

Section 9. Study Product Considerations for Non-Pharmacy Staff

9.1	Study Product.....	2
9.1.1	Study Product Temperature	2
9.1.2	HPTN 058 Study Product	2
9.1.3	Requirements Prior to Shipment to Sites	3
9.1.4	Study Product Acquisition	3
9.1.5	Study Product Accountability	4
9.2	Chain of Custody	4
9.3	Dispensing Study Product during On-Site Visits.....	4
9.3.1	Dispensing from the Pharmacy to Clinic Staff	4
9.3.2	Dispensing from the Pharmacy to Transporters	7
9.4	Dispensing for Take Home Doses	9
9.5	Dispensing from Mobile Units.....	10
9.6	Administration of the Participant-Specific Study Product.....	10
	Figure 9-1. HPTN 058 Record of Receipt of Participant-Specific Study Product	6
	Figure 9-2. HPTN 058 Daily Record of Administration of Participant-Specific Study Product ...	6
	Figure 9-3. HPTN 058 Record of Return of Participant-Specific Study Product.....	7
	Figure 9-4. HPTN 058 Daily Transporter Log (from Transporter to Clinic Staff)	8
	Figure 9-5. HPTN 058 Daily Transporter Log (from Clinic Staff to Transporter)	9

Section 9. Study Product Considerations for Non-Pharmacy Staff

This section provides information and instructions for non-pharmacy staff related to the ordering, transport, and delivery of HPTN 058 study products for study participants. Record keeping requirements for non-pharmacy staff also are provided. Associated instructions for pharmacy staff are provided in the HPTN 058 Pharmacist Study Product Management Procedures Manual, which will be made available to each study site Pharmacist of Record (PoR) by the DAIDS Protocol Pharmacist. In addition to these specifications, sites must adhere to the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks* and the site Pharmacy Establishment Plan approved by the Pharmaceutical Affairs Branch (PAB).

9.1 Study Product

Throughout this section, the term “study product” refers to two dosage strengths of 2 mg buprenorphine with 0.5 mg naloxone tablet (Suboxone® 2 mg tablet) and 8 mg buprenorphine with 2 mg naloxone tablet (Suboxone® 8 mg tablet).

9.1.1 Study Product Temperature

The pharmacist-prepared study product must be stored at a controlled room temperature of 25 °C (77 °F) while in the clinic with excursions permitted to 15-30 °C (59-86 °F). Temperature must be monitored at all times.

Temperature should be controlled in the clinic area where study products are stored with access limited to pharmacy and select study staff and monitored using a continuous temperature recorder or a minimum/maximum thermometer with manual daily recordings on a log during the days when clinic is open. Site SOPs should specify procedures for reading and logging minimum/maximum thermometers and site training records should document that clinic staff involved in monitoring and recording storage temperatures have been trained in these procedures.

The PoR will use this information to determine whether participant-specific study products dispensed but returned unused to the pharmacy the same day can be held for the participants to receive at a later date.

9.1.2 HPTN 058 Study Product

The Pharmacist of Record at each site will be provided with:

- 2 mg buprenorphine with 0.5 mg naloxone tablet (Suboxone 2 mg tablet) in bottles of 30 tablets per bottle.
- 8 mg buprenorphine with 2 mg naloxone tablet (Suboxone 8 mg tablet) in bottles of 30 tablets per bottle.

9.1.3 Requirements Prior to Shipment to Sites

Before study product and supplies are sent to the Pharmacist of Record at a study site, the site must:

- Have a PAB approved HPTN Pharmacy Establishment Plan with Standard Operating Procedures (SOPs)
- Be registered to the study protocol by the DAIDS Regulatory Compliance Center (RCC)
- Have documentation of local drug authority approval for importation of the study drugs (to be submitted to DAIDS PAB)
- Have any additional documents required by the country for import of the study drugs.

The Pharmacist of Record must keep copies of all of the above documents.

It is the responsibility of the Site Investigator and Pharmacist of Record to know the local and country requirements for study product management and to obtain the necessary approvals for study product importation. The Clinical Research Products Management Center (CRPMC) will notify the consignees each time a shipment has been sent.

The Pharmacist of Record should direct questions regarding shipment of study products to sites to the HPTN 058 Protocol Pharmacist.

*Katherine Shin, PharmD
Protocol Pharmacist
Pharmaceutical Affairs Branch (PAB)
Division of AIDS (DAIDS)
National Institutes of Health
6700-B Rockledge Drive, Room 4227
Bethesda, MD 20892
Phone 301-594-1517
Fax 301-402-1506
E-mail: kashin@niaid.nih.gov*

9.1.4 Study Product Acquisition

Each site pharmacy will receive an initial order of study products and ancillary supplies. To order subsequent study product from the CRPMC, the Pharmacist of Record must complete a *Study Product Request Form* and fax it to the CRPMC or send a PDF file via email. The *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks* contains a blank form as well as instructions for completion.

Upon receipt of each shipment, the Pharmacist of Record will verify the content of the shipment against the Packing List from the CRPMC. Once verified, the pharmacist will sign that it was received and fax the list back to the CRPMC. If study product is missing, damaged or inconsistent with the information on the packing list, the pharmacist should contact the Protocol Pharmacist and the CRPMC immediately by phone, fax or email.

If the study product appears damaged, the pharmacist should not dispense it until she/he has been notified by the Protocol Pharmacist or the CRPMC that study product is safe for use. A hard copy of such notification and the signed verification of receipt should be retained in the site pharmacy records.

9.1.5 Study Product Accountability

The Pharmacist of Record is responsible for maintaining detailed records regarding all study products used in HPTN 058. The accountability records will include, but are not limited to, logs for study product received, dispensed, returned, destroyed, and stored. The Pharmacist of Record is responsible for documenting all information related to study product dispensing. The inventory balance documented on the study product accountability form(s) must match the actual study product inventory on hand at all times. The Pharmacist of Record is responsible for maintaining all study product-related documents including original prescriptions, shipping invoices, study drug destruction log in the pharmacy file.

The designated clinic staff for HPTN 058 is responsible for maintaining detailed records of pharmacist prepared, participant-specific study product received from the pharmacy, administered to participants, and returned to the pharmacy if the participant-specific study product was not administered to the participant. The accountability records will include, but may not be limited to, logs for participant-specific study product received in the clinic, administered to the participant, and returned to the pharmacy if not administered to the participant.

Important: Study product accountability form(s) or log(s), and any participant specific records are highly confidential and must be stored in a secure location within their respective areas. These records should be accessible to authorized pharmacy and clinic staff only.

9.2 Chain of Custody

In addition to the requirements of the Pharmacist of Record (specified in HPTN 058 Study Product Management Procedures Manual provided by the Protocol Pharmacist), the non-pharmacy study staff must help to ensure the chain of custody of study product by completing any applicable sections and/or the following documents in their entirety, as directed for each participant:

- HPTN 058 Prescription
- Record of Receipt of Participant-Specific Study Product
- Record of Return of Participant-Specific Study Product
- Record of Administration of Participant-Specific Study Product
- Daily Transporter Logs

Each study site must designate its dispensing method(s) in HPTN 058 standard operating procedures (SOPs) for participant-specific study product supply during clinic visits. These SOPs should be developed with input from both pharmacy and clinic staff. They must be approved by the DAIDS Protocol Pharmacist prior to study activation and may only be modified after consultation with the DAIDS Protocol Pharmacist.

9.3 Dispensing Study Product during On-Site Visits

An authorized prescriber listed on the Form FDA 1572 must sign a written prescription for the pharmacist to dispense study products. The individual who is responsible for actually giving the study product to the participant can be a trained study staff member who meets local requirements and is authorized to administer study products to study participants.

Upon receipt of a completed and signed HPTN 058 Prescription, pharmacy staff will dispense study product for study participants per instructions in the HPTN 058 Pharmacist Study Product Management Procedures Manual provided by the Protocol Pharmacist.. Study product tablets will be

dispensed by the pharmacist in re-sealable plastic bags for dispensing in the clinic to be administered to the participant by authorized site staff or in amber vials with a child resistant capped closure for take home doses containing the participant’s prescribed dose. Plastic bags and Amber vials with participant’s prepared dose will be labeled by the pharmacist in accordance with US and local regulations. In all cases, labeling will include the PTID of the participant for whom the supplies have been prepared and to whom they should be dispensed/delivered.

Note that during the induction phase for each arm (Days 1-3), the authorized clinician must submit a prescription for each dosing of the participant each day. These prescriptions cannot be sent all at once as each prescription will be completed based on the COWS score of the participant after study product dosing. The same chain of custody will be followed for each prescription submitted on these days as will be done for all other dosing throughout the course of the trial.

In the remainder of this section, study products prepared by the pharmacist for dispensing to participants will be referred to as “participant-specific study product.”

Participant-specific study product may be dispensed to participants in one of the following ways:

- From the pharmacy to authorized clinic staff who will deliver the participant-specific study product to the participant for administration in the clinic.
- From the pharmacy to authorized transport staff (“transporters”) who will transfer the participant-specific study product to authorized clinic staff who will then dispense the participant-specific study product to the participant for administration in the clinic

9.3.1 Dispensing from the Pharmacy to Clinic Staff

At sites choosing to dispense participant-specific study product to clinic staff who will then administer it to participants, prescriptions are expected to be delivered to the pharmacy by the clinic staff. Upon receipt of a completed and signed prescription, the PoR will prepare the participant-specific study product as prescribed on the prescription. Participant-specific study product may be prepared based on either original documents or faxed copies, but participant-specific study product will not be released to clinic staff until the original prescription is received.

The HPTN 058 Record of Receipt of Participant-Specific Study Product (Figure 9-1) must be used to document dispensing of participant-specific study product to clinic staff. Pharmacy staff will complete the top section (site name, site number, clinic name) and the first six columns on the Record of Receipt. When receiving participant-specific study product from the pharmacy, clinic staff will verify the PTIDs, confirm the number of 2 mg and 8 mg Suboxone tablets received for each PTID, and complete the remaining columns on the Record of Receipt for each PTID. The date that the product is received by the clinic staff or transporter must be the same as the date of dispensation by the pharmacist. Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. All Records of Receipt will be retained in the pharmacy.

Figure 9-1. HPTN 058 Record of Receipt of Participant-Specific Study Product

Clinical Research Site Name:	Clinic Location:
Clinical Research Site Number:	

PHARMACY STAFF						CLINIC STAFF or TRANSPORTER		COMMENTS /staff name/date (English)
Date Dispensed by Pharmacy dd-MMM-yy	PTID	Dose (mg)	No. of 2 mg Suboxone Tablets Dispensed by Pharmacy	No. of 8 mg Suboxone Tablets Dispensed by Pharmacy	Pharmacist Initials	Date Received from Pharmacy by Clinic Staff or Transporter dd-MMM-yy	Clinic Staff or Transporter Initials	

The clinic staff is responsible for controlling access to the participant-specific study product dispensed into their custody and ensuring that the tablets are delivered and administered properly to the participants for whom they were dispensed. Clinic staff must document delivery and administration of the study product to designated participants on the Daily Record of Administration of Participant-Specific Study Product (Figure 9-2). The clinic staff member who receives the product will complete the first four columns on the Record of Administration, and clinic staff authorized to administer study product to participants will complete the remaining columns (one staff member can complete all columns if she/he both receives and administers the study product). Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. A copy of the completed Record of Administration must be sent to the pharmacy at the end of each work day. The original will be maintained in the clinic study file.

Figure 9-2. HPTN 058 Daily Record of Administration of Participant-Specific Study Product

Clinical Research Site Name:
Clinical Research Site Number:

Clinic Location:
Date (dd-MMM-yy):

RECEIVING CLINIC STAFF				ADMINISTERING CLINIC STAFF			Comments/staff name/date (English)
PTID	No. of 2 mg Suboxone tablets Received by Clinic Staff	No. of 8 mg Suboxone tablets Received by Clinic Staff	Receiving Clinic Staff Initials	No. of 2 mg Suboxone tablets Administered to Participant	No. of 8 mg Suboxone tablets Administered to Participant	Administering Clinic Staff Initials	

In the event that all study product dispensed for a participant is not administered to the participant, clinic staff will document this in the participant’s study chart and return the unused study product to the pharmacy as soon as possible on the same day it was dispensed by the pharmacy. The HPTN 058 Record of Return of Study Product (Figure 9-3) must be used to document the return of participant-specific study product to the pharmacy. Clinic staff will complete the top section (site name, site number, clinic name), the first six columns on the Record of Return, and the comments field. When receiving returned participant-specific study product from the clinic, pharmacy staff will verify the

PTID, confirm the number 2 mg and 8 mg tablets returned, and complete the remaining two columns. The date that the product is returned to the pharmacy by the clinic staff or transporter must be the same as the date of receipt by the pharmacist. Reasons for return (e.g. participant unavailable, temperature excursion, etc.) must be recorded in the Comments column and on the back of the record if additional space is needed. All Records of Return will be retained in the pharmacy.

Figure 9-3. HPTN 058 Record of Return of Participant-Specific Study Product

Clinical Research Site Name:					Clinic Location:		
Clinical Research Site Number:							

CLINIC STAFF or TRANSPORTER					PHARMACY STAFF		COMMENTS /staff name/date (English)
Date Returned to Pharmacy by Clinic Staff or Transporter (dd-MMM-yy)	PTID	No. of 2 mg Suboxone tablets Returned to Pharmacy by Clinic Staff or Transporter	No. of 8 mg Suboxone tablets Returned to Pharmacy by Clinic Staff or Transporter	Clinic Staff or Transporter Initials	Date Received from Clinic Staff or Transporter by Pharmacy (dd-MMM-yy)	Pharmacist Initials	

9.3.2 Dispensing from the Pharmacy to Transporters for Further Transfer to Clinic Staff

At sites choosing to dispense participant-specific study product to transporters who will transfer the study product to clinic staff for subsequent delivery and administration to participants, prescriptions are expected to be delivered to the pharmacy by a transporter. Upon receipt of a completed and signed prescription, the PoR will prepare the participant-specific study product as prescribed on the prescription. Study product may be prepared based on either original documents or faxed copies, but study product will not be released to a transporter until the original prescription is received.

The HPTN 058 Record of Receipt of Participant-Specific Product (Figure 9-1) must be used to document dispensing of participant-specific study product to transporters. Pharmacy staff will complete the top section (site name, site number, clinic name) and the first six columns on the Record of Receipt. When receiving participant-specific study product from the pharmacy, transporters will verify the PTIDs, confirm the number of 2 mg and 8 mg Suboxone tablets received for each PTID, and complete the remaining columns on the Record of Receipt for each PTID. The date that the product is received by the clinic staff or transporter must be the same as the date of dispensation by the pharmacist. Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. All Records of Receipt will be retained in the pharmacy.

HPTN 058 Daily Transporter Logs (Figures 9-4 and 9-5) must be used to document transfer of participant-specific study product between transporters and clinic staff. Although all information on the transporter log will also be documented on the Record of Receipt and Record of Administration of Participant-Specific Study Product, the purpose of this document is to monitor chain of custody while the study product is not maintained in the pharmacy or study clinic. At the beginning of each work day, transporters will complete the top section (site name, site number, clinic name, date) of their Daily Transporter Logs. When receiving study product from the pharmacy, in addition to completing the Record of Receipt for each PTID, transporters will complete the first four columns on the Daily Transporter Log (from Transporter to Clinic Staff) for each PTID.

Figure 9-4. HPTN 058 Daily Transporter Log (from Transporter to Clinic Staff)

Clinical Research Site Name:	Clinic Location:
Clinical Research Site Number:	Date (dd-MMM-yy):

TRANSPORTER				CLINIC STAFF			COMMENTS/staff name/date (English)
PTID	No. of 2 mg Suboxone tablets Received from Pharmacy by Transporter	No. of 8 mg Suboxone tablets Received from Pharmacy by Transporter	Transporter Initials	No. of 2 mg Suboxone tablets Received from Transporter by Clinic Staff	No. of 8 mg Suboxone tablets Received from Transporter by Clinic Staff	Clinic Staff Initials	

Transporters are expected to deliver participant-specific study product to authorized clinic staff directly after collecting the participant-specific study product from the pharmacy. During transport, participant-specific study products should be stored securely (e.g., in a locked box), with access limited to authorized clinic staff. Transporters must control access to the participant-specific study product dispensed into their custody and deliver the study products only to authorized clinic staff. Transporters also must retain and control access to their Daily Transporter Logs until the logs are returned to the pharmacy, at which time pharmacy staff assumes responsibility for the logs. If completed logs are not returned to the pharmacy by the end of each work day, the PoR will notify appropriate clinic or pharmacy supervisory staff (per site SOPs) to ensure timely recovery of the logs. If completed logs are not recovered and delivered to the pharmacy within five calendar days, the PoR will notify the DAIDS Protocol Pharmacist via email.

When receiving participant specific study product from transporters, clinic staff will verify the PTIDs, confirm the number of 2 mg and 8 mg Suboxone tablets received for each PTID, and complete the remaining three columns on the Daily Transporter Log for each PTID. Comments may be recorded in the designated column and, if additional space is needed, on the back of the log.

Clinic staffs are responsible for controlling access to the participant-specific study products transferred into their custody, ensuring that the study products are stored appropriately while in their custody, and ensuring that the study products are delivered to the participants for whom they were dispensed. Clinic staff must document delivery of study product to designated participants on the Record of Administration of Participant-Specific Study Product (Figure 9-2). The clinic staff member who receives the product will complete the first four columns on the Record of Administration, and clinic staff authorized to administer study product to participants will complete the remaining columns (one staff member can complete all columns if she/he both receives and administers the study product). A copy of the completed Record of Administration should be sent to the pharmacy at the end of each work day. The original will be maintained in the clinic study file.

In the event that all study products dispensed for a participant are not administered to the participant, clinic staff will document this in the participant’s study chart and return the unused study product to the pharmacy as soon as possible on the same day it was dispensed by the pharmacy. The Record of Return of Study Product (Figure 9-3) must be used to document the return of study product to the pharmacy. Clinic staff will complete the top section (site name, site number, clinic name), the first six columns on the Record of Return, and the comments field. When receiving returned study product from the clinic, pharmacy staff will verify the PTID, confirm the number of tablets returned,

and complete the remaining two columns. The date that the product is returned to the pharmacy by the clinic staff or transporter must be the same as the date of receipt by the pharmacist. Reasons for return (e.g. participant unavailable, temperature excursion, etc.) must be recorded in the Comments column and on the back of the record if additional space is needed. All Records of Return will be retained in the pharmacy. If the clinic staff gives the unused participant-specific study product to a transporter for return to the pharmacy, then a Daily Transporter Log (from Clinic Staff to Transporter) must be completed (Figure 9-5).

Figure 9-5. HPTN 058 Daily Transporter Log (from Clinic Staff to Transporter)

Clinical Research Site Name:				Clinic Location:			
Clinical Research Site Number:				Date (dd-MMM-yy):			

CLINIC STAFF				TRANSPORTER			COMMENTS/staff name/date (English)
PTID	No. of 2 mg Suboxone tablets Delivered to Transporter by Clinic Staff	No. of 8 mg Suboxone tablets Delivered to Transporter by Clinic Staff	Clinic Staff Initials	No. of 2 mg Suboxone tablets Delivered to Pharmacy by Transporter	No. of 8 mg Suboxone tablets Delivered to Pharmacy by Transporter	Transporter Initials	

9.4 Dispensing for Take Home Doses

Suboxone dosing is intended to be closely supervised, with the product dispensed to the participant at the study site with direct observation of dosing. However, if allowed by in-country authorities, study staff may on rare occasions give participants a supply of study product to take home when the participant is unable to come to the study site for dosing (e.g., because of travel). Under rare circumstances, such as serious participant illness or disability, study staff may visit the participant at home (with consent) to deliver the study medication.

In the event of take home dosing, authorized study staff should follow local requirements for writing the prescription(s). Clinic staff must notify the pharmacy of the quantity of 2 mg and 8 mg Suboxone tablets needed to last until the participant can return to the clinic and allowed by local and country regulations. The pharmacy will dispense the study product in amber vials with child resistant caps. Clinic and pharmacy staff should document the take home dose(s) on the Record of Receipt and Daily Record of Administration of Participant-Specific Study Product and in the participant’s study chart. Pharmacy staff will also complete other documentation as instructed by the DAIDS Protocol Pharmacist.

9.5 Dispensing from Mobile Units

Some sites may require the dispensing of participant-specified study product in the field for participants living in remote areas. However, this can only be done with the approval of local health authorities and the protocol team. Any site wishing to dispense product in the field must submit a Mobile Dispensing Plan to DAIDS for approval before such a plan can be enacted. The mobile plan must minimally meet the requirements of the HPTN 058 protocol, this SSP manual and the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*.

9.6 Administration of the Participant-Specific Study Product

Regardless of the method used to get the participant-specified study product to the participant, in most circumstances the administering of the dose must be observed by a qualified staff member. It is important that the participant properly takes the dose of BUP/NX for its maximum effect to be recognized.

Staff members are to inform the participant that the BUP/NX is to be administered sublingually (under the tongue). The tablets may be placed under the tongue all at once or at least two at a time (if the participant cannot fit more than two comfortably). The participant may take a sip of water to wet her/his mouth **before** the pills are placed under the tongue, but no water is to be taken after the tablets are placed under the tongue. The pills should remain under the tongue until they completely dissolve. Remember to tell the participant that if they swallow the tablets they will not work as well. The observer should check under the participant's tongue at least once to make sure the tablets are placed correctly.

The participant is to be observed during the induction period (Days 1-3) for at least one hour after taking the Suboxone at which time the COWS will be repeated and dose adjustment is made. After the induction period there is no requirement for continued observation after tablets have dissolved. The clinic staff should refer to the BUP/NX Treatment Manual for a full discussion of study product administration. Any side effects or adverse experiences are to be noted in the participant's source documentation and handled according to the specifications of the protocol and Section 12 of this manual.