

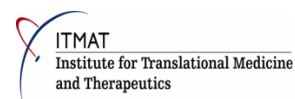
# A Guide to Working with the Investigational Drug Service

for: *Coordinators, Investigators, Data Managers and Business Administrators*

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*Investigational Drug Service*  
*University of Pennsylvania – Perelman School of Medicine – Philadelphia, PA*



## Introduction

The Investigational Drug Service (IDS) is a RESEARCH PHARMACY. We ONLY work with studies involving medications or devices. We do NOT carry a full inventory of medications like a traditional pharmacy and we do NOT bill insurance carriers.

We are affiliated with both ITMAT and the CTRC units (HUP, PPMC and CHOP), however, **we are self-sustaining through user fees**. We operate like a traditional pharmacy in that we are bound by the same state and federal regulations as other pharmacies. That means that we need an actual PRESCRIPTION to dispense a medication. Whether a medication is or isn't already on the market, is irrelevant.



We operate out of our main facility (IDS MAIN) in the Maloney Building, 36<sup>th</sup> & Spruce Streets; and a satellite (IDS NORTH) at 51 N. 39<sup>th</sup> Street, 103 Mutch Building. We coordinate pharmacy services for ALL inpatient trials at both HUP and PPMC, assist in trials at VHUP and provide outpatient services to all Penn schools and UPHS clinics, as well as all CTRC units. As time allows we also provide assistance to investigators at CHOP and at other local institutions.

## Submitting a New Trial to IDS

Generally IDS should receive a copy of the protocol BEFORE grant (or contract) submission to sponsor and BEFORE IRB submission. **Why?**

- To determine costs for budget planning
- For more complex trials, or trials which involve manufacturing, packaging or procurement, the IDS needs to consider feasibility and logistical issues and might suggest changes.

### TO SUBMIT A PROTOCOL FOR COST ANALYSIS:

1. On our website [www.itmat.upenn.edu/ids.shtml](http://www.itmat.upenn.edu/ids.shtml) under the 'FORMS' tab you'll see a 'Protocol Cover Sheet' to use with complete protocols, or a 'Preliminary Cost Estimate' sheet to use if you don't have a complete protocol yet.
2. Complete the correct form and send to IDS along with your protocol (or summary if no protocol yet). All new requests should go to [PennIDS@mail.med.upenn.edu](mailto:PennIDS@mail.med.upenn.edu) first, regardless of location.
3. Someone from IDS will prepare you an estimate of costs.

## IRB Approval and Study Initiation

Once your study is approved to start, contact the IDS to get things started.

1. **When scheduling your SIV, make sure IDS is included.** Someone will begin working on a dispensing procedure before the SIV and this is our opportunity to bring up our questions while the sponsor is here.
2. During the SIV, we'll ask about "electronic" vs. "hand written" inventory logs. The IDS uses a state-of-the-art electronic inventory system – and many industry sponsors do not require separate paper logs if all the data they need is captured already. **Be aware that separate "paper" logs may incur additional monthly costs.**

3. Ask your business administrator to complete and return the cost estimate worksheet that IDS prepared beforehand (see the box on previous page).

### ***Drug and Supply Purchases:***

IDS keeps some general supplies, however many medications are actually **purchased FOR a specific trial and charged back to that study account** when we make the purchase.



We rarely purchase ‘everything’ at once –most things expire and there may be no way to get ‘credit’ for what’s unused. We can buy most things that a sponsor may want, but sometimes we can only buy a ‘case’ or ‘box’ (not 1 or 2 pieces). We look for the lowest price at time of purchase, but be aware that price can change at any time. When we provide a ‘cost’ for purchases, it’s guidance for putting together your budget – it’s never a ‘quote’ or ‘firm price’ if it hasn’t been purchased yet.

### ***While the Study is Active and Recruiting***

- PRESCRIPTIONS should be sent to IDS BEFOREHAND, not when the patient arrives.
- If an IVRS/IXRS call must be made during the visit, make sure that the IDS is aware of the visit date/time beforehand (either send the prescription, or provide a schedule or e-mail).
- If your monitor needs to visit IDS, this MUST be scheduled in advance!



### ***What about Trials that Require 24/7 Access?***

Whenever possible, IDS will handle all preparation and dispensing. Note that for some studies, due to the complexity, it may be necessary to limit the initial enrollment/randomization to weekdays when IDS is on-site, though afterwards IDS can make arrangement for subsequent dosing on nights or weekends.

When weekday preparation isn’t possible, IDS will involve the inpatient pharmacists at either HUP or PPMC, which are open 24/7. There are additional costs with this, sometimes significant, as well as additional time to plan and set up. Due to the large number of people involved – most of them unfamiliar with the study when your patient enrolls – we typically prepare ‘starter kits’, pre-package doses, pre-print labels, etc. The IDS still maintains all records and replenishes supplies the next weekday when something has been used.

### ***When the Last Patient is Off Treatment***

- **Inform IDS right away.** Especially if we’re ordering supplies or purchasing medications based on use. We can’t always return what we purchase!
- **If a study closeout visit needs to be scheduled,** use our scheduling app!
- For pharma trials, we’ll ask the monitor if IDS files must stay on-site (eg. if a ‘final’ closeout visit hasn’t taken place yet) or if we can archive right away.
- For investigator-initiated trials, we just need to determine the fate of remaining drug/supplies, as well as (for blinded trials) who should receive the list of treatment assignments.



## **Monitoring Visits and SIV’s**

ALL visits must be scheduled in advance. The IDS maintains a master visit calendar. **Either YOU or your MONITOR can request a visit directly using our scheduling app** (see link below). Your request will go in as a ‘tentative’

appointment until IDS ‘accepts’ it. You’ll receive an e-mail link back, to use if you need to change or cancel the appointment later.

<https://www.med.upenn.edu/apps/ids/scheduler>

**Make sure to select ‘PENNIDS’ for the main facility or ‘IDSNORTH’ for the satellite, depending on which location is managing your study. If your study involves both, contact the IDS to discuss!**

**ALL IDS staff participate in all trials**, we do not assign a ‘specific’ person to one trial. Some monitors may be used to dealing with one person when they visit small pharmacies (or sites without a pharmacy). We discourage that here as it keeps the rest of our staff out of the loop. We use a team approach for all trials. One person may attend the SIV and prepare written instructions for the rest of the staff, but once that’s done, everyone is involved.

**If your monitor is running late (or early)**, call IDS before coming down. If another monitor is here at that time, we might need to look for another open time later in the day.

### **Shipping Information to Provide to Sponsor**

Make sure that you list the correct shipping information – this is found either on the back of this booklet, or we have a separate informational flyer for monitors/sponsors.

- For studies involving both locations, generally medication should be shipped to the main facility.
- For studies involving DEA schedule medications:
  - At IDSNORTH (satellite), our DEA registration matches the shipping address.
  - At PENNIDS (main), the DEA registration we use does NOT match our regular mailing address – please contact the IDS if you have a study requiring controlled substances.

IDS uses an electronic inventory system, which is in compliance with 21CFR11 and is integrated with other functions, such as labeling, billing, patient profiles, etc. The system eliminates math errors, maintains a complete audit trail and is easily accessible after a study has been closed/archived. We will inquire at the SIV, whether the sponsor will accept those logs, or will require we transcribe them onto paper. If paper transcription is requested by the sponsor, monthly costs for the study will generally be higher.

### **IVRS/IWRS**

If the sponsor uses IVRS or IWRS to register drug shipments or assign treatments to subjects, request **AT LEAST TWO user accounts** for IDS staff.

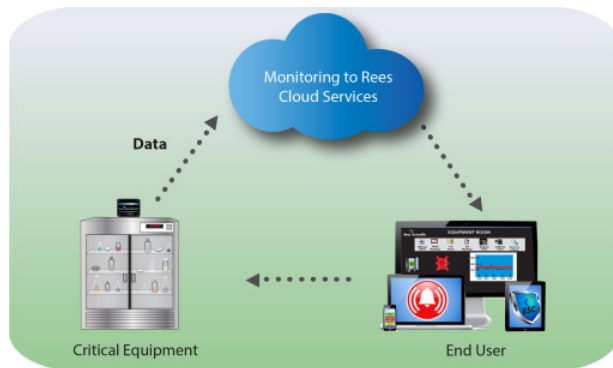


### **Temperature Monitoring**

IDS uses a wireless sensor grid to continually monitor temperature in every refrigerator, freezer and room-temperature location. Sensors are calibrated annually by an outside testing company. IDS will NOT use separate

paper temperature logs; special requests by sponsors are passed on to the study account at an hourly labor rate.

Temperature reports are provided to monitors at each visit in graph form, with the actual high, low and average temperature for that time period. Because we have hundreds of readings per day, we generally do not print out a report of each individual reading.



## Drug Returns

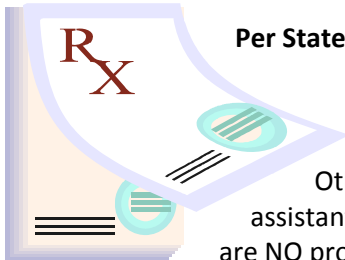
Medications returned by study participants, should come back to IDS promptly, to be logged in and then stored securely in quarantine. IDS staff can generate electronic drug return reports for the study team or monitor as needed. Do NOT return dangerous substances or infusion bags or tubing that have been used to infuse into a patient, these should be discarded as biohazard waste in the clinic or on the inpatient unit.

**IMPORTANT: Patient returns cannot be processed on the day of a monitoring visit. Returns brought to IDS “with a study monitor” or right before a monitoring visit, will be processed after the visit. If your monitor needs to see these at his/her visit, make sure they are returned to IDS at least 2-3 days prior!**

Once returns have been “monitored” we can either store them, return them or destroy them. We have regular pickups from both UPS and FedEx and the monitor should leave a copy of the return paperwork in IDS. For destruction, IDS contracts with an incinerator company.

## Prescribing

The IDS follows the SAME rules and regulations as any other pharmacy.



Per State of Pennsylvania Code (049 Pa Code § 27.1) a licensed prescriber is:

***“A physician, dentist, veterinarian or other individual authorized and licensed by law to prescribe drugs”***

Other authorized individuals can include a CRNP (nurse practitioner) or PA (physician assistant) when practicing under a collaborative practice agreement with a physician. There are NO provisions currently in state regulations, for other healthcare providers – including RNs, LPNs, RDs, RTs or un-licensed personnel – to sign a legal prescription.

**For OUTPATIENT TRIALS:** The IDS is in the EPIC WILLOW database as a retail pharmacy option. We can put in an EPIC ticket to have a custom drug code created for your study, or if you’re using a drug that’s commercially available, you can order it using the existing drug code, just make sure that you (a) select the IDS in place of the patient’s default preferred pharmacy; (b) indicate ‘eFAX’ to send the prescription; and (c) indicate the STUDY (and any other important information) in the COMMENTS section before sending.

- **Main facility: “INVESTIGATIONAL DRUG SERVICE PHARMACY”**
- **North Satellite: (pending)**

When a subject is going to receive the same medication for a period of time, a PROPERLY WRITTEN prescription with enough refills on it, may cover the duration of the study course (maximum one year). Once the signed prescription is in place, other study personnel can then REQUEST REFILLS when a patient is returning to clinic. IDS staff can discuss this during study planning. A NEW PRESCRIPTION is needed if a NEW medication is added, a NEW dose is ordered or if the original prescription is expired or the refills are used up.

**Don’t forget to send prescriptions IN ADVANCE, not the day of the visit!**

**USING EPIC BEACON:** This version of EPIC does not transmit prescriptions, instead it adds orders to a ‘work queue’. BEACON doesn’t automatically know that a drug is ‘investigational’ and should be coming from the IDS.



**When using BEACON, let IDS know your patient schedule in advance!**

**We'll search for the patient in BEACON that morning to find and print the orders. For medications that are expensive or short stability, we'll still wait for a phone call before we prepare the dose, but we pull all the supplies as soon as we have the orders.**

**PAPER PRESCRIPTIONS (NO EPIC):** In these situations, you can either use a traditional prescription (fax it to IDS or drop it off in advance), or we can help create a pre-printed order fax sheet (with medications and regimen already filled in).

**NARCOTICS (SCHEDULE-II):** In all 50 states, prescriptions for Schedule II medications are limited to a 30 day supply AND require an ORIGINAL signature by a prescriber with a DEA prescriber registration. We can PREPARE a prescription based on a fax, however in that situation the ORIGINAL must be presented at the time the medication is picked up (NO EXCEPTIONS).

### ***Inpatient Trials***

For hospital inpatients, medication orders must be entered in SCM (Sunrise Clinical Manager). However, similar to EPIC BEACON, these do not “automatically” come to IDS. Therefore, IDS might create an ‘enrollment notice’ for the coordinator to complete and fax to IDS, telling us who the patient is, where they are, when they’re expected to start treatment and if necessary, the information IDS might need to be able to randomize or calculate the dose.

When orders are properly entered in this system, separate notices sent to IDS are not considered a ‘prescription’. IDS staff will look up the actual written order in SCM and print a copy of it. That printed copy of the electronic order, is treated as a copy of the prescription.

## **Pickups and Deliveries**

While patients are welcome to visit IDS to pick up their medications, this is uncommon. Most medications are delivered to clinic, or picked up by the study team at IDS.

**When is My Prescription Ready?** We use an electronic system, in which every pickup is ‘logged’ including the time/date and person who picked it up, while every ‘delivery’ is logged with the time/date, location and which IDS staff member delivered it. The system offers a READY ALERT - this is an **opt-in feature** that will send you alerts when meds are ready for pickup (please inquire at our pickup window in either location, if you would like to receive alerts).

**Pickups:** There is a pickup window at each location. Make sure that you bring an ID with you – our electronic tracking system logs the person who picked up each prescription.

**Deliveries (local):** There is no charge for deliveries to from IDS MAIN to HUP inpatient units or CTRC (Dulles), or from IDS NORTH to the PPMC (Mutch) CTRC or PPMC inpatient units. However we do have a nominal charge for deliveries beyond that, to cover the time we have staff out of the IDS.



**Deliveries (off-campus):** We use an express courier which can deliver throughout the metro area ‘same day’. Most pickups are within 30-60 minutes (may be longer during peak times) and delivery time depends on distance. We receive an electronic confirmation of delivery. Cost varies by distance and time.

**Shipping:** We use UPS for shipments that do not need to reach their destination ‘same day’, including shipments directly to study participants.



## Budgeting and Billing Process

The IDS follows OMB-A21 ([http://www.whitehouse.gov/omb/circulars/a021/a21\\_2004.html](http://www.whitehouse.gov/omb/circulars/a021/a21_2004.html)) guidelines and University policy 2115 (<http://www.finance.upenn.edu/vpfinance/fpm/2100/2115.asp>). We are a service center, supported through user fees and required to adjust these fees periodically to ensure we operate at 'break even'. We are also required to apply our fees equitably based on our actual costs (materials and labor).

### ***In Planning***

IDS will prepare a cost estimate for your trial, which includes recommended costs to budget for, including recommendations for medications or supplies that may need to be purchased. **See 'Submitting a New Trial to IDS' on page 2.**

### ***Study Start***

- The cost estimate worksheet should be completed and returned to IDS (copy/fax/scan is fine).
- Purchased medications or supplies are pass-through costs. **We cannot purchase anything without a valid account number on file first.**

### ***University (Internal) Accounts***

The IDS debits expenses monthly. Our batch file is created on the last day of the month and uploaded the first week of the next month. An itemized statement is sent in PDF format to the business administrator and investigator.

### ***External Accounts***

- Affiliated institutions (CHOP, Wistar, UPHS) - an invoice will be sent out, either by mail or PDF, with instructions for payment. Checks should be returned to our business administrator and made out to "Trustees of the University of Pennsylvania".
- Outside institutions – invoicing works the same way, except that higher 'external user' rates may apply.

## Other Services We Provide

A primary function of the IDS is to facilitate investigator-initiated research by providing services that would otherwise not be available to investigators, or would be available elsewhere only at a much higher cost. Some of these services are only provided in our Main facility, however finished products can then be transferred to IDS North for dispensing if that location is more convenient to where patients are seen.

### ***Medication Compounding, Formulations***

The IDS prepares blinded medications or customized products for oral, topical, ophthalmic, rectal or other routes. Each product is different and some products are much easier to 'blind' than others. When a study involves customized products or blinding, we encourage discussing the project with a pharmacist early in protocol development, to determine what is feasible and to estimate costs. All manufacturing and repackaging is performed in the IDS MAIN facility only; finished products can be transferred to IDS NORTH for dispensing from that location, once made.

### ***Capsules***

A wide range of sizes and colors are available for blinding, as well as methods to mask the taste or scent of a product. Our equipment is cGMP grade and all products are prepared in a positive-pressure room with trained personnel wearing protective garb. We also have equipment capable of filling individual capsules with drug only, with 0.1mg precision.



## Tablets

Tablets are difficult to copy, because they are very customized – in shape, size, color and coating, as well as a unique imprint which can be used to identify the product in poison control databases. IDS can work with outside companies that can manufacture placebo tablets – however these may be expensive and minimum quantities may be high. If the manufacturer will not donate placebo tablets, then we typically recommend having them made only for large trials where the economics make more sense.



## Packaging

IDS can prepare medications in bottles with tamper-evident seals, as well as blister cards in various sizes. At this time we do not have equipment to prepare entirely custom blister cards, but we do often ‘modify’ the products that are available commercially – we can trim them, add custom labeling or sometimes have them custom printed (if the study requires a large quantity). IDS can also put together treatment ‘kits’.

## Sterile Products

IDS maintains three aseptic glovebox isolators – one negative pressure (for toxic compounds) and one positive pressure. Both maintain an ISO-5 (Class-100) or better environment inside. For trials which require specialized preparations or creation of placebos or blinding for sterile products, we encourage discussing the trial needs with a pharmacist before finalizing the protocol.



## Product Testing

While the IDS is not a ‘laboratory’ we do frequently perform testing on products that we prepare in-house:

- **Endotoxin/Pyrogen:** Endosafe-PTS™ system (FDA-licensed alternative for USP<85>)
- **Sterility:** Becton Dickinson Bactec™ is an established method for microbial testing. It’s considered an alternative method for sterility testing, not the official method in USP<71>, however there is solid literature to document the acceptability of these results and the FDA (CBER) has published a whitepaper to that end as well.
- **Particulates:** The IDS can perform the test for particulates in solution as described in USP<788>.
- **Microbial Bioburden Testing** (USP<61> and <62>): IDS uses both a luminometer for same-day results or pre-prepared media paddles for traditional colony counting (48-72h incubation).
- **eColi** testing
- **Chemical Identity:** Raman spectrophotometer
- **Gram Stain**
- **Cell Viability** (Trypan Blue stain)



## Other Services

The IDS can assist with protocol language to describe services IDS is going to perform, writing up parts of the Chemistry, Manufacturing and Control (CMC) section of your IND submission, or training study personnel. However, these services are performed “as time allows” and time is billed at an hourly rate.

## Study Closure and Records Archival

At the end of the trial, or once all medications/supplies have been shipped out or destroyed (if the sponsor indicates that a later closeout visit isn't needed), we will pack up the records and prepare them to ship to archives.



We use the **University Records Center** for archival. Their website is <http://www.archives.upenn.edu/urc/urc.html>. They have a 'main' storage facility at 4015 Walnut St and other storage facilities within a short drive. The records are secure and the box contents are tracked in our electronic inventory system – so that we can find the 'study' quickly and determine which box the records are in, as well as when they were archived.

We maintain files in IDS for an average of 3 months before archiving.

***Why can't records just be handed over to the investigator and filed with everything else?*** We can either provide copies of records to the investigator, OR if the sponsor requests the originals, we need to make a copy that we archive ourselves. If the study is ever audited in the future, questions about inventory/accountability, preparation/dispensing, etc will involve the IDS. We can much better address these questions if we have direct access to the records ourselves.

Additionally – one benefit of our electronic inventory system, is that the dispensing records are retrievable 'same day' without having to pull the paper records. If the sponsor requests hand-written records, then those would have to be retrieved from archives first. Another reason to encourage that study sponsors migrate to electronic records!

## CONTACT US!

### **Penn Investigational Drug Service**

3600 Spruce St - Maloney Building – Ground Floor

Philadelphia, PA 19104

Phone: 215-349-8817

Fax: 215-349-5132

Email: [PennIDS@mail.med.upenn.edu](mailto:PennIDS@mail.med.upenn.edu)

### **Penn Investigational Drug Service North**

51 N. 39<sup>th</sup> St – 103 Mutch Building

Philadelphia, PA 19104

Phone: 215-662-9995

Fax: 215-243-4645

Email: [IDSNorth@mail.med.upenn.edu](mailto:IDSNorth@mail.med.upenn.edu)

Web: [www.itmat.upenn.edu/ids.shtml](http://www.itmat.upenn.edu/ids.shtml)

