
HOPA

INVESTIGATIONAL DRUG SERVICE

BEST PRACTICE STANDARDS



HOPA
Hematology/Oncology
Pharmacy Association



HOPA
Hematology/Oncology
Pharmacy Association

8735 W. Higgins Road, Suite 300
Chicago, IL 60631-2738
877.467.2791 • info@hoparx.org • www.hoparx.org

Copyright © 2014 Hematology/Oncology Pharmacy Association

All rights reserved. No part of this publication may be used or reproduced in any manner whatsoever without written permission except for brief quotations embodied in critical articles and reviews.

Editor

Barry R. Goldspiel, PharmD BCPS BCOP*
Deputy Chief
National Institutes of Health Clinical Center
Pharmacy Department
10 Center Drive, RM 1C240 MSC 1196
Bethesda, MD 20892-1196
301.496.5869
bgoldspiel@nih.gov

Lead Authors

Sapna R. Amin, PharmD BCOP
Manager, Investigational Pharmacy Services
Division of Pharmacy
MD Anderson Cancer Center
1515 Holcombe Boulevard, Unit 376
Houston, TX 77030
713.563.6646
samin@mdanderson.org

Joyce S. Lee, PharmD BCOP BCPS
Clinical Pharmacist, IDS/Oncology
Department of Pharmacy
Assistant Professor, Division of Hematology/Oncology
University of California–Davis Medical Center
2315 Stockton Boulevard
Sacramento, CA 95817
916.734.7176
joyce.lee@ucdmc.ucdavis.edu

Authors

Jorge G. Avila, PharmD BCOP
Infusion Services and IDS Pharmacy Manager
Department of Pharmacy
Moffitt Cancer Center
12902 Magnolia Drive
Tampa, FL 33612
813.745.1677
jorge.avila@moffitt.org

Robert Enos, RPh MBA
Clinical Pharmacist
Dartmouth-Hitchcock Medical Center
Norris Cotton Cancer Center
1 Medical Center Drive
Lebanon, NH 03756
603.650.5590
robert.enos@hitchcock.org

Matthew J. Boron, RPh
Senior Clinical Research Pharmacist
Pharmaceutical Management Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive
RM 5W228 MSC 9725
Bethesda, MD 20892
240.276.6575
boronm@mail.nih.gov

Kathy Galus, PharmD BCOP
Phase I Clinical Pharmacist
Investigational Drug Service
Roswell Park Cancer Institute
Elm & Carlton Streets
Buffalo, New York 14263
716.845.8370
kathy.galus@roswellpark.org

Stefanie Conley, PharmD RPh
Oncology Investigational Drug Service Pharmacist
University of Texas Southwestern Medical Center
Simmons Cancer Center-Pharmacy
2201 Inwood Road, Suite NC2.852
Dallas, TX 75390-9015
214.645.2616
stefanie.conley@utsouthwestern.edu

Theresa A. Mays, PharmD BS BCOP FASHP
Director, Investigational Drug Section
South Texas Accelerated Research Therapeutics (START)
4383 Medical Drive, Suite 3046
San Antonio, TX 78229
210.593.5264
theresa.mays@start.stoh.com

Authors (continued)

Gopal Patil, PhD MBA RPh
Manager, Oncology and Investigational Drug Pharmacy
UMass Memorial Medical Center
55 Lake Avenue N
Worcester, MA 01655
774.443.8965
gopal.patil@umassmemorial.org

Jennifer L. Thompson, PharmD BCOP CCRP
Senior Clinical Research Pharmacist
Pharmaceutical Management Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive
RM 5W228 MSC 9725
Bethesda, MD 20892
240.276.6575
jennifer.thompson3@nih.gov

Peer Reviewers

Linda R. Bressler, PharmD BS
Clinical Associate Professor Emerita
University of Illinois–Chicago, College of Pharmacy
bressler@uic.edu

Michael P. Kane, RPh BCOP
Director, Oncology Pharmacy Services and Research
Pharmacy Shared Resource
Rutgers Cancer Institute of New Jersey
Rutgers, The State University of New Jersey
195 Little Albany Street
New Brunswick, NJ 08903-2681
732.235.8236
kanemp@cinj.rutgers.edu

Jennifer LaFollette, PharmD BCOP
Clinical Pharmacist Specialist, Hematology/Oncology
Director, Hematology/Oncology PGY2 Residency Program
Grady Health System
Department of Pharmacy
80 Jesse Hill Jr. Drive
Atlanta, GA 30303
404.489.9182
jlafollette@gmh.edu

Susan Rogers, RPh
Director, Investigational Drug Service
Emory University Clinic
Building A, Suite 1200
1365 Clifton Road, NE
Atlanta, GA 30322
404.712.7485
sroger2@emory.edu

Reviewed and endorsed by:

Association of Community Cancer Centers
Institute for Safe Medication Practices
Oncology Nursing Society

The HOPA Standards Committee last reviewed the content of these practice standards for accuracy and relevancy on July 20, 2018.

**The opinions expressed in this publication are those of the editor and do not necessarily reflect the views of the National Institutes of Health (NIH) or the NIH Clinical Center.*

Executive Summary

The mission of the Hematology/Oncology Pharmacy Association (HOPA) is to help hematology and oncology pharmacy practitioners and their associates provide the best possible cancer care. The *HOPA Investigational Drug Service Best Practice Standards* addresses the pharmacist's crucial role in investigational studies across the life cycle of a protocol, the investigational drug service's roles and responsibilities, and special circumstances related to medication therapy access on protocols. The document is directed at institutions conducting clinical research in cancer patients; however, the principles and practices are applicable to any setting conducting clinical research that involves medications. Investigational agents often are considered high-risk or hazardous medications and therefore require consideration for additional safe practices. This guideline should be used in conjunction with other applicable state and federal guidelines.

Investigational Drug Service Responsibilities

Institutions conducting clinical trials using investigational medications should establish an investigational drug service (IDS).

IDS General Best Practices

The IDS should

- develop policies and procedures for investigational medication management
- be responsible for investigational medication inventory maintenance for research protocols
- establish policies and procedures for tracking expiration dates of investigational medications
- use computer software for investigational medication management
- develop policies regarding prospective, periodic investigational medication audits
- establish a procedure to assess investigational medications as hazardous agents
- develop a policy for investigational medications that includes storage, returns, and disposal
- establish policies and procedures to perform continuous temperature monitoring and reporting
- develop policies and procedures to establish fees for using the IDS
- participate in sponsor visits
- create a process for coordinating studies across multiple sites
- develop policies and procedures for mailing investigational medications
- establish institutional policies and procedures for allowing the use of an investigational medication from another institution
- assist the principal investigator with study closeout.

IDS Best Practices for Prescribing Investigational Medications

The IDS must ensure that protocol information is available to essential pharmacy personnel at the time of prescribing.

The IDS should

- train pharmacy and relevant study team personnel
- establish and maintain a list of authorized prescribers for each investigational medication
- create protocol-specific medication order templates for prescribing investigational medications.

When computerized physician order entry is used, clinical decision support should be incorporated into electronic investigational medication ordering.

IDS Best Practices for Dispensing Investigational Medications

The IDS should

- facilitate the dissemination of investigational medication information
- establish policies to ensure adequate investigational medication order review and verification
- establish a process for informed consent verification
- establish investigational medication labeling policies
- establish dispensing and labeling requirements for oral investigational medications
- establish procedures to dispense investigational medications for single- or double-blind studies.

IDS Best Practices for Administering Investigational Medications

The IDS should identify administration information required by investigational medication sponsors.

The Pharmacist's Role in Investigational Studies Across the Protocol Life Cycle

Pharmacists' Best Practices for Protocol Development

Pharmacists should

- develop the medication information section for the protocol
- provide recommendations on supportive care to meet institutional guidelines and provide consistency within and across investigational studies
- participate in scientific review committees
- participate in institutional review board (IRB) protocol reviews
- review all medication-related information used in the informed consent process.

Pharmacists' Best Practices for Patient Counseling and Monitoring

Pharmacists should

- provide medication counseling for patients receiving investigational medications
- assess medication adherence
- participate in reporting of unanticipated problems, adverse events, and protocol deviations.

The Pharmacy Technician's Role in Investigational Medication Management

Institutions should define a pharmacy technician role for the IDS.

Minimum qualifications should be established for pharmacy technicians to practice in the IDS.

Pharmacy technicians' duties should be established to facilitate IDS operations.

Expanded Access to an Investigational Medication

The IDS pharmacist should

- be familiar with resources used to locate expanded access protocols when other options have been exhausted
- determine whether the medication manufacturer is willing to make the agent available through a single-patient IND
- verify U.S. Food and Drug Administration (FDA) and local IRB approval for use of the medication through non-emergency expanded access
- verify FDA approval and local IRB notification for use of the medication through emergency expanded access
- be familiar with the FDA and National Cancer Institute websites regarding expanded access.

Introduction

Pharmacists have become an integral part of clinical research trial support in a variety of practice settings, specializing in all aspects of medication therapy management for investigational research protocols. Oncology pharmacists in particular often are involved in clinical research activities and drug development.¹ In addition to an increasing number of clinical trials and novel therapies in oncology, trial designs also have increased in complexity. Early phase, combined-phase, and blinded trials can require specialized investigational drug service (IDS) procedures.

The IDS performs the logistical duties of medication procurement and provision of investigational medications. IDS pharmacists often have added roles of protocol review and implementation processes that promote patient safety, facilitate regulatory compliance with all state and federal guidelines, and ensure ethical and equitable conduct of human research involving investigational agents. Consistent with their role in advanced pharmacy practice models, pharmacy technicians have an important role in investigational medication distribution and control.

The IDS is charged specifically with providing oversight and direction for the use of investigational medications in research protocols from both an operational and a clinical standpoint. Operational activities include medication acquisition, storage, preparation, dispensing, and disposal; documentation of accountability; and recordkeeping as required by Good Clinical Practices (GCP), the Code of Federal Regulations (CFR), and any applicable state laws. Clinical roles include, but are not limited to, institutional review board (IRB) participation (or participation in an equivalent ethical review committee), expert scientific or medication therapy consultation to investigators, and service as a liaison between the sponsor and the institutional research or pharmacy staff regarding coordination of protocol-directed medication therapy.

The purposes of *HOPA Investigational Drug Service Best Practice Standards* are to

- discuss the regulatory and guiding principles for medication use in human subjects research
- describe the role of the pharmacy department, pharmacist, and pharmacy technician in clinical research
- provide guidance to pharmacists and institutions about best practices for investigational drug management
- establish and recommend uniform practice standards defining the role of a pharmacist or pharmacy service for medication management for a clinical research protocol.

The *HOPA Investigational Drug Service Best Practice Standards* was compiled by a working group led by content experts in IDSs. The guidelines were written with a

focus on pharmacies that provide investigational medications to cancer patients; however, the principles are applicable to managing all investigational medications. These standards are based on the interpretations of the applicable federal laws, GCP regulations, and current practice standards for research pharmacists. This document should not be used as a substitute for state or federal regulations; rather, it should be used as a supplement to help establish practice standards.

Regulatory Background

In the United States, regulatory standards concerning the conduct of clinical research are set forth by the Food and Drug Administration (FDA) as established by the CFR.² An Investigational New Drug (IND) application is required by the FDA to conduct investigational medication research in human subjects. IND status permits an unapproved medication or biological product to be shipped lawfully across state lines for the purpose of conducting research. For any medication or biologic being studied under an IND application, investigators must comply with CFR medication control regulations. Under certain circumstances, clinical research involving marketed drugs may be considered IND exempt and therefore not subject to IND requirements.³ The IDS can be a valuable asset in aiding investigators with medication information, acquisition, storage, distribution, and accountability for both IND and IND-exempt research protocols. In addition to the regulatory standards, the International Conference on Harmonisation (ICH) E6 GCP provides ethical and scientific standards for designing, conducting, recording, and reporting of trials.⁴

IDS operations are contingent upon the following CFR parts and ICH GCP Consolidated Guideline sections:

- IRBs/independent ethics committees (CFR Title 21 Part 56; ICH E6 Section 3)
- informed consent (CFR Title 21 Part 50; ICH E6 Section 4.8)
- investigator's responsibilities (CFR Title 21 Part 312.60-312.70; ICH E6 Section 4)
- IND holder's responsibilities (CFR Title 21 Part 312.50-312.59; ICH E6 Section 5).

Regulatory compliance can be aided by use of institutional standard processes to establish control and safety. The Joint Commission includes investigational drugs in the Medication Management Standards, and the American Society of Health-System Pharmacists (ASHP) provides Guidelines on Clinical Drug Research.^{5,6} IDSs should maintain and adhere to standard operating procedures (SOPs) detailing the proper acquisition, storage, dispensing, labeling, distribution, and disposal of investigational medications.

Investigational Drug Service Responsibilities

Institutions Conducting Clinical Trials Using Investigational Medications Should Establish an IDS.

The purpose of an IDS is to support clinical investigators by providing general pharmaceutical review of the protocol and informed consent, developing investigational medication information for study personnel, and obtaining, storing, dispensing, and returning medications used in clinical research studies. The IDS should be part of the conduct of clinical trials in both the inpatient and outpatient settings. Pharmacy personnel are best suited for providing comprehensive services; however, an IDS can include other research professionals.

IDS General Best Practices

The IDS Should Develop Policies and Procedures for Investigational Medication Management.

The IDS should coordinate the procurement and dispensing of all investigational and commercial products (sponsor-provided) used in a research protocol. The IDS should develop SOPs to ensure compliance and consistency with policies and procedures. SOPs also allow others to follow the same procedures if the primary IDS staff is not available. The policies and SOPs should include

1. Investigational medication inventory control
 - a. Study initiation
 - b. Investigational medication acquisition
 - c. Accountability
 - d. Study closeout
2. Storage and handling of investigational medication
 - a. Safe handling
 - b. Temperature monitoring
3. Preparation and dispensing of investigational medication
 - a. Labeling
 - b. Blinding
 - c. Protocol compliance
4. Investigational medication disposal and destruction or return
5. Investigational medication management
 - a. Transferring investigational medication between protocols
 - b. Using patient's own investigational medication
 - c. Using an investigational medication from another institution
6. Investigational medication shortages

The IDS Should Be Responsible for Investigational Medication Inventory Maintenance for Research Protocols.^{4,7}

The IDS must be able to account for each dose of medication it receives, dispenses, disposes, transfers to another site, or returns to the pharmaceutical sponsor.

The IDS is responsible for maintaining adequate levels of study medication for the duration of the trial. A survey conducted in 1997 by ASHP⁸ reported that maintenance of drug accountability record forms (DARFs) is the service most often provided by pharmacies to clinical investigators. The inventory may be maintained on paper; however, an electronic inventory system is recommended.

The standard for medication accountability should be consistent with the information as it pertains to 21CFR312 Subpart D and the FDA's Compliance Guidance Manual for drug accountability requirements.⁹ Whenever possible, barcodes should be incorporated into the inventory, dispensing, and administration process.

Electronic or paper DARFs should include the following information:

- name of investigator
- name of investigative site
- dispensing location
- protocol number
- full protocol title
- medication name, strength, formulation
- transaction types
 - medication receipt (date, quantity, lot number/medication kit ID), if applicable
 - medication dispensing (subject information, date, quantity, lot number/medication kit ID)
 - medication transfer, undispensed medication disposition (i.e., transfer, return, disposal/destruction)
- recorder's initials and date
- unused, patient-return medication information can be captured as applicable per institutional policies and procedures.

Sponsor-based DARFs, however, need to meet federal requirements. DARFs should be maintained in a real-time environment (i.e., each event should be recorded on the day it occurred).

The IDS Should Establish Policies and Procedures for Tracking Expiration Dates of Investigational Medications.

The IDS should maintain a method for tracking expiration or retest dates of investigational medications at its site. Labeling of expiration dates for investigational medications is not part of the labeling regulations outlined in CFR Part 312. The sponsor is ultimately responsible for providing

each investigational site the investigational product's expiration date; however, each site should perform its own due diligence in this area.

The IDS Should Use Computer Software for Investigational Medication Management.

Use of IDS computer software offers many advantages, such as improved safety, efficiency, quality, and compliance. Investigational sites may decide to create their own electronic DARF or purchase one that is commercially available. All software used for investigational drug accountability must meet FDA 21 Part 11 compliance and accountability should be consistent with the information as it pertains to 21CFR312 Subpart D and the FDA's Compliance Guidance Manual for drug accountability requirements.^{9,10} FDA 21 Part 11 guidance requires the investigational site to perform its own assessment of each electronic program used in the conduct of the clinical trial. If an electronic system is used, then a down-time procedure should be developed in case the system is unavailable.

Other considerations in the choice of a software package include features related to managing change control, medication dispensing, labeling, barcoding, and accountability record printing. The IDS computer software can also provide a mechanism to bill and charge for the services provided on a clinical trial through the course of the study.

The IDS Should Develop Policies Regarding Prospective, Periodic Investigational Medication Audits.

Periodic audits ensure that a study is being conducted in an appropriate manner and follows federal and state laws, sponsor or network group requirements, and institutional policies and procedures. An IDS audit includes reviewing medication accountability, shipment, transfer, destruction, and return forms; conducting a physical inventory; checking for expired medications; and assessing the storage and security of investigational agents. Audits may be internal (conducted by the investigational site) or external (conducted by the sponsor, an outside contractor hired by the sponsor, or the FDA).

The IDS should establish procedures to conduct periodic DARF audits. If study medication is transferred to another location or satellite site for dispensing, these records must be obtained by the control dispensing location and closely reviewed. Siden and colleagues¹¹ published a management consultation for preparing for clinical audits. They recommend the use of an audit checklist to help sites prepare and include an example in their publication. Other resources are available that are helpful for developing audit checklists.^{9,12}

The IDS Should Establish a Procedure to Assess Investigational Medications as Hazardous Agents.

Prior to opening a study, each investigational agent should be reviewed to determine the appropriate storage, preparation, dispensing, disposal, and transportation requirements. Information related to the agent can be found in the investigator's brochure, the safety data sheet, or the protocol. It is the responsibility of the sponsor to provide this information to the pharmacy. The institution should have a standard policy for addressing the handling of hazardous substances.

The IDS Should Develop a Policy for Investigational Medications that Includes Storage, Returns, and Disposal.

The IDS is responsible for maintaining and documenting appropriate storage conditions for the investigational medication during the entire conduct of the study protocol. Access to the IDS is restricted to essential personnel. All investigational medication should be stored in a designated, secure area separate from non-investigational medications and according to the manufacturer's instructions.¹³ Appropriate storage conditions should be reviewed by the study monitor, if applicable to the protocol, at each visit to the IDS.⁴ Investigational medication may be provided in more than one strength for a trial. In addition, an IDS may have several studies open using the same investigational medication. It is essential to separate the medication by different strengths and by protocol. Patient-returned hazardous medication should be disposed of or returned to the sponsor immediately upon reconciliation. The site should follow standard procedure for disposal of hazardous medication.

The IDS Should Establish Policies and Procedures to Perform Continuous Temperature Monitoring and Reporting.

Investigational sites must provide continuous, around-the-clock monitoring of storage temperatures. This requirement also applies to any remote or satellite sites storing investigational medication. Standard definitions of temperature ranges and excursions should be consistent with USP definitions for storage conditions. Temperature monitoring can be accomplished by using minimum/maximum thermometers, which record the lowest and highest temperatures reached in each 24-hour period, using continuous temperature graph wheels, or purchasing a continuous monitoring system. The temperature monitoring system must also be able to alert an individual if a temperature excursion occurs (i.e., if a storage temperature goes out of range). The IDS should also have a planned outlined for a down-time procedure if the primary monitoring system is unavailable.

Each IDS must have a response plan outlined for temperature excursions affecting investigational medications. If a temperature excursion occurs, investigational medications must be quarantined, and the study sponsors must be notified by the site. Quarantined investigational medi-

cation cannot be used to treat a patient until the sponsor approves its use following a temperature excursion.

The IDS Should Develop Policies and Procedures to Establish Fees for Using the IDS.

The IDS should establish a budget for each protocol based on the costs for pharmacy services and supplies including, but not limited to, personnel costs, maintenance, preparation, and distribution of the investigational medication for each study. The IDS pharmacist should review the protocol, the investigator's brochure, and the pharmacy manual, if applicable, to create a proposed pharmacy budget for each study. The proposed pharmacy budget should be provided during the development period for each study to whomever the IDS will be receiving the reimbursement from (e.g., directly from the sponsor, from the institution's research office, or from the principal investigator at the institution). Budgeting for IDS fees will vary across institutions. The following are recommended items for consideration during budgeting for clinical trials and services that involve pharmacy:

- initiation or setup fee
- annual fee
- drug costs (i.e., procurement costs, special handling costs)
- dispensing fees
 - labor per dose dispensed
 - supplies per dose dispensed
 - mailing costs
- inventory management fee
- clinical service fee
- study closeout fee.

The IDS Should Participate in Sponsor Visits.

The protocol sponsor, who may be an on-site investigator, may conduct site initiation visits, study monitoring visits, and closeout visits. During the site initiation visit, details regarding the institution's expectations for sponsor visit, initial supply shipment, resupply procedures, storage, preparation for dispensing and handling, investigational medication accountability requirements, procedures for medication destruction or returns, and storage temperature documentation requirements will be discussed. The pharmacy's SOPs should be reviewed to ensure that the sponsor is aware of the site's requirements. Training materials should be obtained during this visit for the pharmacist to use to adequately train staff.

The IDS Should Create a Process for Coordinating Studies Across Multiple Sites.

The IDS may be requested to coordinate treatments at multiple sites. This coordination may include delivery and administration of investigational doses at another location or

the actual storage, dispensing, and administering of investigational medication at another site. SOPs must be in place to outline how this coordination will occur. If investigational medication is being stored at other locations, then the IDS must have a process in place for auditing remote sites.

The IDS Should Develop Policies and Procedures for Mailing Investigational Medications.

Each IDS should have an SOP outlining how and when investigational medications can be mailed to patients who are unable to come into the clinic.¹⁴ Study sponsors may or may not permit secondary shipment of investigational medications directly to patients. Important items to consider when shipping investigational medications are

- transportation regulations pertinent to the investigational medication
- the ability to maintain the agent at an appropriate temperature and monitor temperature during the shipping process
- where the shipment should be sent (i.e., the patient's home or the physician's office)
- how the shipment will be tracked through the delivery process.

The IDS Should Establish Institutional Policies and Procedures for Allowing the Use of an Investigational Medication from Another Institution.

Even if a location does not participate in clinical trials, patients who are on investigational trials may be admitted to a hospital or receive treatment at the location. Institutions should therefore establish policies for using investigational medications that are not currently studied at that institution, and the policy should incorporate, and be consistent with, the institution's policy to allow patients to use their own medication while admitted to the institution.

An important part of this process is allowing the hospital where the patient is admitted to find information regarding the investigational medication. This can be accomplished by providing the patient with an appropriately labeled medication that contains a phone number for the study site. The investigational site can then provide the necessary documents for the hospital, including a copy of the informed consent document and applicable study medication information following confirmation of appropriate Health Insurance Portability and Accountability Act (HIPAA) authorization.

The IDS Should Assist the Principal Investigator with Study Closeout.

According to CFR Title 21 Volume 5 Part 312.59, the sponsor shall ensure the return of all unused supplies of the

investigational medication from each individual investigator whose participation in the investigation is discontinued or terminated.¹⁵ A sponsor may require that the unused study medication be returned to the sponsor or sponsor's designee or that it be locally destroyed with permission per site policy. The sponsor should be provided, upon request, with copies of the final medication accountability log and record of destruction because the sponsor maintains written records of any disposition of the medication, in accordance with CFR Title 21 Volume 5 Part 312.57.¹⁶ Records must be retained by the investigator for 2 years after a marketing application is approved for the medication (for the indication for which it was investigated) or, if an application is not filed or not approved for the medication, for 2 years after the investigation is discontinued and the FDA is notified.¹⁶

IDS Best Practices for Prescribing Investigational Medications

The IDS Must Ensure That Protocol Information Is Available to Essential Pharmacy Personnel at the Time of Prescribing.^{17,18}

IDS personnel involved in clinical trial implementation must have real-time access to the current study protocol, investigator's brochure, pharmacy manual, and safety data sheets. The IDS must ensure that the most current IRB-approved versions of both the protocol and the investigator's brochure are available for reference when dispensing medications.⁶ This information can be made available electronically on secure Intranet servers; this practice facilitates updating the information and avoids delays typically associated with distributing paper copies. If electronic systems are used, a procedure should be developed to make this information available during system down times.

The IDS Should Train Pharmacy and Relevant Study Team Personnel.

All pharmacy staff involved in activities related to medications used in clinical research should receive standardized training on the relevant institutional policies and procedures, as determined by the IDS. Pharmacy personnel should be instructed on how to access all medication information documents so that they are able to answer questions and perform tasks related to provision of patient care for that protocol. Documentation of training and competency assessment should be maintained in the protocol or pharmacy regulatory folder. As part of education, pharmacists should consider educating nursing staff and relevant study team members within the scope of the training related to the investigational medication.

The IDS Should Establish and Maintain a List of Authorized Prescribers for Each Investigational Medication.

Prescribing for all medication in the clinical trials must be restricted to the authorized prescriber only. The investigator and IDS must have a proper communication plan for notifying the IDS and other relevant staff members of authorized prescribers for an investigational trial to ensure that study products are prescribed only by authorized prescribers for the study. It is the responsibility of the sponsor or physician to ensure that FDA 1572 forms for investigators are maintained and updated as needed. For those institutions that use computerized prescriber order entry (CPOE) and configuration settings allow, only authorized prescribers should be given access to investigational medication protocol order sets.

The IDS Should Create Protocol-Specific Medication Order Templates for Prescribing Investigational Medications.¹⁸⁻²⁰

Standardized order sets or templates for clinical trials can improve compliance with recommended processes of care, promote complete orders, ensure compliance with protocol-specific dosing regimens, and promote patient safety. Procedures should be established for independent review, preferably by the principal investigator, prior to activation of the order set and also for maintenance as a result of protocol amendments.

Order sets should be formatted according to the institutional form and order set guidelines, and at a minimum the following information should be included:

- protocol title and institutional study number
- name of the principal investigator and principal investigator's contact information
- patient identifiers
- protocol-defined dose calculations (e.g., weight to be used, body surface area (BSA) calculation formula, area-under-the-curve formula) or dose-rounding requirements
- dose modifications
- supportive care medications, including premedications and hydration
- laboratory parameters required prior to treating the patient on the particular day of the treatment (i.e., the acceptable timeframe for obtaining the lab values)
- pertinent information in categories such as drug interactions, food requirements, venous access device requirements, research-specific procedures, and instructions the treatment nurse should provide to the patient
- monitoring parameters before and after administration of the medication
- date and time of the order and signature of the authorized prescriber.

When CPOE Is Used, Clinical Decision Support Should Be Incorporated into Electronic Investigational Medication Ordering.

CPOE with clinical decision support systems (CDSSs) can help reduce medication-related errors if investigational agents are ordered through such a system. All clinical decision support for investigational medications should be protocol-specific. Considerations for CDSSs should include an alert to confirm patient registration, dose calculations and limits, drug allergy checks, drug–laboratory value checks, and drug–drug interaction checks. Research order sets should be inactivated in the system when the study is complete.

IDS Best Practices for Dispensing Investigational Medications

The IDS Should Facilitate the Dissemination of Investigational Medication Information.

Prior to the opening of a study, each investigational agent should be reviewed to determine the appropriate acquisition, storage, preparation, dispensing, destruction, and transportation requirements. Information related to the agent can be found in the investigator’s brochure, the safety data sheet, or the protocol. The IDS should facilitate the preparation of a document that outlines medication preparation and pertinent information related to dispensing. The data sheet should be developed for each investigational medication; this practice allows the pharmacy to prepare the investigational medication properly and serves as a resource for answering questions about the investigational medication. These data sheets may be based on the ASHP Guidelines for Clinical Drug Research⁶ and suggestion for information to be included can be the following:

- medication designation
- common synonyms (i.e., names to be used in prescribing and labeling of the investigational agent)
- dosage forms and strength
- pharmacology
- pharmacokinetics
- usual dosage range
- dosage schedule
- preparation information
- route of administration
- storage information
- dispensing information
- administration instructions
- appropriate monitoring
- expected therapeutic effect to be studied
- expected and potential adverse events
- potential toxicity prevention and treatment regimens
- symptoms of toxicity and their treatment
- medication-medication and medication-food interactions
- contraindications

- special precautions required for handling the medication
- names and telephone numbers of principal and authorized subinvestigators
- correct disposal methods for unused doses.

Checklists or study-specific reference sheets applicable to the task being performed can be created to ensure consistent processes for all employees working in the investigational pharmacy.²¹

The IDS Should Establish Policies to Ensure Adequate Investigational Medication Order Review and Verification.

Investigational medications should be considered high-risk medications and must be reviewed in the context of the protocol and patient treatment assignment (i.e., treatment arm and dose). The patient profile should be reviewed each time a new order is received. Double checks are vital to the preparation and dispensing process for such agents. For the purposes of safety and accuracy, each institution should have a policy that identifies medications that require verification by a second pharmacist prior to dispensing. The verification process should be clearly documented. Pharmacists should ensure that chemotherapy is prescribed and dispensed according to such policy.

Prior to dispensing investigational or chemotherapeutic agents on the trial, pharmacists should verify that patients have signed the appropriate consent forms and that prescriptions are signed by authorized prescribers. The chemotherapy orders, including medications, dosages, calculations, routes, and schedules, should be checked against the appropriate protocol. Height, weight, date of birth, and BSA should be included on the orders.

In addition, a second verification should be made for each order entry in the computer system. The verifying pharmacist should make every effort to verify orders without interruption. Pharmacists should verify the BSA, dosage calculations, treatment plan, and any other pertinent information provided by the first pharmacist. Pharmacists should inspect the computer label for accuracy. Pharmacists should check the finished product and verify the amount used to reconstitute, the amount of medication withdrawn, and the amount added to the bag, number of tablets or capsules, or volume of medication dispensed. Ideally, the final product should be checked by two pharmacists; however, the final product should be checked by at least two people (e.g., pharmacist and nurse, pharmacist and prescriber). The pharmacist checking the final product ensures that all required checks have been completed prior to the dispensing.

The IDS Should Establish a Process for Informed Consent Verification.²²

To comply with CFR Title 21 Part 50 and prior to dispensing any investigational medications, pharmacists must

have a method for verifying that a patient has consented to participate in the clinical trial.²³ Consent verification can be performed by direct observation of the consent document or through the central patient registration system. The registration system should be designed to improve communication among study team members, store subject enrollment information in a secure location, and run real-time reports. The system should support electronic eligibility checklists and track signed consent forms, patient randomization information, dose-level assignment, and study sponsor information. The system also should support the ability of individual centers participating in a multisite study to retrieve information from a centralized resource.

The IDS Should Establish Investigational Medication Labeling Policies.

Pharmaceutical research sponsors follow federal requirements for product labeling that are outlined by the FDA in Part 312—IND Application.⁷ According to these guidelines, investigational medication containers and packaging must include the following language: “Caution: New drug—Limited by federal or United States law to investigational use.”

Clinical research sites in the United States should follow all applicable state and federal guidelines for medication compounding, dispensing, and labeling, including United States Pharmacopeia (USP) 797 and the Joint Commission standards. However, institutional labeling requirements, when stricter than state and federal requirements, should supersede individual sponsor requirements.

Any location responsible for compounding intravenous (IV) medication must also be familiar with the requirements of USP 797.²⁴ All investigational pharmacies should have SOPs and annual training to ensure USP 797 compliance.

The IDS Should Establish Dispensing and Labeling Requirements for Oral Investigational Medications.

State boards of pharmacy may have specific labeling requirements for oral medications, such as the name, address, and phone number of the dispensing location; name and strength of the medication in the container; instructions for dosing; and quantity dispensed. This information also is useful when the patient is seen by an outside physician or admitted to an outside hospital because it allows the investigational site to be contacted for study-specific information.

Each site should also have SOPs in place addressing how oral investigational medications will be dispensed to the patient. Those writing these SOPs should consider whether a site will dispense additional doses to a patient and whether the medication will be dispensed in the sponsor-provided container or be repackaged. The primary difficulty most

sites face when required to dispense a product in its original container is the ability to place their own package labeling on the container provided by the sponsor. The ASHP guideline on clinical medication research recommends that pharmaceutical sponsors leave ample space on the medication product container to allow further labeling of the product by the pharmacist.⁶

In 2011, Goodin and colleagues published a clinical practice guideline on the safe handling of oral chemotherapeutic agents.¹² Even though this guideline is not specific to investigational medications, it provides an excellent overview of recommendations on safe handling of oral chemotherapy medications.

The IDS Should Establish Procedures to Dispense Investigational Medications for Single- or Double-Blind Studies.

In randomized trials, IDS dispensing procedures may be conducted in a single-blind or double-blind manner. In a single-blind trial, the IDS can be unblinded and responsible for performing patient randomization. Pharmacists should obtain the necessary randomization information from the sponsor or the study staff. Randomization tables can be either electronic or paper. If electronic, the table should be password protected, with access limited to IDS staff. Caution should be taken during communication of subject information to blinded individuals so as not to inadvertently disclose treatment arm or randomization information. The dispensing procedures should be carried out in such a manner that the investigational medication appears identical regardless of the treatment assignment. Emergency unblinding procedures should be defined in the protocol or an ancillary document and typically require that the investigator contact the sponsor.

Double-blinded dispensing procedures may differ in that the IDS may also be blinded to the treatment assignment. The IDS is typically provided with patient-specific supplies or individual kits containing either active drug or matching placebo. In this case, the checking process for the investigational medication should also include verifying patient ID numbers or kit numbers.

IDS Best Practices for Administering Investigational Medications

The IDS Should Identify Administration Information Required by Investigational Medication Sponsors.

Sponsors often request that particular information regarding investigational medication administration be captured. For instance, the start and stop times of IV investigational medications should be recorded for all administrations. A total volume administered should also be recorded. Investigational sites should have an SOP to ensure that patients

receive the complete dose of study medication and that appropriate flushing of IV tubing occurs. Administration information can be obtained from the medication administration record and would be in the scope of the nursing responsibility. Pharmacy can assist in the process and facilitate medication-based questions.

For oral medications, a dosing time should be recorded in the electronic medical record for each in-clinic dose. Dosing of oral medications outside the clinic should be recorded in a patient-specific medication diary, which should be reviewed each time the patient is in the clinic.

The Pharmacist's Role in Investigational Studies Across the Protocol Life Cycle

Pharmacists should be involved in all parts of the protocol life cycle. The following sections provide specific roles for pharmacists when the pharmacist either is part of an IDS or is working directly with a research team.

Pharmacists' Best Practices for Protocol Development

Pharmacists should participate in protocol development by writing or reviewing the pharmaceutical sections in the protocol, consent and supporting documents (e.g., medication diaries, the pharmacy study manual, drug information sheets). The protocol and informed consent documents are approved by scientific review committees (SRCs) and IRBs using a multidisciplinary approach. The SRC focuses on the scientific aspects, while the IRB focuses on the safety aspects, however these research components are integrated.

Pharmacists Should Develop the Medication Information Section for the Protocol.

Depending on the study sponsor, pharmacists can create the medication information section for the protocol to ensure that the preparation, dispensing, and administration of the investigational medication comply with each institution's policies and practices. This step will also ensure that the recommended administration devices and tubing sets are acceptable to the institution.

The medication information section should include

- source/supplier
- how supplied
- reconstitution (if applicable)
- preparation and dispensing
- storage, returns, and disposal
- stability
- compatibility
- administration
- contraindications
- drug interactions.

When it is not possible for the pharmacist to create the medication section—for example, in an industry-sponsored trial where this section may be provided by the pharmaceutical company—a pharmacist should review this section to ascertain that the institution can prepare the drug as described.

Pharmacists Should Provide Recommendations on Supportive Care to Meet Institutional Guidelines and Provide Consistency Within and Across Investigational Studies.²⁵

Pharmacists should recommend and monitor supportive care therapies for study protocols according to the institution's guidelines and study requirements. Special attention should be given to ensure that required and prohibited adjunct medications are appropriate. Pharmacists should make sure that study protocols requiring supportive care are consistent across all the studies and are based on standard hospital guidelines and the institution's formulary.

Pharmacists Should Participate in Scientific Review Committees.

The SRC is responsible for evaluating the overall scientific merit, priority, and feasibility of the trial. An IDS pharmacist or another pharmacist from the pharmacy department (e.g., a clinical pharmacy specialist) should be included in the SRC as an expert in the area of investigational medication information.

Pharmacy review is especially important with in-house or investigator-initiated clinical trials because a majority of investigators are unaware of the complexity and importance of investigational pharmacy's role in the clinical trial and compliance with federal regulations.

SRCs are responsible for assessing the scientific rationale, trial design, sample size, treatment plan and dosing, adverse events and dose modifications, and supportive care. Pharmacists involved in SRC review should focus on answering the following pharmacy-specific questions in addition to evaluating the trial's scientific merit and feasibility:

- Is the medication supplier defined and, if commercially available, who will be paying for the medication?
- Is an IND required for the medication as used in the protocol?
- Is medication information included for all therapeutic agents, including the investigational agents and any other chemotherapeutic agents used in the clinical trial? Is information consistent with the investigator's brochures or approved labeling?
- Is the medication administration procedure completely defined and easily understood? Is it acceptable to have a separate document (such as a pharmacy manual) detailing the instruction for preparation and

- administration of the investigational agent, provided that the protocol refers to such a document? Are treatment regimens for all arms of the study defined?
- Are dose modifications included, completely defined, and appropriate? Are the laboratory parameters that require dose modifications separately and clearly stated for each investigational agent and any other chemotherapeutic medications used in the trial?
 - If established, is the protocol consistent with the Risk Evaluation and Mitigation Strategies (REMS) program requirements and boxed warnings?
 - Are unanticipated problems, adverse events, and protocol deviations related to medication reporting guidelines included and clearly defined?
 - Are protocol-specific standard order sets required per institutional practice, and have research staff members been identified to deal with all aspects of the protocol?
 - For multicenter studies, is the coordinating center identified, is medication distribution clearly defined, and, if applicable, has the pharmacy budget been addressed?

Pharmacists Should Participate in IRB Protocol Reviews.^{25,26}

The research protocol must be submitted to a research ethics committee for consideration, comment, guidance, and approval before the study begins. CFR Title 21 provides detailed guidelines on the formation, structure, and role of the IRB in clinical research. The IRB is responsible for safeguarding the rights and safety of human subjects participating in clinical research. IRB approval is required prior to any subject enrollment or screening.

Pharmacists who participate in IRBs should evaluate each protocol for adherence to the following guidelines:

- All medication information, including dosing, interactions, preparation and dispensing, and patient counseling, is included.
- Aspects of the consent forms related to medication are consistent with protocol.
- Risks from medications are described accurately and are reasonable in relation to anticipated benefits.
- Guidelines for reporting adverse medication reactions are included and are clearly defined.

Pharmacists serving on IRBs also are liaisons between IRBs and pharmacy departments or IDs after the protocol is approved by an IRB. IRB pharmacists should serve as a source of information for all IRB-approved studies at an institution.

Pharmacists Should Review All Medication-Related Information Used in the Informed Consent Process.²⁰

Pharmacists should closely review the informed consent forms to make sure that all medication-related information

- is complete and understandable. The consent form should
- indicate the phase of the trial and explain what the treatment plan entails in terms of the length of therapy and expectations for patient follow-up
 - indicate if any patient costs or insurance coverage are necessary
 - explain to the participant the rationale for comparing or testing the medications
 - provide as much information as is appropriate and understandable about the medication, such as its manufacturer or place of manufacture and the reason for its development
 - explain the known experience with this medication in preclinical or clinical studies
 - explain all the known side effects and toxicity of the medication, as well as the adverse events of all the other medications being used in the trial
 - describe any applicable tools for documenting medication adherence
 - inform participants about the significance of randomization or blinding (if applicable) and their odds of receiving a particular medication (e.g., each participant has one in four chances of getting the study medication)
 - explain and describe possible or anticipated risks; describe the level of care that will be available in the event that harm does occur; and specify who will provide it and who will pay for it.
 - If applicable, explain the need to avoid certain medications while on the study and the rationale for why these medications need to be avoided.

Pharmacists' Best Practices for Patient Counseling and Monitoring

Patients who are participating in clinical trials must be carefully counseled and monitored for adverse events, compliance with study-related procedures, and adherence to investigational medication administration schedules. Everyone involved in the investigational process is responsible for patient monitoring.

Pharmacists Should Provide Medication Counseling for Patients Receiving Investigational Medications.

Pharmacists should counsel patients receiving investigational medications about the requirements of a clinical trial, medication dosing and administration, anticipated side effects, and medication safe handling and storage. For self-administered agents, the patient should also be counseled on what to do if a dose is missed at the scheduled time. Patients should also be made aware of any medications that are contraindicated while they are in the study, and they should be instructed to contact the clinical site

prior to starting or stopping any medication. Patient education should occur throughout the study. This is especially crucial for patients receiving oral investigational medications. Appropriate dosing should be reviewed with the patient during each clinic visit. All patients should be provided both a daytime number and an emergency number of someone they can contact about any questions they have or issues that arise while they are in the study.

Pharmacists Should Assess Medication Adherence.

Patient adherence for self-administered oral and parenteral medications must be assessed for clinical trials. Each patient should be assessed for the ability to understand and follow dosing instructions prior to entering the trial. Ideally, the protocol should specify the method for assessing adherence. Protocols can include medication diaries, either paper or electronic, and patients should be instructed on their use. Family members may have to be asked to assist in ensuring patient compliance with investigational medication dosing. Patients should bring their medication diaries along with their investigational medication to each clinic visit.

Pharmacists Should Participate in Reporting of Unanticipated Problems, Adverse Events, and Protocol Deviations.

Unanticipated problems should be reported in accordance with Office for Human Research Protections regulations and institutional guidelines. Procedures should be in place to continuously monitor patients for adverse events during protocol treatment. Monitoring may include a review of laboratory data, concomitant medications, and any self-reported patient complaints. The seriousness of medication-related problems and requirements for reporting them should be defined in the investigational protocol. Medication-related protocol deviations should be reported in accordance with protocol requirements and reporting guidelines.

The Pharmacy Technician's Role in Investigational Medication Management

Institutions Should Define a Pharmacy Technician Role for the IDS.

The pharmacy technician plays a vital role in the operation of the IDS. In addition to helping with the more traditional role of investigational medication preparation, pharmacy technicians also support the IDS pharmacist by adhering to the various regulatory requirements and maintaining the documentation needed to run clinical research trials. The use of pharmacy technicians in an IDS can allow the pharmacist to focus on other duties such as protocol review

and research order management as well as extend clinical services to study patients.

Minimum Qualifications Should Be Established for Pharmacy Technicians to Practice in the IDS.

The IDS provides a unique opportunity for hospital-based technicians seeking specialized training. Because the IDS is a specialty within pharmacy, the institution should establish minimum qualifications and competencies for a technician to work in the IDS.

Pharmacy Technicians' Duties Should Be Established to Facilitate IDS Operations.

Where applicable, a separate IDS technician position description or a supplement to an existing pharmacy technician description should be developed. Typical duties include the following:

Assist with Investigational Medication Preparation

One of the primary roles of an IDS pharmacy technician is to assist with the preparation of injectable and oral investigational medications. Preparation of injectable investigational medications involves more complex calculations; pharmacy technicians should be able to correctly perform any mathematical calculations required.

Pharmacy technicians also can assist with dispensing an oral investigational agent by generating pharmacy labels and filling the prescription prior to pharmacist verification.

Assist with Investigational Medication Accountability

The pharmacy technician can assist the IDS pharmacist in maintaining the appropriate required accountability records by documenting inventory, lot numbers, and expiration or retest dates, and retest dates. The pharmacy technician can also document agent receipt, dispensing, disposition, and patient returns of investigational medications.

Monitor Storage Conditions

The pharmacy technician can assist with maintaining the necessary temperature monitoring logs required by study sponsors. In the event of equipment malfunction, pharmacy technicians can help coordinate the transfer of investigational agents to functioning equipment in an organized manner and follow up with appropriate documentation for affected clinical trials. They can also manage the return or disposal of temperature-recording devices sent by study sponsors.

Order Investigational Medication Supplies and Handle Returns

Pharmacy technicians can help maintain appropriate inventory levels of study medications as well as maintain non-study-provided inventory for use in clinical trials. They can also ensure that medications are returned and accounted for as required by the study sponsors or at study closure. When receiving and procuring study inventory, they can ensure that properly received medications are checked in

accurately and that the issue of damaged inventory is addressed with the provider of the study medication. Pharmacy technicians can also help maintain an orderly medication inventory to minimize the risk of dispensing errors, separating like inventory or multiple strengths and formulations within the same clinical trial.

Assist with On-Site Visits and Audits

Pharmacy technicians can assist the IDS pharmacist with correspondence and with hosting of on-site monitoring visits. They can facilitate access to regulatory paperwork and field questions regarding drug procurement, preparation, storage, and maintenance of required regulatory pharmacy documents. They can also help prepare for audits by reviewing the accuracy of inventory and pharmacy records prior to any scheduled visits. During the study initiation phase, the technician can assist the pharmacist with organizing the pharmacy study binder, identifying pharmacy needs, and coordinating sponsor processes for the management of study agents.

Expanded Access to Investigational Medication

Expanded access, as defined by the FDA, is the use of an investigational medication (IND agent) outside of a clinical trial for the sole purpose of patient treatment. This access is limited to patients with a serious or immediately life-threatening disease or condition who have exhausted commercial treatment options or have no comparable or satisfactory alternatives (i.e., clinical trials). Currently, FDA regulations define three categories of expanded access based on population size: individual patient (including those using the IND on an emergency basis), intermediate patient population, and large patient population (those receiving a treatment IND or participating in a treatment protocol). According to annual data on the total number of emergency IND/IDE filings, the FDA received 35 in FY 2012.

Interest in these mechanisms has increased during the past few decades as a result of the vast amount of information publicly accessible through the Internet and the consolidated efforts of advocacy groups across the country. The use of investigational medications through an expanded access mechanism presents a number of challenges for pharmaceutical and biotechnology companies, as well as investigators. These mechanisms can also present challenges for company and institutional regulatory personnel, the drug-supply chain, and investigators' staff at the institutional level. The requirements for regulatory reporting are similar to those of large-scale development programs. As a result, these requirements could present a significant unanticipated workload for a number of parties involved in the process. The company perspective also includes questions about the impact of expanded access release on drug

supply and the overall development program (e.g., impact on clinical trials) of the compound. These factors need to be considered when the IDS team is evaluating expanded access treatment options for patients. The IDS team plays an important role in researching and supporting expanded access options for patients who have exhausted commercial and clinical trial alternatives. Although the use of expanded access mechanisms will likely be a small part of any IDS practice, one should be familiar with some of the available resources and the differences between expanded access and clinical development.

The IDS Pharmacist Should Be Familiar with Resources Used to Locate Expanded Access Protocols When Other Options Have Been Exhausted.

Investigational agents released under an expanded access mechanism are still bound by all of the IND regulations under CFR Part 312. Depending on the type of treatment IND, the IDS will have different responsibilities. (Medication accountability and handling are discussed in earlier sections of this document.)

Several resources for locating expanded access protocols are listed below.

- www.clinicaltrials.gov: A searchable list of federally and privately sponsored clinical trials (search "expanded access")
- NCI's Physician Desk Query (www.cancer.gov/clinicaltrials): a list of oncology trials sponsored by the National Cancer Institute
- NCI's Treatment Referral Center (http://ctep.cancer.gov/branches/pmb/referral_center.htm): NCI pharmacists can provide clinical trial searches and references to available expanded access protocols.
 - NCI special exception program: May provide single-patient expanded access to agents in the NCI portfolio of agents. The NCI would act as the sponsor for the single-patient IND and handle FDA regulatory issues. The clinical site will still be responsible for site-level regulatory issues (e.g., generation of treatment protocol, informed consent, and IRB review).
- Company-specific websites

The IDS Pharmacist Should Determine Whether the Medication Manufacturer Is Willing to Make the Agent Available Through a Single-Patient IND.

If an intermediate or large expanded access protocol is not available, the provider or pharmacist should contact the medication manufacturer to determine whether the medication is available on a single-patient basis. Manufacturers are not required to make their medication available through expanded access or to make medications for that purpose.

The IDS Pharmacist Should Verify FDA and Local IRB Approval for Use of the Medication Through Non-Emergency Expanded Access.

Expanded access protocols must be reviewed and approved by the FDA and IRB prior to treatment of patients. Documentation of approval and the current version of the protocol and consent should be filed with the IDS. These documents should be readily accessible for reference by pharmacy personnel during the handling and preparation of the investigational agent.

The IDS Pharmacist Should Verify FDA Approval and Local IRB Notification for Use of the Medication Through Emergency Expanded Access.

FDA regulations permit emergency use of an investigational agent without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify to the appropriateness of the request (21 CFR 50.23).

When an investigational agent is being used under the emergency-use mechanism (21 CFR 312.310d), FDA approval must be obtained (a verbal approval is permitted). Treatment may begin without prior IRB approval or patient consent, provided the IRB is notified of the emergency treatment within 5 working days of treatment (21 CFR 50.23). IRB acknowledgment should be requested and maintained for IDS pharmacy records. Subsequent request to use the same agent will require full IRB approval.

The IDS Pharmacist Should Be Familiar with the FDA and NCI Websites Regarding Expanded Access.

- Guidance on expanded access and charging for expanded access: www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm172492.htm
- Expanded Access page (FAQ): www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccessToInvestigationalDrugs/ucm176098.htm
- Information on treatment use: www.fda.gov/RegulatoryInformation/Guidances/ucm126495.htm
- Instructions for individual patient IND requests: www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm107434.htm
- NCI treatment referral center: http://ctep.cancer.gov/branches/pmb/referral_center.htm

Conclusion

It is critical that institutions participating in clinical trials establish an IDS. Pharmacists and pharmacy technicians play a crucial role in investigational studies across the protocol life cycle. The *HOPA Investigational Drug Service Best Practice Standards* presents expert recommendations on uniform practices in investigational medication management and the establishment of an IDS to provide guidance to institutions that use investigational medications in clinical research.

References

1. Hematology/Oncology Pharmacist Association. *Scope of Hematology/Oncology Pharmacy Practice*. Chicago, IL: Author; 2013. www.hoparx.org/uploads/files/2013/HOPA13_ScopeofPracticeBk.pdf. Accessed January 30, 2014.
2. U.S. Food and Drug Administration. Code of Federal Regulations Title 21. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm. Accessed July 26, 2013.
3. U.S. Food and Drug Administration. Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs)—Determining Whether Human Research Studies Can Be Conducted Without an IND. www.fda.gov/downloads/Drugs/Guidances/UCM229175.pdf. Accessed January 30, 2014.
4. U.S. Food and Drug Administration, Department of Health and Human Services. International Conference on Harmonisation: good clinical practice consolidated guideline. *Fed Regist*. 1997;62: 25692-25709. www.gpo.gov/fdsys/pkg/FR-1997-05-09/pdf/97-12138.pdf. Accessed September 20, 2013.
5. The Joint Commission. Medication management. In: *Comprehensive Accreditation Manual for Hospitals*. Oakbrook Terrace, IL: Author; 2012.
6. American Society of Health-System Pharmacists. ASHP guidelines on clinical drug research. *Am J Health Syst Pharm*. 1998;55:369-75.
7. U.S. Food and Drug Administration. Code of Federal Regulations Title 21, Part 312—Investigational new drug application. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312. Accessed July 26, 2013.
8. Rockwell KJ, Bockheim-McGee C, Jones E, Kwon I-WG. Clinical research: National survey of U.S. pharmacy-based investigational drug services—1997. *Am J Health Syst Pharm*. 1999;56:337-344.
9. U.S. Food and Drug Administration. Inspections, compliance, enforcement, and criminal investigations. Part III—Inspectional. www.fda.gov/ICECI/EnforcementActions/Bioresearchmonitoring/ucm133569. Accessed May 30, 2014.
10. U.S. Food and Drug Administration. Part 11, electronic records; electronic signatures—scope and application. www.fda.gov/RegulatoryInformation/Guidances/ucm125067.htm. Accessed July 26, 2013.
11. Siden R, Tankanow RM, Tamer HR. Understanding and preparing for clinical drug trial audits. *Am J Health Syst Pharm*. 2002;59(23):2301, 2306, 2308.
12. National Cancer Institute. NCI guidelines for auditing clinical trials for the NCI National Clinical Trials Network (NCTN) Program, Community Clinical Oncology Program (CCOP)/NCI Community Oncology Research Program (NCROP) and research bases. http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/ctmb_audit_guidelines.pdf. Accessed June 6, 2014.
13. Goodin S, Griffith N, Chen B, et al. Safe handling of oral chemotherapeutic agents in clinical practice: Recommendations from an

- international pharmacy panel. *J Oncol Pract*. 2011;7(1):7-12.
14. McIntyre C. Regulations guiding the interstate shipment of investigational product. *J Pharm Pract*. 2014 Feb;27(1):101-105.
 15. U.S. Food and Drug Administration. Code of Federal Regulations Title 21, Part 312, Subpart D, Section 59 version date April 1, 2011. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312&showFR=1&subpartNode=21:5.0.1.1.3.4. Accessed July 26, 2013.
 16. U.S. Food and Drug Administration. Code of Federal Regulations Title 21, Part 312, Subpart D, Section 57 version date April 1, 2011. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312&showFR=1. Accessed July 26, 2013.
 17. Kloth DD. Guide to the prevention of chemotherapy medication errors: strategies to prevent chemotherapy errors. *Clinical Oncology News*. 2009;2:107-114.
 18. David JB, Ballard MD, Ogola G, et al. The impact of standardized order sets on quality and financial outcomes. www.ncbi.nlm.nih.gov/books/NBK43723/pdf/advances-ballard_12.pdf. Accessed July 26, 2013.
 19. Institute for Safe Medication Practices. Design of preprinted cancer chemotherapy order forms is critical for patient safety. *ISMP Medication Safety Alert!* 1996;1(3):2.
 20. Institute for Safe Medication Practices. Designing preprinted order forms that prevent medication errors. *ISMP Medication Safety Alert!* 1997;2(8):1-2. www.ismp.org/Newsletters/acutecare/articles/19970423.asp. Accessed February 7, 2014.
 21. Siden R, Tamer HR, Skyles AJ, Weadock S, Redic K. Pharmacist-prepared dispensing guidelines for drugs used in clinical research. *Am J Health Syst Pharm*. 2012;69:1021-1026.
 22. Sweet BV, Tamer HR, Siden R, et al. Improving investigational drug service operations through development of an innovative computer system. *Am J Health Syst Pharm*. 2008;65:969-73.
 23. U.S. Food and Drug Administration. Guidance for sponsors, investigators, and institutional review boards: informed consent elements, 21 CFR § 50.25(c). www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM291085.pdf. Accessed July 26, 2013.
 24. U.S. Pharmacopeia. USP 797 Guidebook to pharmaceutical compounding—sterile products. In: *U.S. Pharmacopeia*; 2008:1-99.
 25. National Comprehensive Cancer Network. *NCCN Guidelines for Supportive Care*. www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed July 26, 2013.
 26. U.S. Food and Drug Administration. Code of Federal Regulations Title 21, Part 56. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=56. Accessed July 26, 2013.

Suggested Reading

- American Society of Clinical Oncology. Quality assurance and educational standards for clinical trial sites. *J Oncol Pract*. 2008;4:280-282.
- American Society of Health-System Pharmacists. ASHP guidelines on clinical drug research. www.ashp.org/DocLibrary/BestPractices/PrepGdlHazDrugs.aspx. Accessed September 24, 2013.
- American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. www.ashp.org/DocLibrary/BestPractices/PrepGdlHazDrugs.aspx. Accessed July 26, 2013.
- American Society of Health-System Pharmacists. ASHP guidelines on preventing medication errors with antineoplastic agents. www.ashp.org/DocLibrary/BestPractices/MedMisGdlAntineo.aspx. Accessed September 24, 2013.
- Collaborative Institutional Training Initiative (CITI) website. www.citiprogram.org. This program is a subscription service providing research ethics education to all members of the research community.
- Shehab N, Tamer H. Dispensing investigational drugs: regulatory issues and the role of the investigational drug service. *Am J Health Syst Pharm*. September 1, 2004;61(18):1882-1884.

Additional Resources for Expanded Access

Office of Special Health Issues
10903 New Hampshire Avenue
Bldg. 32, Room 5367
Silver Spring, MD 20993
301.796.8460
OSHI@fda.hhs.gov



HOPA
Hematology/Oncology
Pharmacy Association

8735 W. Higgins Road, Suite 300
Chicago, IL 60631-2738
877.467.2791 • info@hoparx.org • www.hoparx.org