
Guidance for Industry

Container Closure Systems for Packaging Human Drugs and Biologics

CHEMISTRY, MANUFACTURING, AND CONTROLS DOCUMENTATION

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

May 1999

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Table of Contents

I.	INTRODUCTION	1
II.	BACKGROUND	2
	A. Definitions	2
	B. CGMP, CPSC and USP Requirements on Containers and Closures	3
	C. Additional Considerations	4
III.	QUALIFICATION AND QUALITY CONTROL OF PACKAGING COMPONENTS ..	5
	A. Introduction	5
	B. General Considerations	7
	C. Information That Should Be Submitted in Support of an Original Application for Any Drug Product	17
	D. Inhalation Drug Products	23
	E. Drug Products for Injection and Ophthalmic Drug Products	23
	F. Liquid-Based Oral and Topical Drug Products and Topical Delivery Systems ..	27
	G. Solid Oral Dosage Forms and Powders for Reconstitution	33
	H. Other Dosage Forms	37
IV.	POSTAPPROVAL PACKAGING CHANGES	37
V.	TYPE III DRUG MASTER FILES	37
	A. General Comments	37
	B. Information in a Type III DMF	38
VI.	BULK CONTAINERS	39
	A. Containers for Bulk Drug Substances	39
	B. Containers for Bulk Drug Products	40
	ATTACHMENT A	A-1
	REGULATORY REQUIREMENTS	A-1
	ATTACHMENT B	B-1
	COMPLIANCE POLICY GUIDES THAT CONCERN PACKAGING	B-1
	ATTACHMENT C	C-1
	EXTRACTION STUDIES	C-1
	ATTACHMENT D	D-1
	ABBREVIATIONS	D-1
	ATTACHMENT E	E-1
	REFERENCES	E-1

GUIDANCE FOR INDUSTRY¹

CONTAINER CLOSURE SYSTEMS FOR PACKAGING HUMAN DRUGS AND BIOLOGICS

CHEMISTRY, MANUFACTURING, AND CONTROLS DOCUMENTATION

I. INTRODUCTION

This document is intended to provide guidance on general principles² for submitting information on packaging materials used for human drugs and biologics.³ This guidance supersedes the FDA *Guideline for Submitting Documentation for Packaging for Human Drugs and Biologics*, issued in February 1987 and the packaging policy statement issued in a letter to industry dated June 30, 1995 from the Office of Generic Drugs.⁴ This guidance is not intended to describe the information that should be provided about packaging operations associated with drug product manufacture.

Approaches which differ from those described in this guidance may be followed, but the applicant is encouraged to discuss significant variations in advance with the appropriate CDER chemistry review staff or CBER review staff. This is to prevent applicants or sponsors from spending unnecessary time and effort in preparing a submission that the FDA may later determine to be unacceptable.

¹ This guidance has been prepared by the Packaging Technical Committee of the Chemistry, Manufacturing, and Controls Coordinating Committee (CMC CC) in the Center for Drug Evaluation and Research (CDER) and in conjunction with the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration. This guidance document represents the Agency's current thinking on container closure systems for the packaging of human drugs and biological products. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

² In general, this guidance does not suggest specific test methods and acceptance criteria (except for references to *The United States Pharmacopia* methods), nor does it suggest comprehensive lists of tests. These details should be determined based on good scientific principles for each specific container closure system for particular drug product formulations, dosage forms, and routes of administration. Acceptance criteria should be based on actual data for particular packaging components and container closure systems, and they should be set to ensure batch-to-batch uniformity of packaging components.

³ As used in this guidance, the terms *drug* and *drug product* include biologics unless otherwise noted.

⁴ The policy statement is a document titled *Container/Closure Information Which Should Be Provided In An ANDA/AADA* which was written by the Office of Generic Drugs/Packaging Advisory Group.

II. BACKGROUND

The Federal Food, Drug, and Cosmetic Act (the Act) mandates the need for adequate information related to packaging materials. Section 501(a)(3) of the Act states that a drug is deemed to be adulterated "if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health..." In addition, section 502 of the Act states that a drug is considered misbranded if there are packaging omissions. Also, section 505 of the Act requires a full description of the methods used in, and the facilities and controls used for, the packaging of drugs (see Attachment A).

Section 505(b)(1)(D) of the Act states that an application shall include a full description of the methods used in, the manufacturing, processing and packing of such drug. This includes facilities and controls used in the packaging a drug product.

A. Definitions⁵

*Materials of construction*⁶ refer to the substances (e.g., glass, high density polyethylene (HDPE) resin, metal) used to manufacture a packaging component.

A *packaging component* means any single part of a container closure system. Typical components are containers (e.g., ampules, vials, bottles), container liners (e.g., tube liners), closures (e.g., screw caps, stoppers), closure liners, stopper overseals, container inner seals, administration ports (e.g., on large-volume parenterals (LVPs)), overwraps, administration accessories, and container labels. A *primary packaging component* means a packaging component that is or may be in direct contact with the dosage form. A *secondary packaging component* means a packaging component that is not and will not be in direct contact with the dosage form.

A *container closure system* refers to the sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components, if the latter are intended to provide additional protection to the drug product. A *packaging system* is equivalent to a container closure system.

⁵ These definitions are intended to clarify the use of certain terms in this guidance only and are not intended to supersede the definitions of *container* and *package* as provided for in 21 CFR 600.3.

⁶ This term is used in a general sense for the basic material, which should be defined in the application in terms of its specific chemical composition for a given drug application (e.g., the specific polymer and any additives used to make the material).

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