING PLAN**(Version 9.0 • October 6, 2020)

**Introduction**

The AIDS Malignancy Consortium (AMC) Data and Safety Monitoring Plan (DSMP) outlines the measures employed by the group to monitor the safety of participants and ensure the data validity and integrity for all clinical trials it conducts. This includes methods to: 1) monitor the progress of trials and the safety of participants; 2) comply with regulatory requirements for adverse event (AE) reporting; 3) processes for trial termination or temporary suspension and major modifications; and 4) plans for ensuring data accuracy and protocol compliance. As the AMC conducts protocols of varying research phase, region of conduct (which may include trials conducted in the U.S., international sites, or both), IND sponsor (AMC investigator, CTEP, or industry-sponsored) and clinical data entry system use, this plan addresses broad processes applying to the range of trial designs and requirements. Refer to the individual AMC protocol to identify the applicable study characteristics for the relevant requirements described in this plan.

**Monitoring the Progress of Trials and the Safety of Participants**

*Routine and expedited AE reporting*

All AMC protocols that collect safety data adhere to the *National Cancer Institute (NCI), Cancer Therapy Evaluation Program (CTEP) Guidelines: Adverse Event Reporting Requirements* (https://ctep.cancer.gov/protocolDevelopment/adverse\_effects.htm), as applicable to the clinical protocol. AEs are to be recorded in the source documents, assessed by a clinical investigator for the AE reporting criteria, and promptly reported in the clinical data entry system as required by each protocol. For AMC trials conducted under a CTEP IND and AMC trials conducted within the U.S., all AEs that meet the NCI’s expedited reporting requirements are reported to the NCI via the CTEP Adverse Event Reporting System (CTEP-AERS) web application, either directly or through integration with Medidata Rave where this system is employed for AMC protocols. Use of this system ensures notification to the protocol chair and Investigational Drug Branch (IDB) at CTEP, as required for trials conducted under a CTEP IND, and a uniform expedited reporting and safety review process for AMC domestic trials. The system may also be programmed to include sponsor notification as required for trials with industry support. Alternate process for expedited AE reporting to the AMC protocol chairs and AMC Operations and Data Management Center (ODMC) within the clinical data entry system (AdvantageEDC or Advantage eClinical only) may be defined in the protocol for select trials (international studies and The ANCHOR Study).

All serious adverse events (SAEs) received by the AMC ODMC will be reviewed by the AMC medical monitor at the AMC ODMC for consideration of individual participant safety, safe trial conduct, data reporting quality for AE term selection, and appropriate application of the regulatory criteria for seriousness, expectedness, and relatedness to the investigational therapy. If alternate procedures are followed for SAE review, the process for adequate medical monitoring will be defined in the AMC protocol and the Transfer of Regulatory Obligations (TORO) with the sponsor. AMC medical monitor review includes review of the CTEP-AERS report before CTEP submission for IDB review (if applicable), or review of the SAE report in the data entry system for trials not using CTEP-AERS for expedited reporting. The IND sponsor or its designee will issue the determination as to whether the AE requires IND safety reporting to FDA as a serious and unexpected suspected adverse drug reaction (SUSAR). For protocols not conducted under an IND, in the event of disagreement between the reporting physician and the AMC medical monitor regarding the relationship of the AE to the investigational agent(s) (i.e., determination of whether the attribution is unrelated or unlikely, or possible, probable, or definite), the AMC medical monitor will provide the final determination of the relationship. IND safety reporting to FDA is performed by CTEP for trials conducted under a CTEP IND; IND safety reporting is performed by the sponsor or sponsor’s designee (AMC ODMC or other party defined in the study agreement or TORO) for IND studies sponsored by AMC investigators or industry sponsors.

*Expedited reporting to the Institutional Review Board (IRB)*

The requirements for IRB review will be identified in the protocol section on ethical and regulatory obligations. All AMC trials initiated before September 1, 2020 and all international sites for all AMC studies are subject to local IRB review; only U.S. sites are subject to the NCI requirement to use a single IRB for protocols initiated on or after September 1, 2020. For trials subject to local IRB review, the site principal investigator is responsible for ensuring that expedited AE reports for its trial participants and any unanticipated problems that affect the local institution only are submitted to the local IRB of the reporting institution, per the local IRB’s requirements for such reporting. For studies reviewed by the single IRB, the protocol chair will render a determination as to whether a SAE or other problem constitutes a trial-wide unanticipated problem that requires reporting to that RB, in accordance with its standards of procedure.

To comply with investigator notification requirements for IND studies under 21 CFR 312.32 and 312.55, IND safety reports from all trials the AMC conducts and reports from external sponsors investigating the same agents are made available to all investigators upon receipt from the sponsor or its designee, either via the password-protected section of the AMC Operations web site (AMC trials subject to local IRB review only) or the CTSU website (U.S. trials subject to single IRB review/CTEP IND agents). The site clinical investigator responsible for the applicable AMC protocol(s) is responsible for reviewing any IND safety reports received and documenting submission to the IRB of record (if required by local policy) within the timeline defined by the Clinical Trials Monitoring Branch (CTMB) audit guidelines.

*Procedures for monitoring trial progress and pharmacovigilance*

For trials using AdvantageEDC or Advantage eClinical for clinical data entry, the AMC ODMC provides on demand tabular listings of all reported AEs and SAEs on a participant level to the protocol chair and co-chair(s) for review via the password-protected section of the AMC Operations web site, [www.AIDScancer.org](http://www.AIDScancer.org). For trials using OPEN and Medidata Rave for clinical data collection, data listing will be made available using that system. Summary reports of AEs by frequency and relationship to the investigational agent(s) are provided to all AMC investigators and their staff It is the responsibility of each site to provide trial-specific AE listings to their respective IRB, if required by its policies. For blinded studies, the AE and SAE listings are reviewed and tabulated without treatment assignment.

Accrual summaries for each AMC trial are updated nightly on the password-protected section of the AMC web site. The progress of each AMC trial is reviewed regularly by the protocol chair and also by the appropriate Scientific Working Group (SWG) during scheduled conference calls (monthly SWG calls and as required, protocol-specific monitoring conference calls). Summary accrual, summary AE, and individual SAE reports are provided to SWG leadership and protocol chairs to monitor participant safety during these monthly calls.

The AMC medical monitor reviews listings of all reported AEs on a quarterly basis for assuring compliance with the protocol requirements for AE reporting and the identification of any safety concerns (individual AE or increased frequency/severity of expected AEs) for the agents under investigation. Findings from these reviews are communicated to the protocol chairs and all AMC investigators, and posted to the AMC Operations web site.

*Data and Safety Monitoring Board Review (DSMB) review*

The AMC has formed an independent Data and Safety Monitoring Board (DSMB) for AMC trials and for the ANCHOR Study. As required by NCI policy, the AMC requires DSMB review for all phase III randomized trials. All other clinical trials that the AMC initiates will be reviewed by the AMC ODMC and AMC Statistical Center during protocol development to issue a recommendation as to whether the study requires DSMB oversight, which will require the approval of the AMC Executive Committee. This determination will be based on the phase of the study, experimental design, risk posed by the investigational approach, extent of data available on the safety of an investigational agent, risk posed by the natural course of the health condition under research, and the categories of vulnerable populations involved. The involvement of a DSMB in reviewing an AMC protocol will be identified in each clinical protocol as approved by CTEP and, as applicable, required by the IRB of record.

Regarding the composition of the AMC DSMB, voting members usually include physicians, statisticians, an ethicist, and a patient advocate. All voting members have no other affiliation to the AMC and are appointed by the AMC Executive Committee with the approval of the OHAM Director. Nonvoting members are the AMC group statistician, the protocol statistician, an AMC ODMC staff member, two representatives (normally a clinician or statistician) from CTEP, and the grant program directors from the NCI Office of HIV and AIDS Malignancy (OHAM).

The DSMB reviews all applicable AMC studies in accordance with the National Cancer Institute’s Policy for Data and Safety Monitoring. Confidential reports of all trials under review are prepared by the AMC group statistician with support from the AMC ODMC. A written report containing the current status of each trial monitored, and when appropriate, any toxicity and outcome data, are sent to DSMB members by the AMC ODMC within the timelines specified by the DSMB charter. This report addresses specific toxicity issues and any other concerns about the conduct of the trial, as defined by the protocol plan for DSMB review. The report may contain information for the DSMB to render determinations for participant safety, early trial termination, results reporting, or continuing accrual or follow-up.

The results of each DSMB meeting are summarized in a formal report sent by the DSMB chair to the AMC group chair and AMC ODMC. The DSMB report contains recommendations on whether to close each study reviewed, whether to report the results, and whether to continue accrual or follow-up. A primary recommendation (e.g., continue with no change; recommended or required modification; stop) must be included in the document. The group chair or designee is then responsible for notifying the protocol chair and relevant SWG chair before the recommendations of the DSMB are carried out. In the unlikely event that the protocol chair does not concur with the DSMB, then the OHAM program directors and the NCI division director or designee must be informed of the reason for the disagreement. The protocol chair, relevant SWG chair, group chair, DSMB chair, and NCI division director or designee will be responsible for reaching a mutually acceptable decision about the study. CTEP approval of a protocol amendment will be required prior to any implementation of a change to the study.

Following a DSMB meeting, the DSMB’s recommendations are provided to all AMC investigators and staff. It is each site principal investigator’s responsibility for conveying this information to its local IRB as relevant for its protocol participation. For trials reviewed by a single IRB, the AMC ODMC will support notification to the IRB as required per its procedures.

*Cohort trial reviews not subject to DSMB review*

For phase I dose escalation trials, dose escalation (or dose de-escalation) is based on the rules in the protocol and the protocol chair, AMC medical monitor, and protocol statistician determine whether these criteria have been met based on a review of all safety data for the protocol-defined evaluation period. If applicable for phase II trials, stopping the trial for toxicity or efficacy, or suspending enrollment pending observation of responses in a multi-stage phase II trial, is based on meeting criteria stated in the protocol, and the protocol chair, AMC medical monitor, and protocol statistician determine whether these criteria have been met.

**Plans for Assuring Compliance with Requirements Regarding AE Reporting**

The protocol chair, AMC group chair, and the AMC ODMC share responsibility in assuring that participating investigators comply with applicable regulatory and protocol requirements for AE reporting. The AMC site principal investigator certifies compliance with NCI and FDA requirements for trial conduct by signing the site subaward agreement for the grant and the AMC Adherence Statement for site membership; clinical investigators also certify compliance in completing the protocol signature page for each protocol active at the site, and Form FDA-1572 for CTEP investigator registration, and also for AMC IND studies sponsored by AMC investigators or industry sponsors. Protocol compliance with AE identification, assessment and reporting requirements is assessed by the AMC ODMC using several methods: 1) programmed system checks and messages to instruct the site to complete routine and/or expedited reporting when certain criteria are reported in the clinical data entry system; 2) programmed data reports provided to the protocol chairs that identify reports requiring expedited AE reporting; 3) remote review of data entry or data reports to ensure compliance with protocol and NCI AE reporting requirements; 4) AMC medical monitor review described in the section above; and, 5) routine site audits by reviewing the site’s source documentation.

The clinical data entry systems used for AMC studies include the Oncology Patient Enrollment Network, OPEN for enrollment, and Medidata Rave for clinical data entry for enrolled participants; trials activated before September 1, 2020 or that involve only AMC international sites may be reported in AdvantageEDC/Advantage eClinical, a web-based data entry and enrollment system. These data entry systems are programmed to notify the site investigator, protocol chair, AMC medical monitor, and AMC ODMC via email in the event that a site reports an AE that meets expedited reporting criteria to NCI and/or FDA. Additional reporting conditions may be programmed depending on the sponsor reporting requirements of a given protocol (e.g., adverse events of special interest [AESI]). If the site does not follow with an expedited report, the AMC ODMC contacts sites to request compliance with reporting requirements. Additionally, the protocol chair, AMC ODMC, and the AMC medical monitor review reported AEs on a routine basis to identify AEs reported by sites that require expedited reporting. The protocol chair, AMC SWG chairs, AMC group chair, and IND sponsors have general oversight for assuring that routine and expedited adverse reporting requirements are met by the responsible parties.

For studies monitored by CTEP using the Data Mapping Utility (DMU), cumulative protocol- and patient-specific data will be submitted weekly to CTEP electronically via the DMU. For trials monitored by the NCI’s Clinical Data Update System (CDUS), AE information is transmitted electronically to NCI on a quarterly basis. For trials monitored by NCI’s Clinical Trials Monitoring Service (CTMS), AE information is transmitted electronically to NCI every two weeks.

**Plans for Assuring that any Action Resulting in a Temporary or Permanent Suspension of an NCI-Funded Clinical Trial is Reported to the NCI Grant Program Director Responsible for the Grant**

In the event that temporary or permanent suspension of a trial, or major modification to the protocol is under consideration, the protocol chair will convene the AMC ODMC, AMC Statistical Center, and SWG chair by conference call to discuss the options. Suspension actions will also be reviewed by the AMC Executive Committee for program oversight and direct communication of the action with the OHAM program directors. For phase III trials, closure decisions are typically rendered by the AMC DSMB; if the trial in question is under AMC DSMB oversight but rendered by the AMC investigators, the AMC DSMB will be notified of the suspension and the reason. For phase I and II trials, the protocol chair also has the option of asking the DSMB to review the study. The AMC ODMC will inform the CTEP Protocol Information Office (PIO), with copy to OHAM Directors, when studies are temporarily or permanently closed. In the event of major trial modification, CTEP must approve all protocol amendments prior to distributing to the AMC sites.

**Plans for Assuring Data Accuracy and Protocol Compliance**

All study data for AMC clinical trials are entered directly by AMC clinical site staff into the applicable clinical data entry system for the trial. During data entry, the system performs validation checks on many fields and performs consistency checks between select fields. Range checks are placed on each field to eliminate entry of out-of-range values. Edit check programs are run on the database on a set schedule to identify and resolve inconsistencies between forms or data collected at different points in time. Submitted data entry forms are reviewed for compliance with the protocol and data entry instructions according to the AMC ODMC’s standards for data quality processes. AMC ODMC staff routinely interacts with site staff to resolve any data submission problems.

In accordance with NCI guidelines, the AMC ODMC conducts audits at the AMC sites to evaluate compliance with regulatory issues, and to review data for specific cases by checking source documents. These reports are sent to the site principal investigator and to the NCI. In the event that major violations are identified, sites are asked to provide a written corrective and preventative action plan to correct deficiencies. If needed, a repeat site audit is conducted. In the event that a site does not correct deficiencies in a pre-determined time frame, the AMC Executive Committee has the option to implement remedial action(s) for the site. Possible actions include, but are not limited to, suspending enrollment of new patients to AMC trials until deficiencies are corrected; recommending a decrease in funding to the site; and requiring specific training for site investigators or staff members.