# University of Colorado Anschutz Medical Campus Investigational New Drug (IND) / Investigational Device Exemption (IDE) Program Policy

**Version: 2**
**Date: 2/7/2025**

This document outlines the requirements and support structure for (1) CU Anschutz held INDs/IDEs and (2) CU Anschutz investigator-held IND and IDE research projects. It applies to the University of Colorado Anschutz Medical Campus (CU Anschutz) faculty who conduct research at University of Colorado Hospital (UCH Metro Denver) and Children's Hospital Colorado (CHCO).

Support will be provided by either personnel in the IND/IDE Office within the Office of the Vice Chancellor for Research (oVCR) or by the Cancer Center.

This policy has the following objectives:

1. Alleviate administrative burdens on investigators
2. Standardize processes for research with FDA-regulated products conducted at CU Anschutz
3. Ensure that FDA-regulated projects are initiated with feasible goals and appropriate resources and funding
4. Facilitate efficient startup processes
5. Minimize risk and mitigate compliance risks

## I. Definitions

**Contract Research Organization (CRO):** A third-party entity that assumes, as an independent contractor with the sponsor, one or more of the obligations of the sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials submitted to the FDA.

**Device Compassionate Use**: An expanded access authorization from FDA to use an investigational or unapproved device to treat a patient who meets the criteria for treatment under expanded access. These are sometimes referred to as "sIDEs" or "single-patient IDEs" as shorthand, although this is not technically accurate.

**eCTD:** Electronic Common Technical Document (eCTD) is the standard format for submitting applications, amendments, supplements, and reports to FDA's Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER). eCTD format is required for all submissions that are marked as "Commercial IND".

**Electronic Case Report Form (eCRF):** An electronic document which is used in a clinical trial to record the protocol and required information about each participant.

**Electronic Data Capture (EDC):** Software that stores patient data collected in clinical trials. Data is typically first recorded on paper and is then transcribed into the system and saved in an electronic case report form (eCRF).

**Emergency IND / Emergency Device Compassionate Use**: Single patient INDs or device compassionate use requests for which there is no time to obtain IRB approval prior to treatment of the patient. In these cases, the treating physician obtains FDA permission to treat by rapid means of communication, treats the patient (consenting prior to treatment if time & patient condition allows), and then notifies COMIRB within 5 working days of product use.

**eReg:** Advarra, Inc.'s electronic document filing system that saves money, improves efficiency, and enhances regulatory compliance across an organization with a 21 CFR Part 11-compliant system designed to adapt to regulatory workflows for any size research site.

**Expanded Access**: The use of a drug, biologic, or medical device that is not lawfully marketed in the U.S. (*e.g., because it is still investigational and not yet approved*) to treat patients who meet the following criteria: 1) patient has a serious or life-threatening disease or condition; 2) no comparable or satisfactory treatment alternative exists; 3) the patient cannot enroll in a clinical trial for the product; 4) the potential benefit justifies the potential risks to the patient, and 5) use of the investigational product will not interfere with the product's development or marketing approval for the treatment indication. Expanded access may refer to single-patient treatment protocols or may be approved for multiple patients. These are sometimes referred to as "compassionate use".

**Investigator (regulatory):** An individual who actually conducts a clinical investigation *i.e.*, under whose immediate direction the test article is administered or dispensed to, or used involving a subject, or, in the event an investigation is conducted by a team of individuals, is the responsible leader of the team.

**Investigational Device Exemption (IDE):** An exemption submitted for FDA authorization to allow use of an investigational device in a clinical trial to collect safety and efficacy data for a device/study that meets the definition of a Significant Risk (SR) device/study. IDEs can be thought of as the "device version" of INDs, although the requirements are somewhat different.

**Investigator Initiated Study (IIS):** a study initiated, managed and sponsored by a local investigator.

**Investigational New Drug (IND):** An application to FDA submitted by a sponsor that requests authorization from FDA to ship an investigational drug or biologic across state lines and administer it to research participants. Each submission must be identified as either a Research IND, or a Commercial IND.

**Research IND:** An IND for a product under investigation that is not intended to be commercialized at a later date. Research INDs are generally sponsored by individual investigators, academic institutions and nonprofit entities. May include INDs for emergency use or other expanded access. (21 CFR 312.310, 312.315 and 312.320). (eCTD requirements will not apply).

**Commercial IND:** An IND for a product under investigation that is intended to be commercialized at a later date. (21 CFR 312.320). (eCTD requirements will apply).

**Single-patient IND (sIND)**: An expanded access IND that allows a physician to treat a patient with an unapproved drug or biologic. Patients must meet the criteria for treatment under expanded access.

**Sponsor (regulatory)**: The sponsor is the person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual, pharmaceutical company, governmental agency, academic institution, private organization or other organization (21 CFR 312.3(b)). For administrative reasons, only one individual should be designated as sponsor.

**Sponsor's Authorized Representative (regulatory**): For a sponsor-investigator IND, the sponsor-investigator should be named and must sign form 1571. For an IND sponsored by a firm or organization, the name of the sponsor's authorizing representative should be entered, and that individual must sign the form.

**Sponsor-Investigator**: Sponsor-Investigator means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A sponsor-investigator holds the IND or IDE, whereas an investigator who is not a sponsor may conduct research under IND or IDE held by a different individual or company. A sponsor-investigator must comply with the FDA regulatory requirements for both sponsors and investigators.

## II. Introduction

Many research projects aim to assess the safety and efficacy of products that are not currently approved by the FDA for the proposed use in humans, i.e., the products are investigational. Projects with these investigational products require communication and interactions with the FDA at various time points throughout the product development process, and during the clinical trials.

Interactions with FDA require that an entity (individual, pharmaceutical or medical device company, governmental agency, academic institution, private organization, or other organization) take on the responsibilities of the regulatory Sponsor.

Being the regulatory Sponsor of projects comes with specific responsibilities outlined in the Code of Federal Regulations, 21 CFR 312 for drug products or 21 CFR 812 for medical devices.

**Products manufactured at CU Anschutz:**

The CU Anschutz community is at the cutting edge of several new therapy developments. Each of these programs likely requires significant interaction with the FDA throughout the product development process. Current programs include products manufactured by:

(1) Gates Biomanufacturing Facility (GBF), which manufactures cell therapies and protein biologics on campus.

(2) ClinImmune, which is involved in the development of cell and gene therapies.

(3) CU's Research Imaging Center (CU-RIC), which is involved in the development of radio-pharmaceutical products. These products may be manufactured by Pharmalogic, which is a non-

University entity working in collaboration with the University, per specification from CU-RIC for a specific study.

These facilities and their partnerships with the University (as well as others that may join this list) are a source of pride, prestige, and potentially direct clinical benefit to patients, and they are a key part of positioning CU Anschutz at the cutting edge and as a leader in innovative academic medical research. Because these investigational products are manufactured on campus, studies using them have an increased demand for support services to meet all regulatory requirements, present a different set of challenges, are high risk to the University, and they are more likely to be targeted for FDA audits.

**Investigational products manufactured outside of CU Anschutz:**

Many locally-led research projects aim to assess the safety and efficacy of investigational products that are manufactured by an external entity, such as a pharmaceutical company or a device manufacturer, in an unapproved indication. These studies require that an entity (individual, pharmaceutical company, governmental agency, academic institution, private organization, or other organization) take on the responsibilities of the regulatory Sponsor. CU Anschutz faculty may assume the Sponsor role, in addition to the responsibilities of a site Principal Investigator (“Investigator”) and function as a Sponsor-Investigator. Investigator-Initiated Studies (IIS) with a CU Anschutz faculty member as IND or IDE Sponsor present unique challenges and risks, and these types of studies are often selected for FDA audits. IIS are also vital to the University’s mission as a leading academic research institution and to the ability of researchers to attract federal and industry funding.

## III. Policy Objective Details

1. **Alleviate administrative burdens on investigators**

   Faculty time is costly and scarce. Minimizing time spent learning technical systems and completing administrative tasks that are more efficiently completed by a support staff specialist reduces cost and alleviates unnecessary burdens on faculty researchers. Staying current and learning newly implemented systems and platforms for submissions to the different FDA review branches are becoming increasingly burdensome to CU Anschutz investigators and their regulatory teams. Having a dedicated central team that stays current on FDA requirements for submissions will reduce time spent on these tasks for investigators and their teams.

2. **Standardize processes for research with FDA-regulated products conducted at CU Anschutz**

   Incorrect, incomplete, or poorly designed submissions to FDA increase institutional risk and potential for adverse consequences. Standardizing the format of research protocols, submissions, mandating review of all submissions through this central office, and centrally managing the submission processes will facilitate efficient submissions, compliant study initiation, study maintenance, and close out, and decrease institutional risk.

3. **Ensure that FDA-regulated projects are initiated with feasible goals, and appropriate resources and funding**

   Project feasibility review by expert staff will provide objective evaluation of the investigator's ability to properly conduct and complete the study, and minimize resources wasted on terminated studies.

4. **Facilitate efficient startup processes**

   Startup for studies under IND and/or IDE is complex. Multiple processes must occur in the correct order before a study can begin enrolling study participants. Tracking and completing the required steps may be overwhelming for Investigators, which can significantly delay the start of research, or cause important tasks to be missed entirely. Centralized project management will monitor startup progress and ensure a complete and efficient start-up.

5. **Minimize risk and mitigate compliance risks**

   The University's proud tradition of decentralization and independent thought fosters innovation and allows researchers to engage in new ideas within a flexible framework. FDA requirements can be complex and compliance necessitates clear understanding of FDA regulatory requirements and expectations. Central oversight of locally led FDA-regulated research projects reduces noncompliance risks and ensures the University's awareness of reportable events that occur in the context of these studies.

   Central management of FDA documentation by the Sponsor for studies under IND or IDE will provide further compliance safeguards.

# IV. Overview of Requirements

This document outlines the mandatory requirements managed by central administration through the CU Anschutz IND/IDE Office or the Cancer Center, with other responsibilities retained by the site Principal Investigator. The university recognizes that this hybrid model is essential to maximize compliance and efficiency, while managing risk.

Key processes, such as FDA application compilation and submissions, registrations, training, monitoring, and eCRF support will be centrally managed. Some project management services during start-up will be provided to address bottlenecks and task gaps, ensure compliance, and meet target deadlines.

The requirements to comply with the IND/IDE Sponsor regulations are the same for all studies, but the specific processes to meet these requirements will vary based on the study's risk. Wherever possible the approach will be standardized.

The IND/IDE Office or the Cancer Center staff will be responsible for all submissions to FDA. Centralized support services are mandatory for all locally led projects that require FDA oversight through an IND or IDE pathway, or any kind of communication with FDA, such as a formal IND exemption determination submission to FDA, or a Request for Designation (e.g., is it regulated as drug or device), or a risk determination (e.g., Significant Risk vs Non-significant Risk device), etc.

Support through the Cancer Center is mandatory for all oncology-based studies of Types # 3 and #4 (see descriptions in Section V of this document) that are not facilitated by the IND/IDE Office. These services were previously voluntary.

There will be a single-entry process to initiate communication about locally written projects that require communication with FDA, regardless of the product development status, type of FDA communication that will be needed, or the patient population. Triage to the appropriate entity for assistance with the compilation of the submission package, if outside the IND/IDE Office, will occur from this single point of entry.

Study feasibility assessment and study budget review will be mandatory prior to utilizing IND/IDE Office or the Cancer Center resources.

A study monitoring plan will be required, with details about the appropriate plan for the study being developed in collaboration with the IND/IDE Office's Medical Director, an independent clinical monitoring provider, or per Cancer Center policy. The site PI will remain responsible for study design, research protocol, non-clinical and clinical IND/IDE section authorship, funding procurement, day-to-day study oversight, and all investigator responsibilities per 21 CFR 312 or 812.

Study audits will be a central responsibility.

## V. Project Type Details:

The following types of projects have been identified and are categorized into Type 1-5.

The use of the IND/IDE Office or the Cancer Center, and the use of eReg and EDC will be mandatory as described in the project types below.

All CU Anschutz-held IND/IDEs and CU Anschutz investigator-held IND/IDEs will be submitted to the FDA as "Research" submissions. CU Anschutz will not submit "Commercial" IND/IDE application packages to the FDA.

1. **Investigator-Initiated Studies (even if some resources or funds are provided by an external partner) seeking to use an investigational product for which a University entity owns the manufacturing process and writes the Chemistry, Manufacturing, and Control (CMC) Information for the submission to the FDA [1]**

    1. *FDA submission support for these types of studies will be provided by the IND/IDE Office regardless of treatment indication*
    2. *CU Anschutz will serve as the Regulatory Sponsor*
    3. *Sponsor's Authorized Representative will be a Medical Director of the IND/IDE Office*
    4. *The trigger for collaboration with the IND/IDE Office will be the plan for first communication to the FDA*
    5. *All fee for service costs will be charged at the academic rate*
    6. *Formatting and validation of submissions will be done by an external vendor as applicable; the cost will be covered as outlined in the contract*
    7. *Use of eReg in standard format structure is required*
    8. *Use of 21 CFR part 11 compliant EDC system is required*
    9. *A campus leadership committee will determine if it is appropriate for CU Anschutz to hold the IND/IDE. This determination will occur early in the evaluation of any new project which may request University regulatory sponsorship and before any legal/contractual agreements are executed.*

[1] Exceptions to this are studies that involve the manufacturing of radiopharmaceuticals, where the CMC section may be written by Pharmalogic per specification from the University of Colorado Research Imaging Center (CU-RIC) for a specific study

2. **Industry funded Investigator-Initiated Studies where an external party controls the intellectual property connected to the investigational product, but the investigational product will be manufactured by a University entity**

    1. *FDA submission support for these types of studies will be provided by the IND/IDE Office regardless of treatment indication*
    2. *CU Anschutz may agree to serve as the Regulatory Sponsor under limited circumstances*
    3. *Sponsor's Authorized Representative will be a Medical Director of the IND/IDE Office*
    4. *The trigger for collaboration with the IND/IDE Office will be the start of feasibility between the manufacturing entity and the industry sponsor*
    5. *All fee for service costs will be charged at the industry rate*
    6. *There will be an IND/IDE assignment fee*
    7. *Formatting and validation of submissions will be done by an external vendor as applicable; the cost will be covered as outlined in the contract*
    8. *Use of eReg in standard format structure is required*
    9. *Use of 21 CFR part 11 compliant EDC system is required*

Consideration for CU Anschutz's involvement in these Type 1 or 2 projects will be based on an assessment of the following:

- Significant clinical interest in accessing this product for clinical use
- Clinical team has appropriate experience in clinical research
- Sufficient clinical population to recruit
- Sufficient resources to serve in this capacity without jeopardizing academic IND/IDE pipeline
- Industry funder needs academic partner as there are scientific issues to address in the development of this product – potential collaboration on IP
- Investigational product is manufactured at CU Anschutz or at the instigation of CU Anschutz researchers (e.g. Pharmalogic for radiopharmaceuticals)
- As sponsor, Industry funding partner agrees that CU Anschutz has complete control of production and clinical research – CU Anschutz provides periodic reports and notification of significant changes only
- Industry funder agrees to IND/IDE assignment fee and industry rate

If CU Anschutz has licensed intellectual property to a commercial entity for translation development of the product, then that commercial entity will be considered an external industry funder and the criteria above will apply.

Based on an evaluation of the criteria listed above, a campus leadership committee will determine if it is appropriate for CU Anschutz to hold the IND/IDE. This determination will occur early in the evaluation of any new project which may request University IND/IDE sponsorship and before any legal/contractual agreements are executed. The committee membership will include:

- Vice Chancellor for Research or delegate
- Executive Vice Chancellor for Administration and Finance
- Institutional Sponsor and Medical Director, IND/IDE office
- Legal Counsel
- Other ad hoc members as needed, including:
  - Associate Vice Chancellor for Regulatory Compliance
  - Risk Management
  - with other ad hoc members as needed and determined by the core committee.

3. **Investigator-Initiated Studies where the DRUG manufacturing process is owned and controlled by an external entity, and the Chemistry, Manufacturing, and Control (CMC) information for the submission to the FDA is either provided in its entirety or via Letter of Authorization to Cross-Reference an FDA filing or similar documentation.**

    1. *FDA submission support for these types of studies will be provided by:*
        a) *IND/IDE Office – all studies for non-oncology indications*
        b) *Cancer Center – all studies for oncology indications*
    2. *The Investigator will serve as the IND/IDE sponsor*
    3. *Sponsor's Authorized Representative will be the Investigator*
    4. *The trigger for collaboration with the IND/IDE Office will be the plan for first communication to the FDA*
    5. *All fee for service components will be charged at the academic rate*
    6. *Use of eReg in standard format structure is required*
    7. *Use of 21 CFR part 11 compliant EDC system is required**

**Exceptions may be made to this requirement based on the institutional risk determination of the study*

4. **Investigator-Initiated Studies where the DEVICE manufacturing process is owned and controlled by an external entity, and the Design and Manufacturing information for the submission to the FDA is either provided in its entirety or via Letter of Authorization to Cross-Reference an FDA filing or similar documentation.**

    1. *FDA submission support for these types of studies will be provided by:*
        a) *IND/IDE Office – all studies for non-oncology indications*
        b) *Cancer Center – All studies for oncology indications*
    2. *The Investigator will serve as the IDE sponsor*
    3. *Sponsor's Authorized Representative will be the Investigator*
    4. *The trigger for collaboration with the IND/IDE Office will be the plan for first communication to the FDA*
    5. *All fee for service components will be charged at the academic rate*
    6. *Use of eReg in standard format structure is required*
    7. *Use of 21 CFR part 11 compliant EDC system is required**

**Exceptions may be made to this requirement based on the institutional risk determination of the study*

5. **Single patient and multi-patient compassionate use requests (both drug and device requests) where local investigator is regulatory sponsor for IND/Compassionate Use**

    1. *FDA submission support for these types of studies will be provided by the IND/IDE Office regardless of treatment indication*
    2. *The Investigator will serve as the sponsor*
    3. *Sponsor's Authorized Representative will be the Investigator*
    4. *The trigger for collaboration with the IND/IDE Office will be the plan for first communication to the FDA*
    5. *All fee for service components will be charged at the academic rate*
    6. *Files will be stored in OnCore*
    7. *IRB Submissions:*
        a) *IND/IDE Office will submit to COMIRB for single patient requests in this type*
        b) *The Investigator will be responsible for all internal regulatory submissions including the HSR Portal and Full Board IRB review for multi-patient requests in this type.*
    8. *Use of eReg is preferred for these requests but use of OnCore is acceptable*

## VI. Other Projects

### Multi-Site Trials

- Central support for FDA communications and submissions will be determined on a case-by-case basis for all type 1-4 projects.
- Contracting with a CRO may be necessary to fulfill Sponsor-Investigator responsibilities, including but not limited to: creating and managing a complete Trial Master File (TMF), electronic data capture, multi-site monitoring and safety oversight.

### Guidance, Templates and Compliance Assistance ONLY Provided

- Single Patient *Emergency* INDs/IDEs
    a) The Investigator will serve as the Sponsor
    b) Sponsor's Authorized Representative will be the Investigator
    c) Due to the urgency of these requests, initial authorization and approval will remain the responsibility of treating physicians via direct communication with the appropriate FDA branch, with engagement from the IND/IDE Office prior to submission as needed
    d) After initial approvals are obtained, IND/IDE Office will provide support to ensure compliance with the required reporting requirements to FDA and IRB
        - Tracking of reporting requirements will occur in OnCore via the IND/IDE Office

- **Industry-Initiated Expanded Access** protocols that offer clinical trial participants the opportunity to continue on the investigational product beyond the clinical trial.
    - These projects will continue to be managed by the research team as the regulatory sponsor continues to be the industry entity.

- **Single Patient Expanded Access** protocols with local IND holder that offer clinical trial participants the opportunity to continue on the investigational product beyond the clinical trial.
    - These projects will continue to be managed by the research team as the regulatory sponsor continues to be the industry entity.

### Projects Not Supported by the IND/IDE Office

- Any industry-initiated projects with industry IND or IDE sponsors

## VII. Document History

| Date | Version Number | Section(s) Affected | Summary of Changes |
|---|---|---|---|
| 15-Feb-2023 | 1 | All | New document |
| 07-Feb-2025 | 2 | Overview of Requirements, Project Type Details | Update trigger for Type 2 IND/IDE Office involvement to the start of feasibility between the manufacturing entity and the industry sponsor; Add independent clinical monitoring provider as an option for development of the clinical monitoring plan; Clarify that the study's risk level may allow an exception to the Part 11 Compliant EDC requirement; Administrative edits for clarity. |

| Approval | | |
|---|---|---|
| Document Version Date: 07Feb2025 | | |
| **Name:** Dr Thomas Flaig | **Title:** Professor, Vice Chancellor | **Signature:** February 12, 2025 \| 1:12:18 PM MST DocuSigned by: E0CEF4F1B734441... |