

Alliance for Clinical Trials in Oncology

Policies and Procedure

Table of Contents

1	Introduction.....	1-1
1.1	Specific aims	1-1
1.1.1	Scientific aims	1-1
1.1.2	Operational aims	1-2
1.1.3	Collaborative aims.....	1-2
1.2	Overview of program structure.....	1-4
1.2.1	Office of the Group Chair	1-6
1.2.2	Statistics and Data Management Program.....	1-7
1.2.3	Central Protocol Operations Program	1-8
1.2.4	Translational Research Program (TRP)	1-9
1.2.5	Cancer Control Program	1-10
1.2.6	American College of Surgeons Clinical Research Program.....	1-12
1.2.7	Member institutions.....	1-13
1.3	Committees.....	1-14
1.3.1	Scientific committees.....	1-14
1.3.2	Administrative committees	1-15
2	Institutional membership.....	2-1
2.1	Membership criteria	2-1
2.2	Applying for membership.....	2-2
2.3	Membership activation.....	2-3
2.3.1	Roster.....	2-3
2.3.2	NCI Tiers.....	2-3
2.3.3	Regulatory documentation.....	2-4
2.3.3	Financial documentation for institutions	2-4
2.4	Responsibilities of a main member	2-5
2.4.1	Communications.....	2-5
2.4.2	Electronic communication.....	2-5
2.4.3	Management of network data	2-6
2.4.4	Investigational drug handling	2-6
2.4.5	Human subjects protection.....	2-6
2.4.6	Training	2-7
2.5	Institutional roles and responsibilities	2-8
2.5.1	Main member principal investigator.....	2-8
2.5.1.1	Network responsibilities.....	2-8
2.5.2	Institutional responsibilities	2-8

Alliance for Clinical Trials in Oncology

Policies and Procedure

2.5.3 Affiliate member principal investigator.....	2-9
2.5.4 Clinical research professionals.....	2-9
2.5.3.1 Lead CRP.....	2-10
2.5.5 Withdrawn or terminated institutions.....	2-10
2.6 Office for Human Research Protections assurances.....	2-11
2.6.1 Assurances.....	2-11
2.6.2 Reporting institutional assurance compliance	2-11
2.7 Institutional Review Boards	2-12
2.7.1 Reporting and review requirements.....	2-12
2.7.2 Federal record-keeping requirements for IRBs	2-13
2.8 Institutional audits	2-14
2.8.1 History	2-14
2.8.2 Quality assurance.....	2-14
2.8.3 NCI audit participation	2-15
2.8.4 Overview of Alliance auditing policies and procedures.....	2-16
2.8.5 Scheduling of audits	2-16
2.8.5.1 Selection of main member and affiliate member institutions for audit	2-16
2.8.5.2 Scheduling audits for NCORPs and NCPOR components.....	2-17
2.8.5.3 Scheduling of audits for inactive sites.....	2-18
2.8.5.4 Single-Site Audit Initiative (Multi-Group Audits [MGA])	2-18
2.8.5.5 Case/protocol selection.....	2-18
2.8.5.6 Notification of audit.....	2-19
2.8.5.7 Audit team	2-19
2.8.6 Audit preparation by the institution	2-20
2.8.7 Conduct of an Alliance audit	2-21
2.8.7.1 Regulatory requirements.....	2-21
2.8.7.1.1 Critical, Major and lesser deficiencies.....	2-22
2.8.7.2 Review of IRB documentation and informed consent content	2-22
2.8.7.2.1 IRB documentation.....	2-22
2.8.7.2.2 Informed consent content (ICC).....	2-24
2.8.7.2.3 Review of the Delegation of Task Log (if applicable)	2-26
2.8.7.2.4 Assessing the IRB, ICC and DTL.....	2-26
2.8.7.3 Review of accountability of investigational agents and pharmacy operations	2-27
2.8.7.3.1 Guidelines for conducting the review	2-29
2.8.7.3.2 Assessing the accountability of investigational agents and pharmacy operations.....	2-34
2.8.7.4 Review of patient case records	2-35

Alliance for Clinical Trials in Oncology Policies and Procedure

2.8.7.4.2	Assessing the findings from patient case records	2-41
2.8.7.5	Exit interview	2-42
2.8.8	Re-audits	2-43
2.8.9	Audit review	2-43
2.8.9.1	Audit evidence of scientific misconduct	2-43
2.8.9.2	Action taken based on audit results	2-44
2.8.9.3	Report submission to CTMB	2-46
2.8.9.4	Changes to the Alliance database subsequent to audit.....	2-46
2.9.	Continuing Alliance membership.....	2-47
2.9.1.	Main members.....	2-47
2.9.2.	Affiliates	2-48
2.10	Institutional Network Performance Evaluation	2-49
2.10.1	Institutional Network Performance Evaluation Scoring System.....	2-49
2.11	Institutional probation	2-51
2.11.1	Probation based on institutional network performance evaluation.....	2-51
2.11.1.1	Criteria for warnings of substandard institutional network performance.....	2-51
2.11.1.2	Criteria for IPEC recommendation of probation of main member networks	2-51
2.11.2	Recommendation of probation for an affiliate member	2-52
2.11.3	Probationary process	2-52
2.11.4	Probation based on unacceptable audits.....	2-54
2.11.4.1	Implications of probationary status	2-54
2.12	Institutional retention of study records	2-56
2.13	Non-member Collaborators	2-57
3	Participants.....	3-1
3.1	Participant Categories.....	3-1
3.2	Membership and participant registration.....	3-3
3.2.1	Applying for membership and registration	3-3
3.2.2	Alliance person database.....	3-4
3.3	Traveling on official Alliance business.....	3-5
3.4	Individual scientific misconduct	3-6
3.4.1	Receipt of allegations of scientific misconduct	3-6
3.4.2	Processing of allegation within Alliance	3-7
3.4.3	Investigation of the allegation	3-7
3.4.4	Actions to be taken if allegation of scientific misconduct is proved	3-8
3.4.5	Publication and retractions	3-8
3.4.6	Actions against individuals.....	3-9
3.4.7	Confidentiality	3-9

Alliance for Clinical Trials in Oncology
Policies and Procedure

3.5	Conflict of interest	3-10
3.5.1	Disclosure.....	3-10
3.5.1.1	Introduction.....	3-10
3.5.1.2	Study chairs/co-chairs.....	3-10
3.5.1.3	Committee chairs/group leaders/institutional investigators/Alliance staff.....	3-11
3.5.1.4	Data and Safety Monitoring Board	3-11
3.5.2	Decisions on matters of conflict of interest.....	3-12
3.5.3	Definitions of potential conflict of interest	3-12
3.5.3.1	Professional interest.....	3-12
3.5.3.2	Proprietary interest.....	3-14
3.5.3.3	Miscellaneous and multiple financial interests	3-14
3.5.4	Management plan for conflicts of interest	3-15
3.5.5	Review of disclosure statements	3-17
3.5.6	Actions on conflict of interest	3-17
3.5.7	Penalties for failure to observe conflict of interest policies	3-17
3.5.8	Public disclosure.....	3-17
3.5.9	Record keeping	3-17
3.5.10	Reporting Financial Conflicts of Interest(FCOI).....	3-18
3.5.11	Alliance Conflict of Interest Committee.....	3-18
4	Committees.....	4-1
4.1	Committees and their function in Alliance.....	4-1
4.1.1	Disease committees.....	4-1
4.1.2	Discipline committees.....	4-1
4.1.3	Modality committees.....	4-1
4.1.4	Administrative committees.....	4-1
4.2	How to form a committee.....	4-2
4.3	Committee membership.....	4-3
4.4	Roles and responsibilities in committees.....	4-4
4.4.1	Committee chair nomination and approval.....	4-4
4.4.2	Committee chair responsibilities.....	4-4
4.4.2.1	Administration.....	4-4
4.4.2.2	Protocol development and management.....	4-5
4.4.2.3	Publications.....	4-6
4.4.2.4	Intergroup collaborations.....	4-7
4.4.2.5	Finances.....	4-7
4.4.3	Committee vice chairs.....	4-8

Alliance for Clinical Trials in Oncology
Policies and Procedure

4.4.4	Subcommittee chairs/cadre leaders.....	4-8
4.4.5	Committee members.....	4-8
4.5	Electing Executive Committee members.....	4-9
5	Meetings.....	5-1
5.1	Group Meetings.....	5-1
5.1.1	Attendance.....	5-1
5.1.2	Travel funding for group meetings.....	5-1
5.1.3	Study accrual reports and publications.....	5-2
5.2	Identification of funded travelers and expense reports.....	5-3
5.2.1	Committee member funding and roster updates.....	5-3
5.2.2	Travel funding notification.....	5-3
5.2.3	Expense reports.....	5-3
5.3	Continuing Education (CE) Credit.....	5-4
5.3.1	Continuing Education (CE) Requirements.....	5-4
5.3.2	Continuing Education (CE) Credit Certificates.....	5-4
6	Study protocol.....	6-1
6.1	Study types.....	6-1
6.1.1	Treatment studies.....	6-1
6.1.2	Non-treatment studies.....	6-1
6.1.2.1	Companion studies.....	6-1
6.2	Study participation.....	6-3
6.2.1	Limited access studies.....	6-3
6.2.2	Credentialing.....	6-3
6.2.3	Non-Alliance members.....	6-3
6.3	Study team roles and responsibilities.....	6-4
6.3.1.1	Moving study chair to a non-Alliance institution.....	6-4
6.3.1.2	Replacing study chair.....	6-4
6.3.2	Study co-chair.....	6-5
6.3.2.1	Moving study co-chair to a non-Alliance institution.....	6-5
6.3.2.2	Replacing study co-chair.....	6-5
6.3.3	Committee chair.....	6-5
6.3.4	Primary statistician.....	6-5
6.3.4.1	Primary statistician.....	6-5
6.3.4.2	Secondary statistician.....	6-6
6.3.5	Data managers.....	6-6
6.3.6	Protocol coordinator.....	6-6
6.3.7	Executive officer	6-7
6.4	Protocol development.....	6-8

Alliance for Clinical Trials in Oncology
Policies and Procedure

6.4.1	Protocol numbering.....	6-8
6.4.2	Concept.....	6-9
6.4.2.1	Concepts other than translational research and data-only requests.....	6-9
6.4.2.2	Concepts containing data-only requests.....	6-10
6.4.3	Developing the protocol.....	6-11
6.4.3.1	Communications post-SCRC and NCI concept approval.....	6-11
6.4.3.2	Protocol authoring.....	6-11
6.4.3.3	Determining the trial participant eligibility criteria.....	6-12
6.4.3.4	Inclusion of women and minorities.....	6-12
6.4.3.5	Determining the trial participant follow-up period.....	6-12
6.4.3.6	External protocol review.....	6-13
6.4.4	Developing case report forms.....	6-13
6.4.4.1	Determining data to be collected.....	6-13
6.4.4.2	Making use of standard Alliance forms.....	6-13
6.4.4.3	Using Translated Patient-Reported Questionnaires.....	6-14
6.4.4.4	Using copyrighted forms.....	6-14
6.4.4.5	Forms design.....	6-14
6.4.4.6	Forms review and approval.....	6-15
6.4.4.7	Forms revision.....	6-15
6.4.5	Participation in intergroup studies.....	6-16
6.5	Activating a study.....	6-17
6.6	Waivers	6-18
6.6.1	Eligibility waivers.....	6-18
6.6.2	Other waivers.....	6-18
6.7	Updating a study.....	6-18
6.7.1	Revisions and amendments	6-19
6.8	Suspending a study.....	6-20
6.9	Unblinding trial participants.....	6-21
6.9.1	Emergency unblinding.....	6-21
6.9.2	Protocol specific unblinding.....	6-21
6.9.3	Elective unblinding.....	6-21
6.10	Closing a study.....	6-23
6.10.1	Procedures for closing a study.....	6-23
6.10.2	Notifying patients about early closure of clinical trials.....	6-23
6.11	Release of data.....	6-24
6.11.1	Studies monitored by the DSMB.....	6-24
6.11.2	Studies not monitored by the DSMB.....	6-24

Alliance for Clinical Trials in Oncology
Policies and Procedure

6.11.2.1	Adverse event/toxicity data.....	6-24
6.11.2.2	Mature endpoint data.....	6-24
6.11.2.3	Immature endpoint data.....	6-24
6.11.2.3.1	Study is closed to accrual.....	6-24
6.11.2.3.2	Study is open to accrual.....	6-25
6.11.2.4	Appeal process.....	6-26
6.12	Completing a study.....	6-27
6.12.1	Archiving paper records.....	6-27
6.12.2	Archiving study database.....	6-27
6.12.3	Study chair access to additional data.....	6-28
6.13	Terminating a study.....	6-29
6.14	Retrospective data collection from closed or completed studies.....	6-30
7	Patient registration.....	7-1
7.1	Authorization of institutions to register patients.....	7-1
7.1.1	Limited access studies.....	7-1
7.2	Authorization of participants to register patients.....	7-2
7.3	Credentialing.....	7-3
7.4	Confirming patient eligibility.....	7-4
7.5	Procedures to register patients to Alliance studies.....	7-5
7.5.1	Pre-registration.....	7-5
7.6	Registration on weekends or after business hours.....	7-6
7.7	Registration to companion studies.....	7-7
7.8	Procedure to register patients to intergroup studies.....	7-8
8	Data management.....	8-1
8.1	Data submission.....	8-1
8.1.1	Competing Forms.....	8-1
8.1.1.1	Alliance general instructions: all forms (electronic CRFs and paper forms).....	8-1
8.1.1.2	Instructions for forms submitted during treatment and follow-up.....	8-1
8.1.2	Submission of data forms.....	8-3
8.1.2.1	General data submission instructions.....	8-3
8.1.2.2	Registered patients who never receive treatment (canceled patients).....	8-5
8.1.2.3	Transfer of patient to another institution.....	8-6
8.1.2.4	Withdrawn consent to treat or follow.....	8-7
8.1.2.5	Confirmation of lost to follow-up status.....	8-8
8.1.2.5.1	Procedure for confirming a patient is lost to follow-up.....	8-8
8.1.2.5.2	Retrospective data submission.....	8-9
8.1.3	Submission of samples, specimens, and modality materials.....	8-10

Alliance for Clinical Trials in Oncology
Policies and Procedure

8.1.4	Submission of samples for intergroup studies.....	8-10
8.2	Receipt and distribution of data forms by SDC.....	8-11
8.3	Quality assurance performed by Data Management Unit.....	8-12
8.3.1	Quality checks of on-study and eligibility data.....	8-12
8.4	Alliance case evaluation process.....	8-13
8.4.1	Objectives.....	8-13
8.4.2	Studies requiring case evaluation.....	8-13
8.4.3	Case evaluation form.....	8-14
8.4.3.1	Patient summary report.....	8-14
8.4.4	Procedures.....	8-15
9	Information systems.....	9-1
9.1	Member information.....	9-1
9.1.1	Member account request and setup.....	9-1
9.1.1.1	Individual institution members.....	9-2
9.1.2	Institution registration.....	9-2
9.1.3	Alliance application accounts.....	9-2
9.1.4	User names and passwords.....	9-3
9.1.5	Roles and permissions.....	9-3
9.1.6	System availability.....	9-3
9.1.7	User support.....	9-4
9.1.7.1	Alliance Service Center.....	9-4
9.2	SMU/ISU operations.....	9-5
9.2.1	Software development.....	9-5
9.2.2	Documentation policies.....	9-6
9.2.3	Technology selection and change management.....	9-6
9.2.4	Usage of computing resources.....	9-7
9.2.4.1	Alliance staff and members.....	9-7
9.2.4.2	Alliance staff.....	9-7
9.2.5	Security.....	9-7
9.2.5.1	Alliance Statistical Center facilities security.....	9-8
9.2.5.2	Network and server security.....	9-8
9.2.5.3	Database security.....	9-9
9.2.5.4	Application security.....	9-10
9.2.6	Backups and data retention.....	9-10
9.2.6.1	System and database backups.....	9-10
9.2.6.2	Servers.....	9-10
9.2.6.3	Retention and storage.....	9-10

Alliance for Clinical Trials in Oncology
Policies and Procedure

9.2.7	Disaster recovery.....	9-11
10	Publications Committee charter and mission guidelines.....	10-1
10.1	Data ownership.....	10-1
10.2	Committee members.....	10-2
10.3	Group Review members.....	10-3
10.4	Abstract and manuscript preparation.....	10-4
10.4.1	General principles.....	10-4
10.4.2	Cover page.....	10-4
10.4.3	Authorship.....	10-5
10.4.3.1	Publication on the primary study endpoint.....	10-5
10.4.3.2	Publication on a secondary (correlative) study.....	10-8
10.5	Abstract and manuscript timelines.....	10-11
10.5.1	Timelines for abstract and manuscript preparation.....	10-11
10.5.2	Delinquency in manuscript preparation.....	10-11
10.5.3	Timelines for review and revision of abstracts	10-12
10.5.4	Timelines for review and revision of manuscripts.....	10-12
10.5.5	Approval of abstracts and manuscripts.....	10-13
10.6	Abstract or manuscript submission to meeting or journal.....	10-14
10.7	Publication of abstract or manuscript.....	10-15
10.8	Publicizing Research Information.....	10-16
10.9	Summary of study results for the public.....	10-17
10.10	NIH Public Access Policy compliance.....	10-18
10.11	Quick view of Alliance publication timelines.....	10-20
11	Alliance Biorepositories and Biospecimen Resource (ABBR) and Translational Research.....	11-1
11.1	ABBR Infrastructure and Oversight.....	11-1
11.1.1	ABBR.....	11-1
11.1.1.1	Alliance Biorepository at the Ohio State University.....	11-1
11.1.1.2	Alliance Hematological Malignancy Biorepository (HEME).....	11-1
11.1.1.3	Alliance Lung Cancer Tissue Bank (LCTB).....	11-1
11.1.1.4	Alliance Biorepository at Washington University in St. Louis (WUSTL).....	11-1
11.1.1.5	Alliance Biorepository at Mayo Clinic (MAYO).....	11-1
11.2	Biorepository Functions.....	11-4
11.2.1	Biospecimen Collection.....	11-4
11.2.2	Storage.....	11-4
11.2.3	Processing.....	11-4
11.2.4	Quality Assurance.....	11-4
11.2.5	Regulatory Compliance.....	11-4

**Alliance for Clinical Trials in Oncology
Policies and Procedure**

11.2.6	Distribution.....	11-5
11.2.7	Direct submission.....	11-5
11.2.8	ABBR support for different study types.....	11-5
11.2.8.1	Integral Biomarker Studies.....	11-5
11.2.8.2	Integrated (Embedded) Correlative Studies.....	11-6
11.2.8.3	Biobanking for Stand-alone Secondary Correlative Studies.....	11-6
11.3	Biospecimen Collection Funding.....	11-7
11.3.1	NCI U24 Biorepository Funding.....	11-7
11.3.2	Clinical Trial Budget.....	11-7
11.3.3	BIQSFP.....	11-7
11.3.4	Non-NCI Funding	11-7
11.3.5	Research Grants (Federal and Non-federal).....	11-8
11.4	Correlative Science and Biospecimen Collection Protocol Development.....	11-9
11.5	Biospecimen Collection Policies.....	11-12
11.6	Biospecimen Processing and Storage Policies.....	11-13
11.7	Biospecimen Reporting and Tracking.....	11-14
11.8	Patient Consent, Confidentiality, and Regulatory Compliance.....	11-15
11.9	Biospecimen Pathology Review.....	11-18
11.10	Accessing Banked Biospecimens Overview.....	11-20
11.11	Stand-alone Secondary Biospecimen Use Studies.....	11-22
11.12	Data Generation, Ownership, and Publications.....	11-23
12	Investigational agents.....	12-1
12.1	Agent Accountability and Procurement.....	12-1
12.1.1	National Cancer Institute (NCI) Investigational Agents.....	12-1
12.1.2	Investigational Agents distributed by the Alliance.....	12-1
12.1.3	Shipment of investigational agents	12-2
12.1.4	Use of Investigational Agents.....	12-2
12.1.5	Storage and Accountability of Investigational Agents.....	12-3
12.1.6	Deviation from Study Protocol.....	12-3
12.2	Investigational New Drug Applications.....	12-4
12.2.1	Investigational New Drug (IND).....	12-4
12.2.1.1	IND Required.....	12-4
12.2.1.2	IND Exemption	12-4
12.2.2	Investigational Device Exemption (IDE).....	12-4
12.2.3	FDA Reporting.....	12-4
13	Industry relations.....	13-1
13.1	Industry documents.....	13-1

Alliance for Clinical Trials in Oncology
Policies and Procedure

13.1.1 Legal agreement for provision of financial support.....	13-1
13.1.2 Protocol document.....	13-2
13.1.3 Letter of understanding regarding drug or device/services provision.....	13-2
13.2 Confidential and proprietary information.....	13-3
13.3 Data ownership in the context of industry collaboration.....	13-4
13.4 Release of data.....	13-5
13.5 Indemnification.....	13-6
13.6 Intellectual property and patent rights.....	13-7
13.7 Publication of study results.....	13-8
13.8 Use of agent/devise provided by industry collaborator.....	13-9
14 Public relations.....	14-1
14.1 Authorized group representation.....	14-1
14.2 Public service.....	14-2
14.3 Dissemination of information to the general public.....	14-3
14.4 Confidentiality of patient information.....	14-5
15 Data sharing.....	15-1
15.1 Guidelines for availability of datasets.....	15-1
15.2 Request procedures.....	15-3
15.3 Regulatory considerations.....	15-4
15.4 Genomic data sharing.....	15-5
15.4.1 NIH data sharing policies.....	15-5
15.4.2 Alliance genomics studies.....	15-5
15.4.2.1 Genotype data.....	15-6
15.4.2.2 Phenotype data.....	15-6
15.4.2.3 Results databases.....	15-6
15.5 Release conditions and disclaimer.....	15-8
15.6 Appeals process.....	15-9
15.7 Fees.....	15-10
16 Study monitoring and interim analyses.....	16-1
16.1 Study monitoring by the DSMB.....	16-1
16.1.1 Studies requiring DSMB monitoring	16-1
16.1.2 Function of the DSMB.....	16-1
16.2 Overview of DSMB procedures.....	16-2
16.2.1 Confidentiality.....	16-3
16.2.2 Membership.....	16-3
16.2.3 Meetings.....	16-4
16.2.4 Recommendations.....	16-4

Alliance for Clinical Trials in Oncology
Policies and Procedure

16.2.4.1	Study change for patient safety reasons.....	16-5
16.2.4.2	Study closure due to slow accrual.....	16-5
16.2.4.3	Study change for non patient safety reasons.....	16-5
16.2.5	Study modifications.....	16-6
16.2.6	Release of results.....	16-6
16.2.7	Presentation of results by treatment group.....	16-7
16.2.8	Phase 2/3 trials.....	16-7
16.2.9	Industry-supported studies.....	16-8
16.2.10	Conflict of interest.....	16-8
16.3	Monitoring phase 1 and 2 studies.....	16-9
16.3.1	Phase 1 studies.....	16-9
16.3.2	Phase 2 studies.....	16-9