CLINICAL AND LABORATORY STANDARDS INSTITUTE®

1st Edition

CLSI EP47™

Evaluation of Reagent Carryover Effects on Test Results

CLSI EP47 provides guidance for planning, performing, evaluating, and documenting reagent carryover experiments and guidance for ensuring that no significant reagent carryover occurs.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Evaluation of Reagent Carryover Effects on Test Results

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Abstract

Clinical and Laboratory Standards Institute EP47—*Evaluation of Reagent Carryover Effects on Test Results* provides guidance for planning, performing, evaluating, and documenting reagent carryover experiments along with establishing that no significant reagent carryover occurs by a developer during the Establishment Stage of the Test Life Phases Model (see CLSI EP19[1]). End-user laboratories can use CLSI EP47 to investigate if suspect results are caused by reagent carryover. Assessment and mitigation of carryover risk is described.

CLSI EP47 is intended to promote uniformity in the evaluation of reagent carryover characteristics of medical laboratory measurement procedures across developers of *in vitro* diagnostic tests, regulatory organizations, and medical laboratories.

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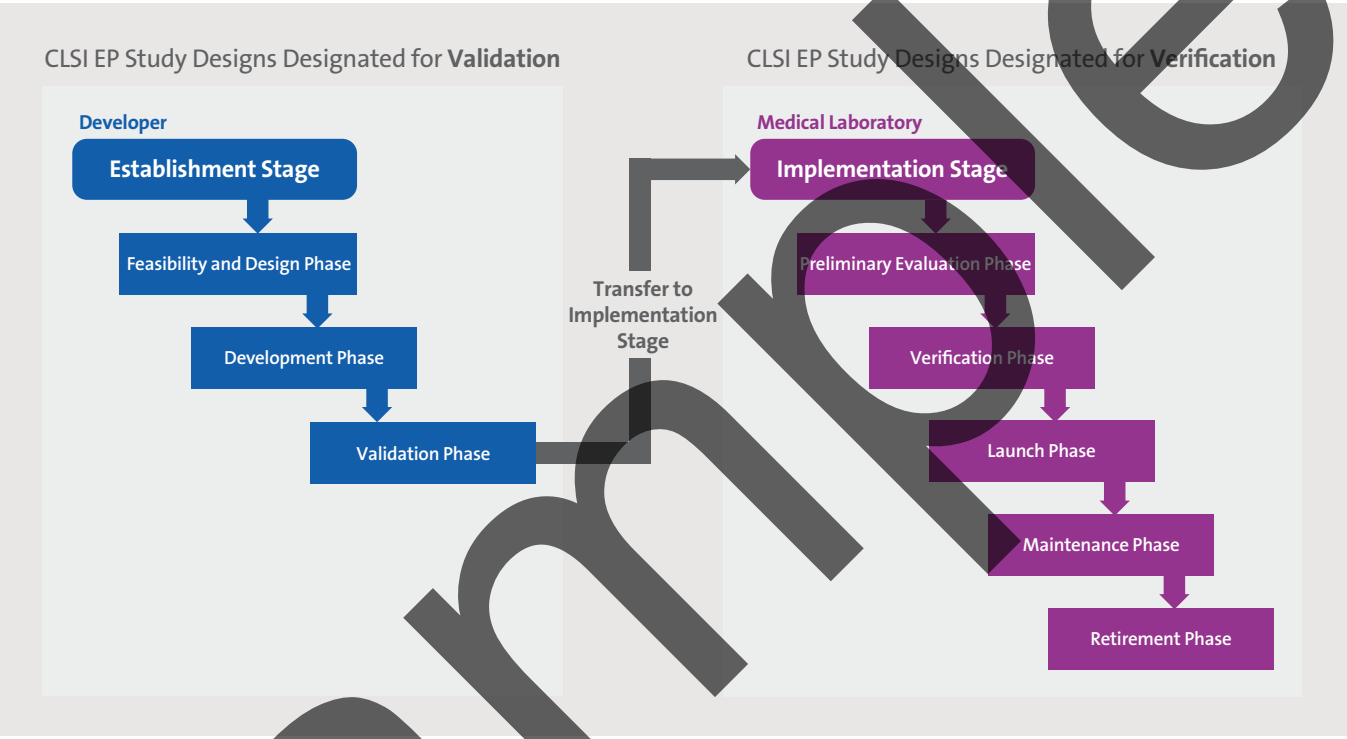
Contents

Foreword

Carryover is the unintended transfer of material from a patient sample or reagent into other samples, reagents, materials, or parts of the instrument system, potentially causing a carryover effect (ie, a quantifiable difference in a measurement result). CLSI EP47 focuses on carryover from a reagent into adjacent reagents, termed "reagent carryover." Reagent carryover can potentially cause significant errors in reported results and, therefore, has the possibility of affecting medical decisions. Reagent carryover claims should be established as part of the Establishment Stage of a new test method (see Figure 1 and the detailed description of the Test Life Phases Model in CLSI EP19[1]).



Abbreviation: EP, evaluation protocols.

[a] The eight phases separate into the two stages, ie, the Establishment Stage (blue), which is performed by a developer, and the Implementation Stage (purple), which is performed by the end-user laboratory.

Figure 1. The Test Life Phases Model[a]

CLSI EP47 recommends study designs and statistical methods for a developer to estimate a reagent carryover effect and to state the carryover performance, as appropriate. This guideline is also intended to assist developers to reduce carryover effects for commercial test methods. Worked examples are provided to illustrate study design considerations and data analysis.

NOTE: The content of CLSI EP47 is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

clinical effect
qualitative
quantitative
reagent carryover
study design

Chapter 1

Introduction

Evaluation of Reagent Carryover Effects on Test Results

1 Introduction

During the Establishment Stage of the Test Life Phases Model for a new test method, specifically the Feasibility and Design and Development phases, any unacceptable reagent carryover effect should be identified and mitigated. Developers should develop instrument systems and/or test methods (assays) with clinically insignificant or nondetectable carryover effects. Reagent carryover should be experimentally challenged during these two phases of the Test Life Phases Model to ensure any carryover effect is clinically insignificant. CLSI EP47 describes study designs for estimating the extent of reagent carryover. Before method development is concluded, a developer should experimentally determine that reagent carryover is within acceptable limits before finalizing the method. The study design could be used for evaluation or validation of reagent carryover. Reagent carryover is generally not verified by the end-user laboratory.

1.1 Scope

CLSI EP47 is for developers of instrument systems and medical laboratory test methods, both commercially manufactured as well as laboratory-developed tests (LDTs) to eliminate or mitigate reagent carryover. This guideline could also be used for the laboratory end user creating new LDTs, adding open-channel reagents not verified by the manufacturer, or investigating suspect results.

CLSI EP47 provides recommendations for:

- Risk assessment criteria to evaluate the potential for reagent carryover effects
- Statistically valid study designs for evaluation of reagent carryover effects
- Selection of sample(s) and/or reagent(s) combinations to include in reagent carryover studies
- Data analysis and interpretation
- Reporting and/or labeling format for a summary of the reagent carryover effect and performance claims

CLSI EP47 provides recommendations for the evaluation of reagent carryover from one reagent to another and is intended for quantitative test methods. Qualitative binary methods with an internal continual response and internal cutoff are covered by the recommendations in this guideline. However, CLSI EP47 does not cover semiquantitative test methods characterized as multilevel qualitative assays (eg, assays with an equivocal zone).

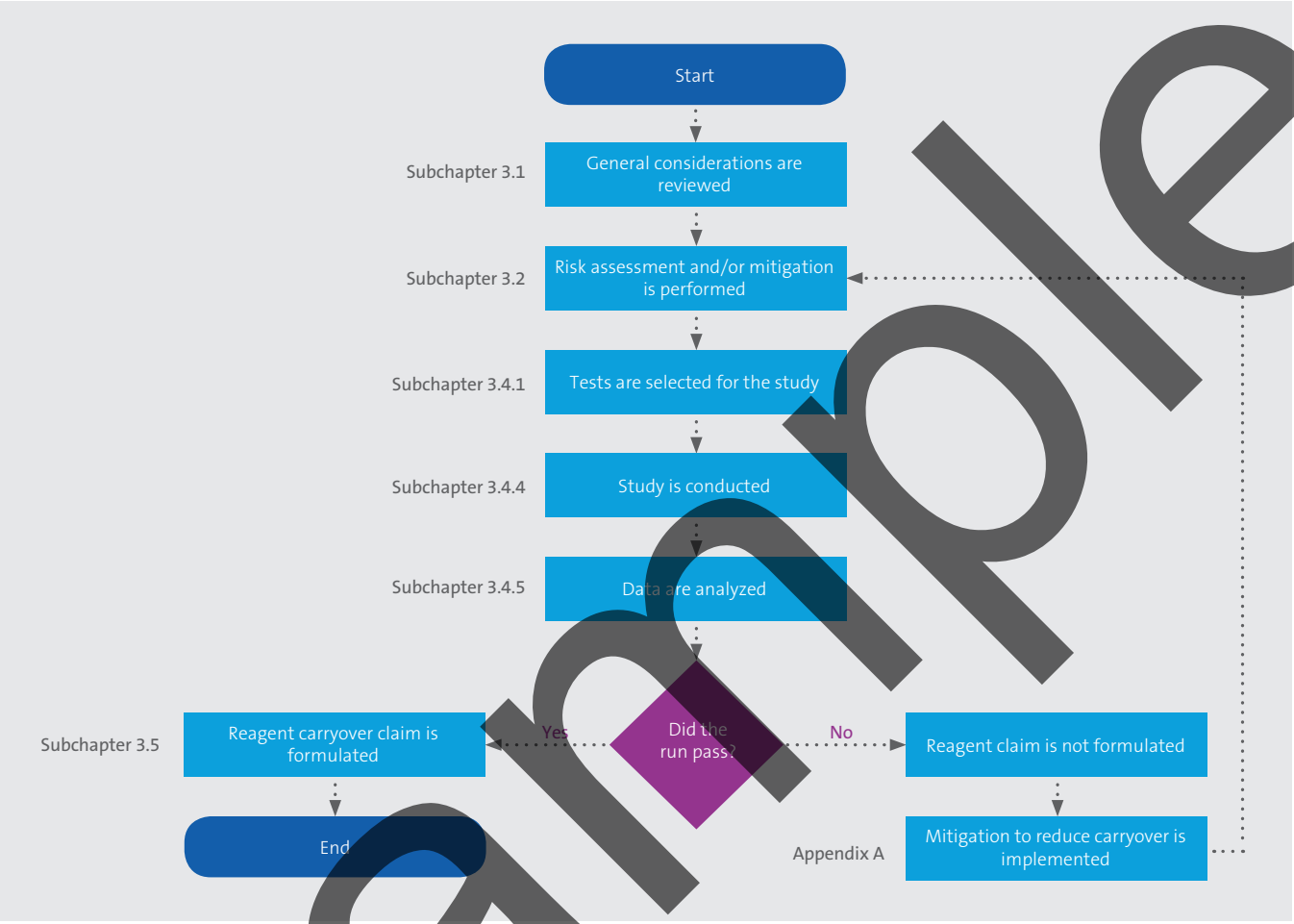
This guideline is not intended to provide detailed guidance for:

- The evaluation of sample carryover
- The combined effects of reagent carryover from several different reagents into a single reagent container
- Carryover between different test methods used to measure the same samples
- Carryover caused by sample interactions with reagents or cross-contamination from preexamination procedures
- Carryover within multianalyte assays and/or algorithmic test method

CLSI EP47 is not intended to be used for verification by the end-user laboratory but can be used to troubleshoot suspect results.

2 Path of Workflow

The steps of evaluation of reagent carryover are detailed in Figure 2. The mechanisms for reagent carryover information to mitigate a carryover effect are provided in Appendix A. Appendix B has an example of a risk assessment, and Appendix C has a detailed example.



[a] Four basic symbols are used in this process flow chart: oval (signifies the beginning or end of a process), arrow (connects process activities), box (designates process activities), diamond (includes a question with alternative "Yes" and "No" responses).

Figure 2. Process Flow Chart for the Evaluation of Reagent Carryover[a]

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