INVESTIGATIONAL drug service (IDS)
Standard Operating Procedures

The Investigational Drug Service (IDS) strives to meet or exceed the standards of Good Clinical Practice (GCP).

1. UC Davis Health (UCDH) policy requires that distribution of all investigational drug product(s) (IP) is coordinated and supervised by IDS.

   **Shipping Address (for ALL IDS shipments):**
   UC Davis Health
   Investigational Drug Pharmacy, Rm DT0762
   2315 Stockton Blvd
   Sacramento, CA 95817

   **IDS Pharmacy Locations & Contact Information:**
   **Main IDS Pharmacy**
   UC Davis Health
   Investigational Drug Pharmacy, **Rm 1107**
   2315 Stockton Blvd
   Sacramento, CA 95817
   hs-ids@ucdavis.edu
   **Main IDS Phone:** 916-703-4093
   **Main IDS Fax:** 916-703-7048
   **IDS Cancer Center (IDSCC) Pharmacy**
   UC Davis Comprehensive Cancer Center
   Investigational Drug Pharmacy
   4501 X Street, **Rm 1008A**
   Sacramento, CA 95817
   hs-idsc@ucdavis.edu
   **IDS Cancer Center Phone:** 916-734-7176
   **IDS Cancer Center Fax:** 916-734-2260

2. **Staffing and Hours of Operation (appointments required)**
   **Main IDS Hours:** Monday – Friday 8:00 am to 4:30 pm (closed weekends and holidays)
   **IDSCC Hours:** Monday – Friday 9:00 am to 4:30 pm (closed weekends and holidays)

   A hospital pharmacist is available to address urgent IDS issues 24-hours a day by calling the 24-hour Inpatient Pharmacy at **916-703-4084**. For non-urgent issues, after regular hours of operation, an e-mail may be sent to the respective IDS Pharmacy.

   **Main IDS Staff**
   Kimmai V. Nguyen, PharmD, BCPS  rxknguyen@ucdavis.edu
   Matthew J. Serna, PharmD, BCPS  mjserna@ucdavis.edu
   Peter B. Trovitch, PharmD  ptrovitch@ucdavis.edu
   Alex Pfaller, CPhT  aappfaller@ucdavis.edu
   Jacob Monares, PhT  jmonares@ucdavis.edu
   Nadir Sarwary, PhT  nsarwary@ucdavis.edu

   **IDS Cancer Center (IDSCC) Staff**
   Joyce Lee, PharmD, BCOP, BCPS  jsylee@ucdavis.edu
   Jennifer Murphy, PharmD, BCOP, BCPS  jemurphy@ucdavis.edu
   Jessica Turner, CPhT  jyturner@ucdavis.edu
3. **Security**
   The Main IDS Pharmacy is located inside the main hospital at UC Davis Health. The IDSCC Pharmacy is located inside the UC Davis Comprehensive Cancer Center. Both IDS pharmacies are in safe and secure locations, behind double locked doors, and made accessible only to pharmacy personnel via badge scanner and passcode. Visitors are permitted to enter the IDS pharmacy areas only when escorted by IDS or other pharmacy personnel.

4. **Technology Protection**
   IDS complies with Federal Regulations (FDA 21 CFR Part 11) that govern the use of computerized systems (e.g. IXRS). PIN numbers, access codes, etc. are not shared without written approval from the sponsor.

5. **IP Storage**
   IP is appropriately stored in accordance with Good Clinical Practice Guidelines and the study protocol. IP is stored separately by protocol and is not co-mingled with non-IP. Returns are isolated.

6. **Temperature Management**
   IDS adheres to institutional policies regarding medication storage and temperature control. IDS medication appliances are maintained in accordance with UCDH Patient Care Standard IV-57: Refrigerator/Freezer Requirements for Medications, Patient Nutrition and Laboratory Specimens and Controls.

   Appliances used for the storage of IP in pharmacy service locations are continuously monitored by Aeroscout®, a remote temperature monitoring device. The appliances are equipped with calibrated monitoring tags that are replaced as indicated. The internal temperature of the appliance is electronically recorded approximately every 20 minutes.

   If a temperature excursion occurs in which the appliance temperature records outside of the acceptable range, an alert is sent to the Temperature Excursion Response Pager. The alert is sent to IDS during operational hours. After IDS hours, the alert is received by the 24-hour Inpatient Pharmacy. Aeroscout®-generated alerts ensure that essential pharmacy personnel receive immediate notification for management of the temperature excursion (e.g. close refrigerator door, relocate IP).

   The Metasys® system serves as the back-up appliance monitoring system and is managed 24 hours a day by the Plant Operations and Maintenance (PO&M) department. Metasys® temperature probes are calibrated as indicated. In the event of an Aeroscout® system failure or positional misreading, IDS will utilize Metasys® data to verify the internal temperature of the appliance.

   The ambient temperature in all IDS and pharmacy drug storage areas is monitored centrally and maintained by PO&M in accordance with UCDH Policy 1689: Temperature, Humidity and Air Exchange Monitoring and Control. Records of automated temperature logs are maintained by the PO&M department.

   Electronic temperature records are maintained for all areas where IP is stored. Under no condition will sponsor temperature logs be utilized for temperature record keeping. Electronic temperature records and calibration certificates can be made available upon request via email in conjunction with monitoring visits (with a minimum allowance of 5 business days for distribution).

   Corrective action is taken and documented for any temperature excursion. Sponsors are notified according to protocol instructions and all IP will be quarantined until approved for use.

   **Acceptable temperature ranges:**
   - Room temperature: 68 to 75°F
   - Refrigerator: 36 to 46°F
   - -20°C Freezer: 5 to -13°F
   - -80°C Freezer: -130 to -94°F

   For more information regarding temperature management, please refer to PCS Policy IV-57.
7. **Power Supply**

The primary power source for the UCDH campus is the UCDH PO&M power plant. In the event of power failure, UCDH has two backup power sources. If UCDH PO&M fails, power is first pulled from SMUD (Sacramento Municipal Utility District). If SMUD is unable to supply power, UCDH has generators to power all critical systems. All the refrigerators and freezers are part of the critical systems.

8. **Receiving and Transport**

IP shall only be shipped to Pharmacy Stores (Room DT0762). Packages are received by Pharmacy Stores and transported to the Main IDS Pharmacy (the “control” pharmacy) for unpacking, integrity assessment, and addition to inventory. Movement of IP is documented from time of receipt by Pharmacy Stores (Room DT0762) to dispensation for patient use. Hazardous IP will be handled in accordance with institutional and department policies.

IP may be transported to other pharmacy service locations (referred to as “satellites”) for storage, preparation and/or dispensation. Appropriate records of the transfer are kept by both the control and satellite locations (consistent with NIH guidelines).

Ambient IP is transported at ambient temperature. Refrigerated/frozen IP is transported in an insulated cooler with ice packs or dry ice. IDS provides the following equipment for inter-pharmacy transfer: insulated containers, ice packs, dry ice. IDS requests that sponsors supply any additional necessary equipment required for transport.

9. **Dispensing and Labeling**

IP dispensing meets all safety requirements required by pharmacy law for non-investigational drugs. Each dispensed IP must be labeled with a standard patient-specific, institution-specific prescription label consistent with local, state, and federal law. Additional labels beyond those generated by the institution, including sponsor-provided labels, will not be affixed to IP preparations.

IP may be dispensed directly from IDS to the investigator, study/licensed personnel or to the participant. IP may also be dispensed from one of the inpatient or outpatient pharmacies or pharmacy service locations. IP not dispensed directly to the patient or licensed personnel will be dispensed in a sealed container. IDS will work with the study staff to develop a safe and efficient dispensing plan in accordance with institutional policies, applicable regulations, and best practice guidelines (e.g. Joint Commission, ASHP Guidelines, HOPA Best Practice, etc.). Once dispensed from a pharmacy service location, the next party in the chain of custody is responsible for transporting the IP under proper conditions.

If consistent with institutional licensing, the investigator may request for IDS to send prescriptions by FedEx, UPS, USPS, or the courier service so long as this is permitted per protocol and documentation of sponsor approval is provided. Costs for shipping and/or courier services will be charged to the study account or patient.

**Standard expected preparation and dispensation times for IP are as follows:**

<table>
<thead>
<tr>
<th>Type of Preparation</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral preparations (simple)</td>
<td>1 hour</td>
</tr>
<tr>
<td>Oral preparations (complex and compounded)</td>
<td>2 hours</td>
</tr>
<tr>
<td>Parenteral preparations (biohazard and injectable)</td>
<td>2 hours</td>
</tr>
</tbody>
</table>

IP requiring compounding prior to administration will be prepared in the manner consistent with current institutional standards (i.e. site-specific drug preparation records).

Randomization or retrieval of IP assignment (e.g. IXRS) will not occur outside of IDS operational hours. The PI will need to determine an unblinded coordinator in such instances or the sponsor will have to provide an alternate assignment method (e.g. advance assignment when applicable or faxed assignment to Inpatient Pharmacy).
10. IP Accountability and Documentation

The inventory record shall document each transaction involving receipt, transfer, return, dispensation and destruction of IP inventory. The assignment of an IP unit in the electronic inventory system will serve as documentation of use and destruction of any residual IP. IDS will maintain IP accountability records electronically using a HIPAA and 21 CFR Part 11 compliant computerized inventory management system. nCoup IDS is considered the sole source for documentation for IP accountability and meets all applicable federal regulations and Good Clinical Practice (GCP) guidelines.

Use of sponsor-provided inventory records, a separate sponsor IP accountability system, central database, or file hosting service is considered duplicative and/or secondary documentation, and as such, is not accommodated. IDS considers IXRS to be an electronic accountability system and transactions beyond IP receipt will not be documented by IDS staff into IXRS. Any transcription of IP accountability and/or uploading into a secondary system is the sole responsibility of the sponsor.

Sponsor-provided IP preparation worksheets are not filled out by IDS staff unless standardized department records and/or policy do not encompass the requirements by the sponsor. Necessity of sponsor-provided worksheets will be determined by an IDS pharmacist. Institutional IDS documents may be provided for sponsor review only.

IDS will not maintain IP accountability records for medications that are considered standard of care (e.g. medications that are not provided or paid for by the sponsor and administered under a study protocol). Should locally-sourced commercial drugs be used in study participants, details about the drugs, including but not limited to the manufacturer, lot number, and expiration date will not be proactively recorded and retained by IDS. Institutional policy and regulatory requirements mandate the recording of manufacturer, lot number, and expiration date during dispensing of compounded medications. This information may be made available upon written request by sponsor and only in the event of drug recall, regulatory agency inspection, and adverse event reporting.

11. Inventory

Inventory is maintained perpetually in the electronic inventory system (nCoup IDS) and a physical inventory is conducted at least quarterly (with monthly expiration date reviews) to ensure accurate inventory and dispensing records are kept for all IP.

12. IP Quaratines

IDS quarantines IP by the following process:

1) IDS places the quarantined IP in a secured bag and labels the bag as “Quarantined”
2) IDS quarantines the IP in the electronic inventory system

13. Patient-Returned IP

All patient-returned IP bottles, packaging, and extra IP will be returned to IDS within a timely manner for reconciliation and appropriate destruction. Patient-returned IP must be provided to IDS in a sealed container labeled with the accurate patient-return date, study name, subject ID/MRN, and (non-hazardous drug) pill count(s). Reconciliation and pill counts by IDS shall only be conducted upon IP return to IDS at the end of each cycle/treatment period and will not occur at any point mid-cycle.

Returned IP accountability will be performed within a reasonable amount of time upon receipt by IDS. All returned IP will be counted by IDS staff, recorded in the electronic inventory system, and then destroyed by IDS personnel in accordance with institutional, local, state, and federal requirements for destruction of medication waste. Destruction will occur on site immediately after accountability as per the IP Destruction/Disposal section below. The exception to this may pertain to controlled substances at the discretion of the IDS pharmacist.

IDS will not retain boxes, containers, or other forms of packaging for IP accountability. Returns and destruction will be documented in accordance with the IP and Accountability Documentation Section of
this SOP. The electronic inventory system will serve as the sole source of documentation for patient returns and destruction.

IP that has been dispensed to/for a subject and then returned to the IDS will not be returned to the sponsor.

Patient-returned IP will not be weighed. Returned IP that will not be accepted include: liquids, syringes, used IV bags/tubing, inhaled devices, ampules, dispensed IP not returned in hygienic conditions, and non-investigational medications.

14. IP Destruction
IP will be destroyed in accordance with the UC Davis Health Policies and Procedures: Policy 3313 (Medication Security), Policy 1630 (Pharmaceutical Waste Management) and Policy 1623 (Management of Hazardous Drug Waste and Spills) in addition to Patient Care Standards Policy X-01 (Hazardous Drug (HD) (Chemo): Safe Handling/Preparation/Administration/Disposal of Waste/Spill Procedures).

To minimize personnel and environmental exposure to substances, injectable IP and packaging once used, opened, or emptied, will not be retained, but rather will be disposed of as waste. Partial and/or used IP vials will be destroyed after compounding. IDS will not document destruction of partial or used vials, including the volume disposed of, after use for compounding. The assignment of a unit of IP in nCoup IDS will serve as documentation of destruction. In the case an IP dose is prepared for facility administration and not administered, IDS will document the disposition of the dose in nCoup IDS.

Hospital Policy 1623 will be extrapolated to include gene-transfer and cellular therapy IP for the purposes of environmental and employee safety.

Unused IP will be retained for up to 60 days from the date of expiration (or last date of potential dispensation for patient-specific IP). If IP is not returned/destroyed by the sponsor (for monitored studies) within the 60-day period, IDS will destroy the IP. Within the 60-day window, unused IP and supplies may be returned to the sponsor or destroyed on-site at the sponsor’s documented request. Disposition (return to sponsor or destruction) must occur within 60 days of study closure or treatment of the final patient. If specific materials are required for return of IP, it is the responsibility of the sponsor or supplier to provide the necessary items. The sponsor or supplier will be responsible for the cost of the shipment and all related materials. Unless otherwise explicitly required by the study sponsor, IDS may utilize a Tech-Check-Tech process for destruction of patient returns. Final disposition for all IP will be documented in the electronic inventory system.

15. Hazardous IP
IDS operates in accordance with USP General Chapters <795>, <797> and <800>. USP <800> outlines practice measures and standards for handling hazardous drugs to promote the safety of patients and healthcare personnel, and environmental protection. IDS determines if an IP is hazardous in accordance with Patient Care Standards Policy X-01 (Hazardous Drug (HD) (Chemo): Safe Handling/Preparation/Administration/ Disposal of Waste/Spill Procedures).

Due to hazardous drug handling, storage, and training requirements, hazardous drugs cannot be made available to clinical trial sponsor representatives, and/or study team members for accountability, review, and/or destruction. USP <800> requires all personnel involved with the handling of hazardous drugs to receive specialized institutional training. Per USP <800> requirements, specific hazardous investigational products must be stored appropriately in negative pressure pharmacy storage areas. These areas are restricted to essential authorized and trained pharmacy personnel. Drugs that are stored in these areas are not permitted to travel outside of these areas except for preparation, administration, or disposal/destruction. As such, only non-hazardous drugs will be made available to monitors for accountability and/or review.
Hazardous IP will not be made available for non-IDS personnel review prior to return or destruction. Additionally, hazardous IP will not be packaged or handled by UCDH personnel for shipping or return to the sponsor, clinical trial sponsor representatives, and/or study team members. Sponsors may hire third parties specifically trained and certified in hazardous and/or dangerous good shipping to return hazardous IP to the sponsor at the sponsor’s expense at the convenience of the IDS. Unused/expired hazardous IP will be destroyed on site by IDS personnel as in accordance with section 14 of this SOP. The only exception may pertain to controlled substances at the discretion of the IDS pharmacist as is in accordance with state and federal regulations.

Under no circumstances will IDS utilize alternative methods of providing proof current inventory (e.g. retaining empty bottles, packaging, photographs, photocopying of labels, sponsor forms, count transcription into secondary systems, etc.) in lieu of the hazardous products being provided for review by the clinical trial sponsor representatives, and/or study team members. IDS will not perform accountability, review, and/or destruction at monitor visits in lieu of the clinical trial sponsor representatives, and/or study team members for their observation. Electronic inventory accountability reports shall be made available for the trial representative to review the inventory and individual unit assignments at the monitor visits. These reports shall serve as the sole source of documentation.

16. Ancillary materials
If a sponsor requires specific ancillary materials to be used for IP preparation and/or administration, the sponsor must provide the materials if they are not standard stock items readily available at UC Davis Health. These materials must be compatible with institutional devices, such as IV pumps, tubing, and closed system transfer devices. Any materials deemed incompatible or with the potential to pose patient safety concerns will not be utilized.

17. IDS Fee Schedule
IDS provides mandated services (Joint Commission Standards, Department of Health Regulations, Hospital Policy and Good Clinical Practice Guidelines) with respect to investigational drugs. IDS services are met at the expense of the Department of Pharmacy Services (DPS). Patients cannot be billed for IDS services and/or investigational drugs. Therefore, the DPS will recharge the study account for IDS services provided. Recharges will occur quarterly.

IDS will provide an IDS Fee Schedule upon request. These fees will be agreed upon prior to the initiation of pharmacy study set-up by IDS and study activation. A study account number must be provided to IDS prior to the first dispense. The start-up and close-out fees are one-time, non-refundable fees. The start-up, annual maintenance, and close-out fees are non-negotiable.

18. Study Documents
Electronic copies of all study documents must be sent to IDS. Updated study documents must be provided to IDS with either a Summary of Changes or a tracked/marked version. Current and previous versions of the study protocol may be kept electronically on IDS’ secure, limited access shared drive. Sponsors and study personnel are required to notify IDS in writing via email when study document modifications occur and must provide IDS with electronic copies of such modified study documents.

19. Randomization
Upon request, IDS will prepare a randomization schedule using a program (Research Randomizer) that uses a computerized random number generator to produce customized sets of random numbers.
20. **Blinding**
Unblinding envelopes (if used) are stored in the secure IDS Pharmacy. Protocol guidelines will be followed in the unlikely event that it is necessary to unblind a treatment. IP and study documents are not accessible to blinded study personnel.

21. **Training and Delegation Logs**
A staff member’s electronic signature captured in the electronic inventory system upon IP receipt or dispense will serve as evidence of self-training. Should a sponsor require documentation of training beyond the above, it is the responsibility of the study team to maintain such documentation.

IDS may assign IP preparation to pharmacy staff within the scope of the staff member’s job descriptions and relevant policies. The IDS pharmacist prepares protocol-specific written instructions that provide pharmacy personnel with information on proper dispensing and preparation procedures.

Delegations logs will be signed by essential and relevant IDS staff only, as determined by IDS.

22. **Archiving**
To comply with ICH E6; section 8.2-8.4 (Essential Documents for the Conduct of a Clinical Trial), and as required by the applicable regulatory requirements, after completion or termination of the trial, all pharmacy documents will be forwarded to the investigator, who will be responsible for retention.

23. **Monitoring Visits**
All visits will occur at the Main IDS Pharmacy. Review and collection of IDS documents is the responsibility of the Monitor/CRA during a scheduled on-site visit. Request to view internal documents beyond accountability documents must be submitted at least five business days in advance. Under no conditions does IDS participate in remote monitoring or close-out visits. Access to sterile pharmacy areas (e.g. Infusion Center Pharmacy and main Central IV Admixture room) is prohibited.

Monitoring visits are scheduled on a first come, first serve basis. IDS will not double book monitoring visit appointments. Please schedule monitoring visits by email at least four weeks in advance. Monitoring visit requests should specify the date(s) of the desired visit and the amount of time needed for each visit. No more than two monitoring visits can be scheduled at any time.

Monitoring visits must conclude within the scheduled appointment time. At the conclusion of each visit, a verbal report of findings must be given by the monitor to an IDS staff member. An email sign-out report shall be sent by the monitor to IDS within 72 hours. Please allow 10 business days for query resolution. Charges per monitoring visit will be according to contract. IDS has a 24-hour cancellation and rescheduling policy. If you miss your appointment, cancel or change your appointment with less than 24-hour notice, you will be charged for the full monitoring visit, per contract.

24. **IRB Participation**
An IDS Pharmacist can be a member of the IRB. The pharmacist is not listed on the FDA 1572.

25. **Licensure and Curriculum Vitae (CV)**
All UCDH pharmacists and technicians, including IDS staff, are required to maintain active licensure, in good standing, with the California State Board of Pharmacy (UCDH Department of Pharmacy Policy 256:00). Verification of pharmacist licensure is monitored by the UCDH Pharmacy Administration and Human Resources staff. Pharmacists and technicians are not permitted to work without evidence of current active licensure. Verification of pharmacist and technician licensure may also be viewed on the California Board of Pharmacy web page (https://www.pharmacy.ca.gov/about/verify_lic.shtml). Signed copies of IDS pharmacist CV’s are maintained in IDS pharmacy. Copies will be provided to the sponsors upon request.