Policy Name: Membership Criteria	**Policy Number:** 2.1
Section: Institutions – 2	**Date Revised:** December 16, 2024

2 Institutional membership

Members of the Alliance will be institutions meeting all requirements for membership, which include accrual, data quality and timeliness, adherence to Alliance policies and procedures, and participation in Alliance scientific activities. See the Alliance Bylaws for additional details. Institutional member networks consist of a main member with or without affiliates or components.

2.1 Membership criteria

Refer to the Alliance Bylaws sections 1-4 for qualifications for prospective members.

The Membership Committee considers the following aspects in their evaluation of prospective members:

- Multi-disciplinary institutional resources for clinical trials
- Scientific interests
- Prior clinical research experience
- Level of participation in cancer research cooperative group trials
- Patient population
- Prior institutional performance evaluation metrics
- Satisfactory audit results
- Other regulatory considerations

Policy Name: Applying for Membership	**Policy Number:** 2.2
Section: Institutions – 2	**Date Revised:** December 16, 2024

2.2 Applying for membership

The Alliance reviews institutional membership applications monthly or as needed. The institutional membership application is available on the Alliance public website under the Membership tab (http://www.allianceforclinicaltrialsinoncology.org). An application will be reviewed by the Membership Committee only if the institution has an active NCI ID, FWA and is enrolled in the NCI Central IRB (CIRB). The Membership Committee evaluates the completed applications for appropriateness of facilities, institutional resources, current open or soon to be open studies and past performance in clinical research. Following a decision by the Membership Committee, applicants will be notified of approval status. If the Membership Committee approves the application, it then submits its recommendation for approval to the Board of Directors for vote Refer to the Alliance Bylaws section 5 for additional details regarding the membership evaluation procedure.

Affiliate applications can be approved by the Membership Committee without Board approval.

2.3 Membership activation

If the Board of Directors approves the Membership Committee's recommendation for approval, applicants will receive a notification of approval status with additional information. Alliance staff will activate the member on the Alliance roster in the Cancer Trials Support Unit (CTSU) Regulatory Support System (RSS) and the Clinical Trials Monitoring Branch (CTMB)-Audit Information System. Alliance staff will manage the PI and Lead CRP roles in the institution roster(s). The Lead CRP will add persons and person roles to the institution roster via the NCORP Management System (NCORP SYS) or CTSU Roster Update Management System (RUMS). Upon activation of Alliance membership, the institutional network will be granted access to the Alliance website and Alliance Web applications. Alliance members will have access to clinical trials on the CTSU menu.

2.3.1 Roster

2.3.1.1 A site must be included on the roster if it meets the following definition of engagement in research as defined by OHRP (45 CFR part 46). An institution is engaged in a particular non-exempt human subjects research project when its employees or agents for purposes of the research project obtain:

1. Data about the subjects of the research through intervention or interaction with them
2. Identifiable private information about the subjects of the research, or
3. The informed consent of the human subjects for the research

2.3.1.2 **NCI Tiers**

The Alliance adheres to the institution membership structure as mandated by the NCI. There are four types of member networks that are structured based on their funding mechanism. The member networks can have up to 3 levels (tiers) of member types:

- Tier 1 members of Lead Academic Performance Site (LAPS) and NCI Community Oncology Research Program (NCORP) represent the administrative offices of the member network. Tier 1 of the Main member networks (non-LAPS, non-NCORP) can either be an administrative office of a health system (if approved by CTSU) or an accruing institution.

- Tier 2 members include affiliates of Main members, NCORP components, and LAPS Main member, LAPS affiliates, LAPS Integrated components as identified in the LAPS grant. LAPS can also have aligned affiliates. Aligned affiliates are institutions/performance sites that are affiliated with the LAPS network but are not included in the LAPS grant. The Alliance Operations Center grant provides the per case payments for aligned affiliates.
- Tier 3 members are sub-component/sub-affiliates. A sub-component or sub-affiliate is an institution or practice site that shares the same FWA, IRB, governance structure and employees of either a Tier I or Tier II member. An example of a sub-affiliate is a physician practice that has a primary clinical site and has additional office locations where the same physicians treat patients. The primary clinic site is the parent and the additional locations are sub-affiliates.

2.3.2 Regulatory documentation

Regulatory documentation includes: documentation that the institution has a current Federalwide assurance (FWA) with the Office for Human Research Protections (OHRP); current Food and Drug Administration (FDA) 1572 forms and financial disclosure forms (FDFs) for all investigators; and certification that all investigators have received training in Human Subjects Protection (HSP) and Good Clinical Practice (GCP).

NCI policy requires all persons participating in any NCI-sponsored clinical trial to register and renew their registration annually. Registration is accomplished via the NCI Registration and Credential Repository (RCR). Additional details can be found on the NCI/CTEP website.

2.3.3 Financial documentation for institutions

Financial documentation for institutions includes a services agreement signed by the principal investigator and institutional official and W-9 form confirming correct legal name and tax-ID of the institution.

2.4 Responsibilities of a main member

The principal investigator will receive a membership letter that includes a summary of key policies and procedures, including conflict of interest, scientific misconduct, membership accrual requirements, confidentiality, audit requirements, institutional performance and publications.

The main member institution is responsible for all aspects of conducting Alliance clinical trials within its network. The main member is responsible for monitoring the conduct of a study both at the main member and all affiliate and sub-affiliate sites within its network.

Responsibilities are listed below. Affiliate and sub-affiliate institution have their own unique characteristics but each main institution must be sure that mechanisms are in place so that these responsibilities are met.

2.4.1 Communications

The main member institution must confirm that all research staff have access to the Alliance electronic distribution of information. This information includes new protocols, addenda, memos, letters, and miscellaneous items from the Alliance. The Alliance clinical research office at the institution is frequently located in the oncology or hematology department of a hospital or medical school and it is vitally important that a good communications network is established so that Alliance members from other modalities (e.g., pathology, radiation oncology, surgery, transplant, imaging, correlative sciences) receive information on a timely basis regarding Alliance protocols, meetings, and other relevant topics. It is the responsibility of the main member to assure that their network institutions have the same type of communications network established to distribute information to all disciplines within the affiliate.

2.4.2 Electronic communication

The Alliance makes use of electronic mail and the website to provide information to its members. It is the responsibility of the main member to confirm that participants are able to access this information. The Alliance requires all members to have a unique e-mail address. All network and site PIs, Co-PIs, Lead CRPs and Secondary Lead CRPs are required to receive broadcast emails.

2.4.3 Management of network data

Data forms should be submitted according to specifications in the protocol. The main member is responsible for the data quality and timeliness of their network sites.

If an affiliate institution changes main member networks, the new main member becomes responsible for the timely submission of data for all Alliance patients at the affiliate institution, including patients registered through the previous main member.

A main member institution is responsible for collection of data for patients at an affiliate institution even if that affiliate is dropped from the network. The Institutional Performance Evaluation Committee (IPEC) includes, in its evaluation of a main network, patients from dropped affiliates who are still in the evaluation window.

2.4.4 Investigational drug handling

All affiliates order drugs directly from either the NCI or from a private source as specified in the protocol. However, the main member is responsible for ensuring that all federal regulations regarding investigational drugs are adhered to by the main member and the affiliates. Annually, each Alliance investigator must sign an FDA Form 1572 stating that the investigator will adhere to the federal regulations and each main member should confirm that its investigators are in compliance and have a current FDA Form 1572 on file with the Pharmaceutical Management Branch. Each institution that orders drugs is responsible for any protocol specific requirements related to drug ordering and shipping. Refer to the Investigator's Handbook on the NCI/CTEP website for more specific investigational drug information. See also Section 12, Investigational Product.

2.4.5 Human subjects protection

The main member is responsible for ensuring that all federal regulations are adhered to regarding protection of human subjects. No patient may be entered on a study until the protocol has been reviewed and approved by the IRB of record for the institution where the patient is being treated. Alliance protocols also require a patient to sign an informed consent and the registering institution must confirm that the informed consent has been signed before the patient can be registered to the study. Protocol-specified research interventions, including interventions conducted at a facility external to the registering institution, must be covered under an IRB approval.

2.4.6 Training

The main member serves as a resource for institutional personnel to further their understanding of clinical studies and to expand and encourage participation in the studies. Training programs should be provided for all personnel. The Alliance conducts education and training sessions during the Alliance Group meetings and posts educational resources on its website and on CTSU sponsored training site CLASS. All Alliance members are encouraged to participate in these training opportunities.

2.5 Continuing Alliance membership

The Alliance Bylaws outline procedurally how Alliance membership status is evaluated. Each institutional member is re-evaluated for accrual requirements and performance in Alliance activities by the Membership Committee semi-annually. The Alliance Institutional Performance Evaluation Committee (IPEC) reviews institutional performance semi-annually. All Alliance institutions are subject to periodic audits. The Membership Committee receives reports from the IPEC, the Audit Committee, and other committee reports as needed to evaluate institutional status. Based on the information received from the various sources, the Membership Committee recommends:

- Continue institutional membership
- Suspend patient registration privileges until specific deficiency is corrected
- Change to probationary status
- Mandated change in membership type or expulsion
- Expulsion from the Alliance

Institutions must annually achieve the required number of patient registrations per year (15 for main member networks, and five for affiliates) based on a rolling three-year average.

2.5.1 Main members

Main members that do not fulfill the accrual requirement of 15 patient registrations per year, based on a three-year rolling average, for two consecutive calendar years will be subject to having their membership type changed to an affiliate in the year following the second year that the three-year rolling average was below 15 patient registrations. They would be allowed four months to find a main member with which to affiliate. It is understood that any affiliates of the main member would also need to find a new main member. If the affiliation agreements cannot be executed in this time frame, the main member (and their affiliates/sub affiliates) will be dropped from participation in Alliance.

At the spring Alliance meeting, the main members likely to be affected by this policy will receive a warning letter from the Membership Committee. Prior to the fall Alliance meeting, main members will be informed of the recommendation for a change in membership type and be given the opportunity to appeal at the fall Board of Directors meeting.

The Membership Committee may recommend exceptions to the Board of Directors for approval. If an exception is granted or an appeal is approved, the affected institution will be granted a grace period of one year. If the network does not meet

their accrual requirement at the end of the grace period, the network will be subject to having their membership type changed to an affiliate, without an opportunity to appeal. If the main member and/or their affiliates do not find another main member with which to affiliate by the end of the grace period, their Alliance membership will be terminated, as of January 1st in the year following the grace period.

2.5.2 Affiliates

Affiliates must achieve at least five patient registrations per year based on a three-year rolling average. Affiliates that do not fulfill their accrual requirement for two consecutive calendar years, will be subject to having their Alliance membership terminated, as of January 1st of the year following the three-year period. At the spring Alliance meeting, the affiliate members likely to be affected by this policy will receive a warning letter. Prior to the fall Alliance meeting, main members will be informed of the recommendation for a change in membership type and be given the opportunity to appeal at the fall Board of Directors meeting. The Membership Committee will include a list of at-risk affiliates to the Board of Directors for approval**.**

2.6 Institutional roles and responsibilities

2.6.1 Main member principal investigator

2.6.1.1 Network responsibilities

The main member principal investigator (PI) is responsible for the conduct of Alliance activities at a main member institution and for the integrity of all data submitted from the institution's affiliate network. The PI is ultimately responsible for the conduct of research and regulatory compliance at affiliate institutions. The PI is responsible for managing the funds to support the work of the Alliance at their institution, and receive other funds from the Alliance in support of Alliance activities.

The obligations of institutional membership are set forth elsewhere in these policies. It is the job of the PI to ensure that these are met by all institutions in the network or to correct deficiencies in institutional performance that are documented by Alliance mechanisms, set forth elsewhere in these policies.

Each main member institution shall also have a co-principal investigator, who shall assume responsibility in place of the principal investigator if for any reason the principal investigator is unable to perform duties required for Alliance institutional membership.

Each affiliated institution in a network must name a responsible principal investigator. This PI may be the main member PI or another investigator responsible for clinical trial conduct at the affiliate institution with oversight from the main member PI.

2.6.1.2 Institutional responsibilities

Membership in Alliance is granted to an institution not an individual. It is the institution's responsibility to ensure that the Alliance research program is vigorously and competently administered at that institution, and to recommend to the group chair and Membership Committee, as appropriate, changes in the institutional PI. Although the Membership Committee considers the qualifications of PIs when approving institutions for membership in the Alliance, and must acknowledge changes in PI when proposed by the institution, the Alliance is not involved in

the nomination or selection process which occurs at the institutional level.

The PI receives Alliance communications concerning activities at his/her institution, or appoints individuals to act on behalf of the PI for these purposes. The PIs name individuals from their institutions as authors on Alliance publications, according to Alliance guidelines on publication. The PI takes responsibility for the performance of their institution's interdisciplinary team of Alliance participants, and for the introduction of new scientists to Alliance activities. The PI ensures that specialists from relevant oncology disciplines are available within the institution to support the activities of Alliance; makes certain that the institution meets minimum accrual standards required to maintain Alliance membership; and oversees all aspects of data and specimen management for Alliance studies within the institution. The PI also ensures that Alliance studies are conducted with appropriate attention to the protection of human subjects in research, all applicable regulations and that the physicians who oversee the conduct of Alliance studies disclose potential conflicts of interest. The PI ensures that the delegation of authority and tasks is documented and that research personnel are adequately trained.

2.6.2 Affiliate member principal investigator

The principal investigator (PI) for an affiliate institution is responsible for the conduct of Alliance activities at an Alliance institution, human subjects protection and the integrity of all data submitted from the institution.

These responsibilities are similar to the responsibilities of the principal investigator at the main member institution.

2.6.3 Clinical research professionals

Clinical research professionals (CRPs) at an Alliance institution may include clinical research associates (CRAs), surgical CRAs, oncology research nurses, and others. In general, responsibilities for CRPs at an Alliance institution include the following:

- Obtain IRB approval for Alliance protocols, consent forms, annual continuing review, and any protocol amendments that require IRB approval

- Obtain patient consent (and re-consents, when appropriate) for participation in Alliance studies
- Maintain study-specific regulatory and training files
- When authorized, register consented eligible patients to Alliance studies.
- Submit accurate protocol-required data, specimens and supporting documents according to protocol requirements
- Maintain a research record of supporting documents for each Alliance patient
- Participate in Alliance audits at the institution
- Maintain a patient notification policy

2.6.3.1 **Lead CRP**

Each Alliance institutional network must designate a lead CRP to receive and distribute communications from the Group and be the primary clinical research professional contact for the network. A secondary CRP should be designated to serve as a backup to the lead CRP. Institutional responsibilities of the lead CRP vary by network.

2.6.4 Withdrawn or terminated institutions

If an institution is withdrawn from the Alliance or terminated by the Alliance, the institution will remain responsible for data submission until such time that there are no longer patients in treatment or follow up, or the patient(s) are transferred to another Alliance member. The main member remains responsible for data from withdrawn affiliates.

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Policy Name: OHRP Assurances	**Policy Number:** 2.7
Section: Institutions – 2	**Date Revised:** December 16, 2024

2.7 Office for Human Research Protections assurances

2.7.1 Assurances

The regulations require that each institution engaged in the conduct of research involving human subjects provide a written assurance of compliance that it will comply with the requirements set forth in these regulations. The document is referred to as an assurance. Each assurance sets forth the commitment of the institution to employ the basic ethical principles of the Belmont Report and to comply with the regulations. There are several kinds of assurance documents. Where an independent investigator is to provide an assurance of compliance to OHRP the document is called an agreement.

Under the Department of Health and Human Services (HHS) human subjects protection regulations at 45 C.F.R. 46.103, every institution engaged in human subjects research supported or conducted by DHHS must obtain an assurance of compliance approved by the Office for Human Research Protections (OHRP).

All institutions applying for membership in the Alliance that do not currently have an assurance must obtain a Federalwide Assurance (FWA). The institution is responsible for ensuring that all institutions and investigators engaged in its U.S. federally supported human subject research operate under an appropriate OHRP or other federally approved assurance for the protection of human subjects.

2.7.2 Reporting institutional assurance compliance

The institution's FWA must be included with the member's roster information and remain current. Alliance must have documentation that there has been prospective review, at least annual continuing review, and review of significant protocol updates.

2.8 Institutional Review Boards

Each Alliance member institution must have an approved institutional review board (IRB) under the HHS Regulations for the Protection of Human Subjects (45 CFR 46) in order to enter patients on Alliance protocols. The IRB must follow the federal regulations regarding IRBs. The IRB must also be registered with the Food and Drug Administration (FDA). If the NCI Central Institutional Review Board (CIRB) is utilized by the local IRB through facilitated review, the CIRB is considered the IRB of record. Each Alliance member institution in the United States must utilize the CIRB as the IRB of record for studies that are activated after March 1, 2019.

At the time of institutional audit, the performance of the IRB with respect to review of Alliance protocols and protocol amendments is evaluated. In addition, consent forms used within the institution are examined in order to determine whether they meet the standards required by OHRP. For institutions using CIRB, documentation of CIRB approvals including the CIRB Facilitated Review Acceptance Form will be reviewed, as well as the local informed consent form.

The Alliance may take various actions including suspension of accrual by an institution when it receives information from any source alleging that an IRB fails to comply with federal regulations. In such instances, Alliance informs the CTMB and an audit team may be assembled by staff at the CTMB, in conjunction with OHRP and the Office of Research Integrity (ORI).

2.8.1 Reporting and review requirements

As noted above, the Alliance must have documentation that there has been prospective review, at least annual continuing review and the review of significant protocol updates. IRB approval documentation is submitted to the CTSU. This information is entered into the CTSU/RSS database and is referred to when a patient is being registered. Documentation must state the type of review, list the protocol number (and if it is a review of a protocol update, it must list the protocol update number) and an IRB member or administrator must sign it. The protocol number and the update number, if applicable, must be clearly documented. Initial and continuing review documents must be submitted to the Cancer Trials Support Unit (CTSU) and Alliance staff will access the information in the CTSU database.

Annual continuing review must continue as long as patient data are being submitted. However, if no patients are currently receiving treatment and only data are being submitted, the Alliance accepts expedited review. Institutions must continue to submit studies that are not yet terminated to the IRB of record for continuing review. The Alliance audit team confirms that informed

consent was obtained after initial review and that appropriate continuing review and significant protocol updates have taken place.

2.8.2 Federal record-keeping requirements for IRBs

The institutional review board that reviewed the study must keep records and minutes of the review per the federal guidelines. Institutions retain their discretion to organize and store IRB records in any manner that is consistent with the requirements of HHS regulations at 45 CFR 46.115. Electronic storage is acceptable as long as all records are accessible for inspection and copying by the Alliance, OHRP, FDA and other regulatory agencies, as applicable.

Policy Name: Institutional Retention of Study Records	**Policy Number:** 2.9
Section: Institutions – 2	**Date Revised:** December 16, 2024

2.9 Institutional retention of study records

The following definitions apply in this policy:

- **Research records** are usually maintained by the investigator or research staff, may be separate from the hospital records, and may contain the original signed informed consent form and copies of key protocol parameters.
- **Source documents** include original patient medical records, hospital charts, lab printouts, radiological reports, correspondence, scans, X-rays, patient-completed forms, etc.
- **Flow sheets and case report forms** are created by the Alliance, completed by the institution, and submitted from the participating sites to the Alliance Statistics and Data Center.

The registering institution identified at registration, or, in the case of a transfer, the institution that accepts the responsibility for the patient, is responsible for maintaining and keeping all regulatory and original source documentation.

If the study treatment does not include investigational agents, then the research records (except for signed informed consent) and Alliance case report forms and flow sheets may be discarded after the study has been terminated. The institutional review board that reviewed the study must keep records and minutes of the review per federal guidelines and their own institutional policies.

If the study includes investigational agents, then in addition to the above requirements, records may only be destroyed two years after the New Drug Application (NDA) or Biologic License Application (BLA) has been approved or withdrawn, or the Investigation New Drug (IND) has been withdrawn/closed. The pharmacy at the institution must keep the ordering records for each agent per the federal requirements and the disposition of the investigational agent must be documented in the drug accountability form.

Source documentation, including the informed consent forms, should be retained indefinitely at the registering institution. In many instances, the signed informed consent form is included in the research records and not in the medical records. The Alliance does not collect signed informed consent forms. If the original signed informed consent form is not charted to hospital source documentation and is maintained in the research records, the signed informed consent form must be removed before the research record is destroyed and retained as would be done for source documents.

Policy Name: Non-member Collaborators	**Policy Number:** 2.10
Section: Institutions – 2	**Date Revised:** December 16, 2024

2.10 Non-member Collaborators

Non-member collaborators (NMCs) are institutions or networks that participate on Clinical Therapy Evaluation Program (CTEP) and Division of Cancer Prevention (DCP) sponsored protocols but are not full member institutions of the Alliance or a participating organization. Most non-member collaborators with the Alliance are international organizations.

In addition to their own country's regulations, International groups must comply with US federal regulations such as:

- Obtaining Federalwide assurance (FWA) with the Office for Human Research Protections (OHRP); and

- Obtaining State Department Clearance. The Alliance will submit State Department Clearance to the NCI on behalf of the international collaborator.

NCI policy also requires all persons participating in any NCI-sponsored clinical trial to register and renew their registration annually. Registration is accomplished via the NCI Registration and Credential Repository (RCR). Additional details can be found on the NCI/CTEP website.

2.11 Participation in AFT

The Alliance adheres to the institution membership structure as mandated by the NCI. The structure includes:

- Tier I members include the LAPS and NCORP administrative offices or umbrella organizations and rostered (non-LAPS, non-NCORP) main members.

- Tier II members include LAPS main members, LAPS Integrated Components (satellite sites of the LAPS main member), NCORP Affiliates, and affiliates of rostered main members

- Tier III members are sub-affiliates. The sub-affiliates are satellites of either a Tier I or Tier II institution and must be owned by the Tier I or Tier II institution and have the same FWA.

The Tier I or Tier II institution and sub-affiliates or integrated components are one entity with multiple locations and considered as a package. Enrollments by these site types are included in the Tier I or Tier II site of which they are a satellite. Accrual and participation in AFT for Tier III sites and integrated component are based on the standing of the Tier I or Tier II package.

Alliance members in good standing may participate in AFT trials. Good standing is defined as meeting the membership accrual requirements and without probation. Member networks must maintain a 3-year average of 15 membership credits and Tier II members, including NCORP affiliates must earn 5 membership credits per year based on a 3-year average before the site(s) can be considered for participation in AFT.

2.11.1 Provisionary Members

Provisionary member networks can participate in AFT trials with approval from the Chief Operating Officer once the member network has accrued 15 patients per year and prior to the acceptance as a full member.

Once the member network has been approved to participate in AFT, Tier II members within the provisionary member network can participate in AFT *if* the site earns 5 membership credits per year. Tier II sites but cannot participate in AFT until the network has been approved, even if the affiliate has met the affiliate level accrual requirement.

2.11.2 Members on Probation

AFT sanctions for members placed on probation for either IPEC or Audit will coincide with the Alliance sanctions. Specifically:

Immediate: No sanctions

1st Year Anniversary: Member will not be selected to participate in additional AFT studies.

2nd Year Anniversary: Accrual to AFT studies will be restricted until the site meets 15 NCTN membership accrual credits. The remaining accrual can be a mix of AFT and NCTN but not to exceed 50% of the average annual NCTN accrual as per Alliance policy.

3rd Year Anniversary: Membership will be terminated.

Policy Name: AFT Membership Accrual Credits	**Policy Number:** 2.12
Section: Institutions – 2	**Date Revised:** December 16, 2024

2.12 AFT Membership Accrual Credits

Enrollments to AFT studies are included in the Main member accrual totals in years in which the Main member meets or exceeds the Alliance accrual requirements via NCTN enrollments credited to the Alliance and are in good standing. AFT accrual will be included in the total accrual only in years in which the NCTN average was met.

2.12.1 Provisionary Members

AFT accrual will not be included in the total Alliance membership accrual during the provisionary period has ended. AFT accrual will be counted once the member has full status and will be retroactively applied.

2.12.2 Affiliate Accrual

Affiliate AFT accrual will be included in the affiliate and main member totals accrual only in years in which the NCTN average was met by the affiliate.