Policy Name: Agent Accountability and Procurement	**Policy Number:** 12.1
Section: Investigational Agents – 12	**Date Revised:** December 16, 2024

12 Investigational Products

In Alliance studies, any product that is provided to institutions is considered "investigational" for purposes of this policy. For investigational products used under an IND or IDE, the IND/IDE holder is either the NCI or Alliance. Investigational products may be provided by NCI/CTEP or directly by the industry partner. Investigational products may be distributed to the institutions by NCI, industry, or a third-party distributor. The Alliance generally follows PMB policies (https://ctep.cancer.gov/branches/pmb/default.htm) and CTEP investigator guidelines (https://ctep.cancer.gov/investigatorresources/investigators_handbook.htm) for all IND/IDE investigational products, irrespective of the IND/IDE holder.

12.1 Investigational Agent Accountability and Procurement

12.1.1 National Cancer Institute (NCI) Investigational Agents

Investigators must have current investigator registration documents (FDA Form 1572, Financial Disclosure Form, HSP/GCP training, biosketches, Agent Shipment Form, and CV on file with the NCI in order to receive investigational agents. These registrations must be renewed annually. Registration must be completed via the NCI Registration and Credential Repository (RCR). Additional information regarding registration types and required documentation is available at the Cancer Therapy Evaluation Program (CTEP) website (https://ctep.cancer.gov/investigatorresources/).

Investigational agents provided or distributed by the NCI are ordered through the Pharmaceutical Management Branch (PMB) Online Agent Order Processing (OAOP)-AURORA application. Access to the OAOP system requires a CTEP Identity and Access Management (IAM) account and the maintenance of an active account status and a current password. Users must complete the ID.me authentication and link the ID.me credential to their CTEP-IAM accounts.

NCI distributes investigational agents for which it holds the IND and may also distribute investigational agents, either Alliance-held IND or IND exempt, provided by industry.

12.1.2 Investigational Agents distributed by the Alliance

Instructions for ordering agents distributed by the Alliance or third-party distributors vary from study to study, and can be found in the Drug Information section of the protocol. The specific order form required to ship drug to an institution is described in the protocol.

12.1.3 Shipment of investigational agents

Multiple pharmacy addresses may be listed on the Agent Shipment Form. By providing accurate shipping information this will assure that the FDA regulations are being followed, along with decreasing investigational agent shipping delays and expense and ensures accountability.

Investigational agent(s) will only be shipped to the designated pharmacies of the investigator who is ordering the agent. Alternatively, investigators at affiliate institutions may order agents directly from PMB and not through their main member institution.

PMB policy allows centralized pharmacies to receive investigational agents for re-distribution to local satellite institutions and affiliated investigators who are registered with PMB and have designated a "central pharmacy" as their shipping address. If investigational agent is ordered through the main member institution, then the agent can be couriered to the satellite location if necessary. When agents are transported between control and satellite locations, care must be taken to ensure all appropriate storage conditions are maintained.

In the instance of investigators who staff more than 1 location, investigational agent(s) should be ordered to the central pharmacy where the patient will be receiving the investigational agent.

PMB policy also forbids secondary distribution of investigational agents to physicians who are not listed on the Delegation of Tasks Log (DTL) or transfer of investigational agents between institutions or other sites. Shipment of agents directly to patients is allowed as described by the CTEP Oral IND Agent Shipment Guideline/Alliance Oral IND Agent Shipment Guideline.

12.1.4 Use of Investigational Agents

Investigational agents must be used only in accordance with the protocol and only for patients registered on the study. Investigators must not charge for or seek reimbursement for investigational agents.

Commercial agents may not be substituted for an investigational agent nor can an investigational agent be used to "pay back" or "replace" commercial supplies.

The Alliance audits the pharmacy according to the NCI Guidelines for Auditing Clinical Trials (CTMB Guidelines) section 5.3 (https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring.htm).

Compliance with investigational drug use and accountability procedures is reviewed at the time of Alliance audits and will result in the pharmacy audit being rated as critical non-compliant, non-compliant, compliant or not reviewed. A rating of critical non-compliant will automatically result in an Unacceptable audit rating for Drug Accountability and Pharmacy. Any Unacceptable rating will require a re-audit within 12 months.

Auditors review investigational agents provided by industry partners according to the same procedures used for agents provided by NCI.

12.1.5 Storage and Accountability of Investigational Agents

A pharmacist or designated individual is responsible for investigational drug ordering, storage, dispensing and accountability. All study site personnel responsible for investigational agent(s) accountability must be listed on the Delegation of Tasks Log (DTL). The appropriate NCI Drug Accountability Record Form (DARF) should be used to record the receipt and disposition of all drugs supplied (by the NCI or pharmaceutical companies) for Alliance protocols. Specific procedures for completing DARFs and policies for storage and accountability are available on the PMB website. Guidelines are also available in the CTEP Investigator's Handbook.

12.1.6 Deviation from Study Protocol

The appropriate Alliance protocol resource must be contacted if the handling or dispensing of the investigational agent(s) deviate from the protocol instructions. The deviation must be reported to the CIRB or IRB of record, documented in a note-to-file, and retained in the records of the site.

12.2 Investigational Devices Accountability and Procurement

12.2.1 Investigational Devices Distributed by the Alliance

Instructions for ordering devices distributed by the Alliance or third-party distributors vary from study to study, and can be found in section 10.0 of the protocol. The specific order form required to ship device to an institution is described in the protocol.

12.2.2 Shipment of Investigational Devices

Investigational device(s) will only be shipped to the designated shipping addresses on the Agent Shipment Form of the investigator who is ordering the device.

Investigational device may be ordered through the main member institution, then couriered to the satellite location if necessary. When devices are transported between control and satellite locations, care must be taken to ensure all appropriate storage conditions are maintained.

In the instance of investigators who staff more than 1 location, investigational devices(s) should be ordered to the facility where the patient will be receiving the investigational device.

12.2.3 Use of Investigational Devices

Investigational devices must be used only in accordance with the protocol and only for patients registered on the study. Investigators must not charge for or seek reimbursement for investigational devices.

Commercial devices may not be substituted for an investigational device nor can an investigational device be used to "pay back" or "replace" commercial supplies.

The Alliance audits the pharmacy or designated facility according to the NCI Guidelines for Auditing Clinical Trials (CTMB Guidelines) section 5.3 (https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring.htm). Any Unacceptable rating will require a re-audit within 12 months.

12.2.4 Storage and Accountability of Investigational Devices

A pharmacist or designated individual is responsible for investigational device ordering, storage, dispensing and accountability. All study site personnel responsible for investigational device(s) accountability must be listed on the Delegation of Tasks Log (DTL). The appropriate Product Accountability Record Form should be used to record the receipt and disposition of all devices supplied for Alliance protocols. Specific procedures for completing forms and policies for storage and accountability are available in the protocol.

12.2.5 Deviation from Study Protocol

The appropriate Alliance protocol resource must be contacted if the handling or dispensing of the investigational device(s) deviate from the protocol instructions. The deviation must be reported to the CIRB or IRB of record, documented in a note-to-file, and retained in the records of the site.

12.3 Investigational New Drug Applications

Alliance reviews each study in development to determine if an IND/IDE application is required for a trial**.**

12.3.1 Investigational New Drug (IND)

12.3.1.1 IND Required

IND applications for Alliance-held INDs are submitted to the FDA by the Alliance Office. The Alliance group chair is the Responsible Investigator on all Alliance IND applications. The FDA will provide documentation of IND approval.

12.3.1.2 IND Exemption

If the FDA determines that an IND is not required, the FDA will provide documentation of IND exempt status.

12.3.2 Investigational Device Exemption (IDE)

Alliance studies may include the use of investigational devices. As in the case of INDs, the Alliance will submit an application for Investigational Device Exemption. The Alliance will also submit an IDE application or request for risk determination of investigational device, if required, for trials in which NCI holds the IND. A Center for Medicare and Medicaid Services (CMS) application will be submitted for the IDE, after study receives CIRB approval. If a study includes an investigational device, the protocol provides instructions on how to obtain the device as well as information regarding any special handling requirements that must be followed.

12.3.3 FDA Reporting

For Alliance-held INDs/IDEs, annual reports, correspondence, amendments, and all other reporting requirements are submitted by the Alliance Office. All serious adverse events (SAE) whose causality may be both related and unexpected (SUSAR) are reported to the FDA by the Alliance within the required reporting timelines.