Standard Operating Procedure

Department	Regulatory Affairs
Version Number	6.0
Document Number/ID	SOP-0574
Document Title	Shipment and Management Investigational Product

1.0 Overview

This document contains the following topics:

Purpose

This document describes how to perform one or more of the following activities involving an Investigational Product (IP), shipped from Pharmacyclics (PCYC) designee to Investigational Sites (Sites) participating in PCYC-sponsored clinical trials:

- Requisition
- Shipment
- Management
- Return
- Destruction

Scope

This document applies to all IPs used in PCYC-sponsored clinical trials at Sites.

Overview, Continued

Definitions

For the purposes of this document, the following terms are defined:

Term	Definition
Clinical Trial Lead (CTL)	Clinical personnel who • oversees conduct of a PCYC-sponsored clinical trial • coordinates clinical trial activities across functional areas, and • acts as the primary liaison with the person or organization contracted to perform specific trial duties and functions
Clinical Trials Management System	System used to • generate hard copy supplies requisitions and shipping receipts, and • provide tracking of IP shipments
Drug Depot	A third-party company contracted by PCYC to • store IP • distribute IP to Sites, and • accept returned IP from the Sites
Interactive Response Technology (IRT)	• Refers to Interactive Voice Response System (IVRS) or Interactive Web Response System (IWRS) • Can be used to generate, track, and document IP shipments

Responsibility

This table lists the roles and responsibilities for performing the tasks in this document.

Role	Responsibility
Clinical Drug Supply Management (CDSM)**[XYZ SME: Please check inserted full form.]**	• Confirms availability of lot and quantities of IP according to trial protocol requirements • Authorizes the shipment of IP to sites • Manages all communication documentation with any PCYC-designated third-party drug depot
• CDSM • Designee	Prepares and ships the IP to sites
Clinical Operations (CO)	• Initiates the collection and QC of the Site regulatory documents • Approves FORM-0023 • Completes and sends Study-Specific Drug Order Form to CSDM when a study does not use IRT for requisition and shipment of IP

2.0 Requirements for Retaining Records

2.1 Filing the Documents

Follow the requirements given below to retain records pertaining to applicable documents.

- File the documents in the TMF as per the trial-specific TMF Management Plan and Index.
- Retain the records according to regulatory requirements**[XYZ SME: Pls provide missing reference.]**.

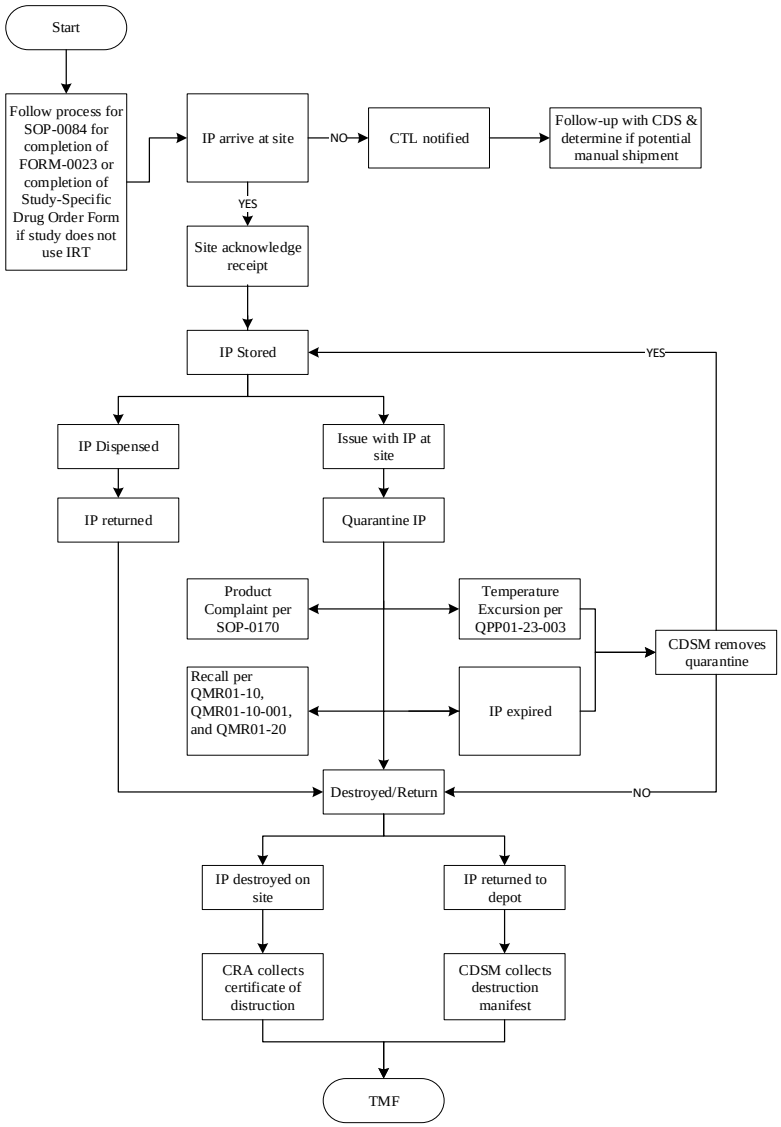
Responsibility: CO**[XYZ SME: Pls check responsibility.]**

3.0 Management of Investigational Products

3.1 IP Management: Flow Diagram

This diagram illustrates the tasks for performing the following activities pertaining to an IP:

- Requisition
- Shipment
- Management



4.0 Requirements for Requesting and Shipping IP to Sites

4.1 Requesting and Shipping Using IRT

Follow the steps in the table below to request and ship IP for trials using IRT.

Step	Responsibility	Action
1	CO	Initiate FORM-0023 per SOP-0084.
2	CDSM	Determine the following information for the IP required: • Availability of lot • Quantities required
3	CDSM	• Activate the site in IRT. • Initiate request to ship IP to sites.
4	CDSM or designee	• Prepare shipment of IP according to site information on FORM-0023. • Manage and ship IP using IRT or CTMS per the trial-specific IRT Pharmacy Manual**[XYZ SME: Pls confirm change in reference.]**.

4.2 Requesting and Shipping Using Drug Order Form

Follow the steps in the table below to request and ship IP for trials using Study-Specific Drug Order Form, that is, for trails not using IRT.

Step	Responsibility	Action
1	CO	Complete the Study-Specific Drug Order Form (for initial and follow-up IP shipments).
2		Enter information into XYZ CDSM ibrutinib Drug Order SharePoint.
3		Email the completed Study-Specific Drug Order Form to the CDSM study lead.

5.0 Storing and Managing IP at Site

5.1 Receipt of IP

Upon the arrival of the IP, the Site

- completes acknowledgment of receipt and files it in the study-specific Pharmacy Binder, and
- stores IP as per protocol/Pharmacy Manual requirements.
  Reference: See topic "4.4 Storing and Dispensing IP" for more information.

Note: Accountability of IP at the Site is managed as outlined in SOP-0077.

5.2 Handling Non-Receipt of IP

Follow the steps in the table below if IP does not arrive at the Site.

Step	Responsibility	Action
1	Site personnel/ CRO	Notify the CTL.
2	CTL	Follow up with CDSM on the status of the shipment. ***Note:*** If there is an event that requires IP replacement, CDSM raises a manual shipment per their process.

6.0 Returning and Destroying IP

6.1 Identifying, Returning and Destroying IP

Perform the following to identify, return or destroy an IP.

- Clearly identify and store IP returned to site from subject in an appropriately dedicated area.
- Mark IP for destruction or return to sponsor or designee only after PCYC representative has completed accountability and reconciliation as per the Clinical Monitoring Plan and Pharmacy Manual.

Responsibility: Site personnel

Note: Destroy all IP at the site except in circumstances

- where they do not have the ability to destroy IP, or
- when otherwise defined or directed by PCYC.

6.2 Destroying IP at Site and Documenting Destruction

Follow the steps in the table below to destroy IP at site and document destruction.

Step	Responsibility	Action
1	Pharmacist or Designee	Destroy IP per the site destruction policy or process.
2		Document the destruction on FORM-0157, or equivalent receipt of destruction with applicable dates and signatures.
3	CO or Designee	Retrieve/receive all destruction certificates or receipts for destruction from the sites throughout the study.
4		Ensure all destruction certificates or receipts for destruction are filed in the site's Pharmacy Binder and in the trial-specific TMF.

7.0 Escalating Deviations

7.1 Escalating Deviations from SOP

Escalate to the CTL or above and to Clinical Process Compliance (CPC) any deviations from the procedures mentioned in this SOP, including the following activities:

- Re-dispensing of returned IP
- Re-dispensing of IP that has been already assigned in IRT
- Re-dispensing IP in original container, not relabeled, only in opened bottles
- Shipping IP to other locations
- Dispensing IP to anyone other than the consented subject
- IP dispensed to subjects that is under evaluation due to temperature excursion

Responsibility: **<Information requested>**

8.0 References

QOS References

- QMR01-10, *Potential Drug Shortage, Quality Defect Report and Product Recall*
- QMR01-10-001, *Quality Defects and Product Recalls*
- QMR01-20, *Product Action for Investigational Medicinal Product*
- QPP01-23-003, *Resolving Temperature Excursions of Investigational Product for PCYC Sponsored Imbruvica Clinical and Investigator-Sponsor*
- SOP-0077, *Conducting Site Monitoring*
- SOP-0084, *Regulatory Document Approval Process for and Authorization of Shipment of Investigational Product*
- SOP-0170, *Product Complaint Reporting Trial-specific Pharmacy Manual*

Non-QOS References

- EU Guideline to GMP Annex 13
- EU Regulation No 536/2014
- ICH E3, E6(R2), E8, E9, E11 and FDA Code of Federal Regulations Title 21CFR Part 312 and European Union Clinical Trials Directive, European Union Good Clinical Practice Directive and any other regulations, guidance, or directive by law in other applicable countries

9.0 Revision History

Summary of changes

Version	Description of Change
6.0	DCR 2670: Added site number to the CSRF and CSSR forms. Added Materials Management's responsibility to obtain details of the clinical supplies shipment request from the initiated CSRF in CRIS. Added CRIS System Administrator's responsibility to provide an electronic spreadsheet to QA once clinical supply lot #s are entered in CRIS. Added QA's responsibility to ensure that the clinical supply lot #'s are accurately entered into CRIS
5.0	DCR 2559: Added CRIS System Administrator responsibilities, changed QA's responsibility in the requisition and shipment process, revised Appendix A to add lot information
4.0	DCR 2219: Biennial review, change to new template format, change in responsibility for allocation, dispensation and inventory control from Quality Control to Materials Management, change in responsibility for Regulatory Affairs approvals to only do initial drug shipment approvals, change to CSRF Appendix to reflect change in approval sign-offs (done in Sierra)
3.0	**<Information requested>**
2.0	**<Information requested>**
1.0	**<Information requested>**

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