ISPE®

GOOD PRACTICE GUIDE:

# Investigational Medicinal Product Reverse Logistics

## *Good Returns and Reconciliation Practices*

GOOD PRACTICE GUIDE:

# Investigational Medicinal Product Reverse Logistics

## *Good Returns and Reconciliation Practices*

**Disclaimer:**
The *ISPE Good Practice Guide: Investigational Medicinal Product Reverse Logistics – Good Returns and Reconciliation Practices* provides best practices to help organizations effectively plan and implement reverse logistics policies and processes. This Guide is solely created and owned by ISPE. It is not a regulation, standard or regulatory guideline document. ISPE cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

*Limitation of Liability*
*In no event shall ISPE or any of its affiliates, or the officers, directors, employees, members, or agents of each of them, or the authors, be liable for any damages of any kind, including without limitation any special, incidental, indirect, or consequential damages, whether or not advised of the possibility of such damages, and on any theory of liability whatsoever, arising out of or in connection with the use of this information.*



ISBN 978-1-946964-45-8

# Preface

Every year the number of clinical trials conducted across the globe rises in a concerted effort to develop new or improved medicinal products that ultimately improve lives. Each trial is supported by dedicated professionals who work tirelessly to uphold the safety of the medicinal products being tested in the trial and to ensure the safety of those participating in the trial. Armed with regulatory guidance, the pharmaceutical industry has developed standards and best practices in almost every aspect of a trial. Additionally, as the pharmaceutical industry has evolved, medicinal products have changed from primarily single small molecules to include biologics, combination product/devices, and personalized medicines such as cell and gene therapies. With each innovation, the industry has typically established new best practices. Despite this progress however, there is one area that lacks foundational best practices: that of medicinal product accountability, reconciliation, and return for destruction, otherwise known as reverse logistics.

Most current reverse logistics processes lack effective planning, thorough application of risk management, and well-defined roles and responsibilities. This results in inefficient and costly processes that often cause delays in study closure as failure to account for study materials can affect the acceptability of trial data. Establishing better standards is also complicated by gaps in and lack of harmonization between Good Clinical Practice (GCP), Good Manufacturing Practice (GMP), local environmental laws and regulations, and import/export and customs regulations. Regulatory scrutiny exists and failure by a sponsor or investigator to maintain accurate, complete, and current records related to the receipt, use, and disposition of investigational products is frequently cited in findings such as US FDA 483 observations and warning letters.

As the industry continues to expand and regulators continue to modernize laws, reverse logistics will need to gather the needed attention and focus to escape from being the weak link in the clinical supply chain. The *ISPE Good Practice Guide: Investigational Medicinal Product Reverse Logistics – Good Returns and Reconciliation Practices* recommends best practices for consideration to improve reverse logistics processes.

# Acknowledgements

The Guide was produced by a Task Team made up of:

| | | |
|---|---|---|
| Neal A. Gordon, PhD | Merck & Co., Inc. | USA |
| Edward Groleau | PCI Pharma Services | USA |
| Catherine (Cat) Hall, MS, MBA | endpoint Clinical | USA |
| Greg Hottell | GSK | USA |

The work was supported by the ISPE Investigational Products Community of Practice (CoP). Input was provided by the Global Clinical Supplies Group (GCSG).

## Special Thanks

The Team would like to thank those that inspired us to complete this work including the ISPE European Investigational Products CoP who initially formed a task team in 2017 with this final output in mind. We would also like to thank the many reviewers of this document within our organizations and all of those that have asked the question can we establish a best practice for Investigational Products Returns and Reconciliation process.

The Team would also like to thank ISPE for technical writing and editing support by Jeanne Perez (ISPE Guidance Documents Technical Writer/Editor) and production support by Lynda Goldbach (ISPE Publications Manager).

Company affiliations are as of the final draft of the Guide.

*Cover photo (background): https://www.istockphoto.com.*


600 N. Westshore Blvd., Suite 900, Tampa, Florida 33609 USA
Tel: +1-813-960-2105, Fax: +1-813-264-2816

**www.ISPE.org**

# Table of Contents

# 1 Introduction

Reverse logistics is the process of planning, implementing, and controlling the efficient and effective inbound flow and storage of secondary goods and related information for the purpose of recovering value or proper disposal. Within the pharmaceutical industry, this is often referred to as Returns, Reconciliation, and Destruction (RRD). While sponsors spend a great amount of time and effort ensuring the security of putting investigational products into the hands of patients, often less energy is spent accounting for used and unused products within a trial. With an increased focus on how falsified products are entering the market, regulators have turned their attention to this portion of the supply chain, re-invigorating the industry to complete the final steps of an investigational product's journey, the one to its destruction.

## 1.1 Purpose and Scope

RRD processes are often clouded with uncertainty as they fall across the Good Clinical Practices (GCP)/Good Manufacturing Practices (GMP) boundaries. While regulatory guidelines (for example, US FDA CFRs [1], EU Annex 13 [2], and ICH E6 [3]) mention RRD, they fail to provide with any certainty who owns what, lacking best practices to guide decisions. The purpose of this *ISPE Good Practice Guide: Investigational Medicinal Product Reverse Logistics – Good Returns and Reconciliation Practices* is to provide further clarity from across the industry on what best practices exist, what nuances can be important to understand, and where the first standards in RRD can be relied on by the industry and health authorities. By far, just establishing clear RRD policies and procedures represents a best practice within the industry, and this Guide recommends areas for consideration to address within such documents.

This Guide primarily focuses on Investigational Medicinal Products (IMP) and does not cover diagnostics, ancillary or laboratory supplies. Although the general principles may be applied to all of these areas, the authors recognize that there are also key differences that may not be addressed. This Guide uses the general assumption of working with solid-dosage forms, as they form the majority of experience in the industry; however, alternative dosage forms and their special considerations are addressed in Chapter 4. In addition, this Guide primarily focuses on sponsor-supplied materials rather than site-sourced materials, which are more of an extension of the commercial supply chain rather than the clinical supply chain, while recognizing that it is a gray area.

## 1.2 Key Considerations

This Guide is structured to denote several key areas of consideration that are commonly taken into account when creating and implementing RRD policies and procedures. It is not intended to cover every scenario and it is assumed that the use of this Guide is accompanied by a risk-based approach in its application.

Every sponsor has different interpretations regarding regulations, and thus it is important to refer to your company's position and policies related to IMP RRD. Additionally, while references to key regulatory documents are provided, this Guide is not intended to be an extensive or in-depth analysis of the regulations, and users must recognize that regulations are always subject to change. Finally, the definitions within this Guide are based on collective best practice and have not been directly endorsed by any regulatory agency.