Compendial Expectations for Dose Content and Uniformity for Biologics

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Agenda

- Introduction
- USP Framework
  - Product Quality Tests
  - Dosage Forms
  - Content Uniformity
  - Container Content
- Challenges and Potential Paths Forward for Biologics

1 Introduction

Why Dose Content Uniformity Matters

- Reliable delivery of labeled dose is necessary to ensure:
  - Patient safety
  - Therapeutic efficacy
  - Regulatory compliance
- Dose uniformity is especially critical for
  - Products with a narrow therapeutic range (e.g. insulins)
  - Low dosage products
  - Products that are prone to inhomogeneity (e.g. lyophilized products, cell and gene therapies)

USP Public Standards

Monographs

- Specifications for pharmaceutical articles in commerce (from release through product shelf life)
  - Tests, assays, and acceptance criteria needed to demonstrate the article meets required quality standards

General Chapters

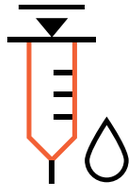
- Procedural chapters numbered <1000
  - Typically contain validated methods and often have associated reference standards
  - Are enforceable when referenced in general notices, monographs

- Informational if numbered 1000 to 1999
  - Best practices, guidance and context for enforceable chapters
  - Often address new technologies and emerging issues
  - Are not enforceable

Physical Reference Standards

- Provide traceable standards to demonstrate broad-based acceptability of procedures

2025-2030 Expert Committees



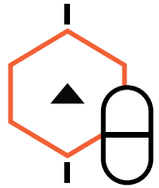
Biologics

Biologics – Therapeutic Peptides, Oligonucleotides, and Complex Carbohydrates
Rosario Lobrutto

Biologics – Therapeutic Proteins
Kenneth R. Miller

Biologics – Vaccines
Mark van Ooji

Biologics – Cell & Gene Therapies
Lili Belcastro



Small Molecules

Small Molecules – Therapeutic Areas 1
Mary Seibel

Small Molecules – Therapeutic Areas 2
Robert G. Buice Jr.

Small Molecules – Therapeutic Areas 3
Eric Kesslen

Small Molecules – Therapeutic Areas 4
Partha S. Mukherjee

Small Molecules – Therapeutic Areas 5
Justin Pennington

Small Molecules – Therapeutic Areas 6
Allan D. Bokser

Excipients

Excipient Monographs 1
Vivek S. Dave

Excipient Monographs 2
Barbara R. Serr

Excipient Chapters
Richard Creekmore

General Chapters

General Chapters – Dosage Forms
Kevin Warner

General Chapters – Chemical Analysis
Anthony C. Bevilacqua

General Chapters – Microbiology
Ed C. Tidswell

General Chapters – Packaging & Distribution
Renaud Janssen

General Chapters – Statistics
Charles Tan

General Chapters – Pharmaceutical Analysis Lifecycle & Data Science
Jaime Marach

General Chapters – Materials Physical Properties Characterization
Eloise Welfare

Healthcare Quality & Safety

Healthcare Safety, Quality, & Nomenclature
Melody Ryan

Compounding
Brenda Jensen

Healthcare Information & Technology
Leslie Lenert

Personalized Medicines
Sara L. Rogers

Dietary Supplements & Herbal Medicines, Food Ingredients

Botanical Dietary Supplements & Herbal Medicines
Thomas Brendler

Non-Botanical Dietary Supplements
Raimar Loebenberg

Dietary Supplements Admission, Evaluation, & Labeling
Amy L. Roe

Food Ingredients
James Brooks

2 USP and Regulatory Framework

Overview of Compendial Resources and Regulatory Relevance

Relevant USP Chapters

- <1151> *Pharmaceutical Dosage Forms*
- <1> *Injections and Implanted Drug Products (Parenterals) - Product Quality Tests*
- <905> *Uniformity of Dosage Units*
- <697> *Container Content for Injections*

Regulatory Requirements and Recommendations

- USP Monographs
  - Required when referenced in monograph
- FDA guidance for industry: *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products* (June 2015)
  - References <1>, <1151>, <697> <659>
- MaPP 5019.1 *Allowable Excess Volume/ Content in Injectable Drug and Biological Products* (Jan 2022)
  - References <1151>, <905>, <697>, <659>, <911>
- MaPP 5019.2 *Assessment of the Appropriate Labeled Content for Injectable Drug Products* (June 2022)
  - References <659>

Monograph Example: Glucagon for Injection

- DEFINITION
- IDENTIFICATION
  - A.
  - B. Glucagon Bioidentity Tests ⟨123⟩:
- ASSAY
  - Procedure
- PERFORMANCE TESTS
  - Uniformity of Dosage Units ⟨905⟩:
- IMPURITIES
  - Organic Impurities
- SPECIFIC TESTS
  - Water Determination ⟨921⟩, Method I, Method Ic:
  - pH and Clarity of Solution:
  - Bacterial Endotoxins Test ⟨85⟩:
  - Sterility Tests ⟨71⟩:
  - Constituted Solution:
- ADDITIONAL REQUIREMENTS
  - Packaging and Storage:
  - Labeling:
  - USP Reference Standards ⟨11⟩

DEFINITION
Glucagon for Injection is a sterile lyophilized mixture of the hydrochloride of glucagon with one or more suitable buffering and stabilizing agents. It contains NLT 65% and NMT 110% of the labeled amount of glucagon

PERFORMANCE TESTS
•**Uniformity of Dosage Units** ⟨905⟩**:**
Meets the requirements

SPECIFIC TESTS
•**Constituted Solution:**
At the time of use, it meets the requirements for *Injections and Implanted Drug Products* ⟨1⟩*, Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and Clarity of Solutions*.

ADDITIONAL REQUIREMENTS
•**Packaging and Storage:**
Preserve as described in *Packaging and Storage Requirements* ⟨659⟩*, Injection Packaging, Packaging for Constitution*.
Change to read:
•**Labeling:**
The labeling states that the material is synthetic or of recombinant DNA origin.

MaPP 5019.1 and 5019.2 Recommendations and Linkage to USP Chapters

Table 1: Quality assessor responsibilities for injectable drug products that are solutions, suspensions, or emulsions

OPQ Office	Deliverable volume (mL per vial) by USP <697> testing[30]	Assay or protein concentration (mg per mL)	Gross content of drug product (mL per vial)[31]	Bulk concentration prior to filling (mg per mL)[32]	Uniformity of Dosage Units by USP <905> testing[33]	USP <1151> compliance	Minimum and maximum fill volume
OPQA I and II	X	X	X	X[34]	X		X[35]
OPQA III	X	X	X	X	X	X	X
OPMA				X		X	X

Table 2: Quality assessor responsibilities for injectable drug products that require reconstitution/constitution

OPQ Office	Net container content (mg per vial)	Labeled concentration after reconstitution/ constitution (mg per mL)	Gross content of drug substance or protein content (e.g., mg per vial)	Bulk concentration prior to filling (mg per mL)[36]	Uniformity of Dosage Units by USP <905> testing	Deliverable volume by USP <697> testing after reconstitution/ constitution	Minimum and maximum fill amounts
OPQA I and II	X	X	X	X[37]	X	X	X[38]
OPQA III	X	X	X	X	X	X	X
OPMA				X			X

- Relevant Footnotes from MaPP 5019.1
  - [10] Typically, USP General Chapters titled with numbers above are considered informational and not requirements. However, in this case, because FDA's regulations, i.e., 21 CFR 201.51(g), specifically require adherence to the USP recommendations on this topic, the recommendations in USP General Chapter for excess volume of injectable drug products are considered requirements.
  - [11] USP General Chapters numbered below 1000 are requirements only if referenced in a USP/NF monograph or made applicable through USP General Notices for products with USP/NF monographs. Otherwise they are general recommendations. Alternative methods and procedures must be validated and demonstrated to be suitable for intended use (see 21 CFR 211.165(e) and 211.194(a)(2)). Specifically, this applies to references to USP General Chapters <697> and <905> throughout this MAPP.

- Relevant Footnote from MaPP 5019.2
  - [11] Per USP General Chapter Packaging and Storage Requirements, Injection Packaging Systems, multiple-dose vials have a maximum container volume sufficient to permit the withdrawal of not more than a total of 30 mL, unless otherwise specified in an applicable USP drug product monograph. Exceeding the 30 mL multiple dose vial limit may be justified if the recommended dose of the drug product packaged in a multiple dose vial is large, making the 30 mL limit impractical.

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USP <1> *Injections and Implanted Drug Products (Parenterals) - Product Quality Tests*

USP GC <1> to <5>: Product Quality Tests

Series of chapters that define general requirements for injections and parenteral dosage forms, including terminology and expectations for sterility, strength, and uniformity.

⟨1⟩ INJECTIONS AND IMPLANTED DRUG PRODUCTS (PARENTERALS)—PRODUCT QUALITY TESTS

⟨2⟩ ORAL DRUG PRODUCTS—PRODUCT QUALITY TESTS

⟨3⟩ TOPICAL AND TRANSDERMAL DRUG PRODUCTS—PRODUCT QUALITY TESTS

⟨4⟩ MUCOSAL DRUG PRODUCTS—PRODUCT QUALITY TESTS

⟨5⟩ INHALATION AND NASAL DRUG PRODUCTS—GENERAL INFORMATION AND PRODUCT QUALITY TESTS

INTRODUCTION

PRODUCT QUALITY TESTS COMMON TO PARENTERAL DOSAGE FORMS

- Universal Tests
- Specific Tests

PRODUCT QUALITY TESTS FOR SPECIFIC PARENTERAL DOSAGE FORMS

- Solutions
- Sterile Powders for Solutions
- Suspensions
- Liposomes
- Sterile Powders for Suspensions
- Emulsions
- Implants
- Drug-Eluting Stents

GC <1> *Injections and Implanted Drug Products (Parenterals) - Product Quality Tests*

Universal Tests

- Identification
- Assay
- Impurities
- Foreign and Particulate Matter
- Sterility
- Bacterial Endotoxins
- Container Content
  - References <697> *Container Content for Injections*
- Packaging Systems
- Container Closure Integrity
- Labeling

Specific Tests

- Uniformity of Dosage Units
  - References <905> *Uniformity of Dosage Units*
- Vehicles and Added Substances
- Antimicrobial Preservatives
- Water Content
  - Applicable to lyophilized products
- Aluminum Content
- Completeness and Clarity of Solutions

Product Quality Tests for Specific Parenteral Dosage Forms

- Solutions
- Sterile Powders for Solutions
- Suspensions
- Liposomes
- Sterile Powders for Suspensions
- Emulsions
- Implants
- In situ Gels
- Microparticles
- Drug-Eluting Stents

<1151> *Pharmaceutical Dosage Forms*

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- Purpose of Chapter
  - Establish standardized terminology for dosage forms
  - Provide guidance on testing requirements for dosage forms
  - Support interpretation of compendial requirements
- Some recommendations are considered requirements in:
  - FDA guidance for industry: *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products* (June 2015)
  - MaPP 5019.1

GENERAL CONSIDERATIONS

- Dose Uniformity
- Stability
- Bioavailability
- Release Profile
- Manufacture
- Route of Administration
- Packaging and Storage
- Labeling Statements

PRODUCT QUALITY TESTS

- Description
- Identification
- Assay
- Impurities
- Physicochemical Properties
- Particle Size
- Uniformity of Dosage Units
- Water Content
- Microbiological Quality
- Antimicrobial Preservative Content
- Antioxidant Content
- Sterility
- Dissolution
- Breaking Force and Friability
- Leachables
- Other Tests

<1151> *Pharmaceutical Dosage Forms*

DOSAGE FORMS

- Aerosols
- Capsules
- Cloths
- Creams
- Emulsions
- Films
- Foams
- Gases
- Gels
- Granules
- Gums
- Implants
- **Injections**
- Inserts
- Irrigations
- Liquids
- Lotions
- Lozenges
- Ointments
- Pastes
- Pellets
- Pills
- Plasters
- Powders
- Rinses
- Soaps and Shampoos
- **Solutions**
- Sponges
- Sprays
- Strips
- Suppositories
- **Suspensions**
- Swabs
- Systems
- Tablets
- Tapes

Injections

(See *Emulsions*, *Foams*, *Powders*, *Solutions*, and *Suspensions* for information on injectable dosage forms.)

Injections are not treated as a dosage form in this chapter. Chapter (1) provides quality and other information about injectable products. Information on specific dosage form terminology can be found in the *Glossary*. For appropriate injection nomenclature, see *Nomenclature* (1121).

EXCESS VOLUME IN INJECTIONS

Each container of an injection is filled with a volume in slight excess of the labeled "size" or the volume that is to be withdrawn. The excess volumes recommended in *Table 1* are usually sufficient to permit withdrawal and administration of the labeled volumes.

Labeled Size (mL)	Recommended Excess Volume	
	For Mobile Liquids (mL)	For Viscous Liquids (mL)
0.5	0.1	0.12
1	0.1	0.15
2	0.15	0.25
5	0.3	0.5
10	0.5	0.7
20	0.6	0.9
30	0.8	1.2

[a] This table pertains only to vials and ampules.

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USP <905> *Uniformity of Dosage Units*

USP <905> *Uniformity of Dosage Units*

- Core standard for **Content Uniformity (CU)**
- Defines two methods for determining uniformity of dosage units
  - Weight variation
    - Applicable to specific listed dosage forms
    - Other dosage forms must be tested by CU
  - Content Uniformity
    - Applicable to all dosage forms
  - Both methods provide:
    - Guidance on # of units to test
    - Calculation of Acceptance criteria (Acceptance Value, AV)
- Harmonization
  - Adopted by Pharmacopeial Discussion Group*
    - EP: *Uniformity of dosage units (2.9.40)*
    - JP: *<6.02> Uniformity of Dosage Units*
  - Referenced in ICH Q4B Annex 6

Dosage Forms that Can Be Tested by Weight Variation

W1)	Solutions enclosed in unit-dose containers and into soft capsules;
(W2)	Solids (including powders, granules, and sterile solids) that are packaged in single-unit containers and contain no active or inactive added substances;
(W3)	Solids (including sterile solids) that are packaged in single-unit containers, with or without active or inactive added substances, that have been prepared from true solutions and freeze-dried in the final containers and are labeled to indicate this method of preparation; and
(W4)	Hard capsules, uncoated tablets, or film-coated tablets, containing 25 mg or more of a drug substance comprising 25% or more, by weight, of the dosage unit or, in the case of hard capsules, the capsule contents, except that uniformity of other drug substances present in lesser proportions is demonstrated by meeting the requirements for *Content Uniformity*.

*Portion of harmonized text in EP and JP was not accepted by FDA/ USP

Weight Variation vs Content Uniformity

- Chapter distinguishes between drug products based on total dose and ratio (w/w) of DS
- EP/JP include provision for items falling into category W4 to be tested by weight variation under certain circumstances
  - This provision was not accepted by FDA and USP and is not included in <905>

Table 1* – List of dosage forms and the applicable test (weight variation or content uniformity).

Dosage Form	Subset Descriptor	Dose* and Ratio** of Drug Substance		Remarks
		≥25 mg and ≥25 wt %	<25 mg or <25 wt %	
Capsules	Containing liquids or semisolids	WV	WV	-
	Containing solids	WV	CU	-
	Containing suspension	CU	CU	
Emulsions		CU	CU	
Implants (including drug-eluting stents)		CU	CU	-
Injections		-	-	See Injections in <1151>
Solids in single-dose containers	A single drug substance	WV	WV	-
	A single drug substance lyophilized in final container	WV	WV	-
	Drug substance(s) with excipients	WV	CU	-
	Drug substances without excipient(s)	WV	CU	-
Solutions	in single-dose containers	WV	WV	
	In multi-dose containers	n/a	n/a	See <698> and <755>
Suspensions		CU	CU	
Tablets		WV	CU	-

Note: WV = weight variation, CU = content uniformity, n/a = not applicable

** Table 1 adapted from <905> and is not official*

Harmonization – ICH Q4B Annex 6 and PDG

2. Q4B OUTCOME

2.1 Analytical Procedures

The ICH Steering Committee, based on the evaluation by the Q4B Expert Working Group (EWG), recommends that the official pharmacopoeial texts, Ph. Eur. 2.9.40. Uniformity of Dosage Units, JP 6.02 Uniformity of Dosage Units, and USP General Chapter <905> Uniformity of Dosage Units, can be used as interchangeable in the ICH regions subject to the following conditions:

2.1.1 Unless the 25 milligrams (mg)/25% threshold limit is met, the use of the Mass/Weight Variation test as an alternative test for Content Uniformity is not considered interchangeable in all ICH regions.

2.1.2 For specific dosage forms that appear in local text in the pharmacopoeias by enclosing the text in black diamond symbols, application of the Uniformity of Dosage Units test is not considered interchangeable in all ICH regions.

2.1.3 If a correction factor is called for when different procedures are used for assay of the preparation and for the Content Uniformity Test, the correction factor should be specified and justified in the application dossier.

2.2 Acceptance Criteria

The acceptance criteria are harmonized between the three pharmacopoeias.

4. CONSIDERATIONS FOR IMPLEMENTATION

4.1 General Consideration

When sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts that are referenced in Section 2.1 of this annex, any change notification, variation, and/or prior approval procedures should be handled in accordance with established regional regulatory mechanisms pertaining to compendial changes.

4.2 FDA Consideration

Based on the recommendation above, and with reference to the conditions set forth in this annex, the pharmacopoeial texts referenced in Section 2.1 of this annex can be considered interchangeable. However, FDA might request that a company demonstrate that the chosen method is acceptable and suitable for a specific material or product, irrespective of the origin of the method.

FDA finds unsuitable for regulatory purposes the not more than 2% Relative Standard Deviation (RSD) exception to the 25 mg/25% threshold that appears in the JP and the Ph. Eur. Therefore, in accordance with the official text in the USP, for those items below the 25 mg/25% threshold, testing by Content Uniformity should be performed.

4.3 EU Consideration

For the European Union, the monographs of the Ph. Eur. have mandatory applicability. Regulatory authorities can accept the reference in a marketing authorisation application, renewal or variation application citing the use of the corresponding text from another pharmacopoeia as referenced in Section 2.1, in accordance with the conditions set out in this annex, as fulfilling the requirements for compliance with the Ph. Eur. Chapter 2.9.40. on the basis of the declaration of interchangeability made above.

4.4 MHLW Consideration

The pharmacopoeial texts referenced in Section 2.1 of this annex can be used as interchangeable in accordance with the conditions set out in this annex. Details of implementation requirements will be provided in the notification by MHLW when this annex is implemented.

4.5 Health Canada Consideration

In Canada any of the pharmacopoeial texts cited in Section 2.1 of this annex and used in accordance with the conditions set out in this annex can be considered interchangeable.

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USP <697> *Container Content for Injections*

and other relevant chapters in development

USP <697> *Container Content for Injections*

- Establishes requirements for determining net content and acceptable variability in containers to ensure patients receive the intended dose.
- Minimum fill, net content, acceptable variability
- Analytical accuracy and precision
- Impact on vials, pre-filled syringes (PFS), cartridges
- Regulatory expectations for investigational/commercial lots

- Chapter is harmonized with EP/JP, with the exception of one sentence
  - EP: *Test for extractable volume of parenteral preparations (2.9.17)*
  - JP: *<6.05> Test for Extractable Volume of Parenteral Preparations*

Each container of an injection contains sufficient excess to allow withdrawal of the labeled quantity of drug (see *Pharmaceutical Dosage Forms ⟨1151⟩, Excess Volume in Injections*). Such withdrawal shall be performed according to labeled directions, if provided.

DETERMINATION OF VOLUME OF INJECTION IN CONTAINERS

This section is harmonized with the corresponding texts of the *European Pharmacopoeia* and/or the *Japanese Pharmacopoeia*. These pharmacopeias have undertaken not to make any unilateral change to this harmonized section. A portion of the present text (see below) is national *USP* text, and therefore not part of the harmonized text; it is marked with symbols (♦) to specify this fact.

Suspensions and emulsions must be shaken before withdrawal of the contents and before the determination of the density. Oily and viscous preparations may be warmed according to the instructions on the label, if necessary, and thoroughly shaken immediately before removing the contents. The contents are then cooled to 20°–25° before measuring the volume. ♦Sterile solid formulations must be constituted according to labeled directions before removing the contents. Contents are then to be measured following the procedures for suspensions, emulsions, or solutions, as appropriate.♦

Single-Dose Containers

Select 1 container if the volume of the container is 10 mL or more, 3 containers if the nominal volume is more than 3 mL and less than 10 mL, or 5 containers if the nominal volume is 3 mL or less. Take up individually the total contents of each container selected into a dry syringe of a capacity not exceeding three times the volume to be measured and fitted with a 21-gauge needle NLT 2.5 cm (1 inch) in length. Expel any air bubbles from the syringe and needle, and then discharge the contents of the syringe, without emptying the needle, into a standardized, dry cylinder (graduated to contain rather than to deliver the designated volumes) of such size that the volume to be measured occupies at least 40% of its graduated volume. Alternatively, the volume of the contents in mL may be calculated as the mass, in g, divided by the density. For containers with a nominal volume of 2 mL or less, the contents of a sufficient number of containers may be pooled to obtain the volume required for the measurement, provided that a separate, dry syringe assembly is used for each container. The contents of containers holding 10 mL or more may be determined by means of opening them and emptying the contents directly into the graduated cylinder or tared beaker.

The volume is NLT the nominal volume in the case of containers examined individually or, in the case of containers with a nominal volume of 2 mL or less, is NLT the sum of the nominal volumes of the containers taken collectively.

Multi-Dose Containers

For Injections in multiple-dose containers labeled to yield a specific number of doses of a stated volume, select 1 container, and proceed as directed for single-dose containers, using the same number of separate syringe assemblies as the number of doses specified. The volume is such that each syringe delivers NLT the stated dose.

Injections in Cartridges or Prefilled Syringes

Select 1 container if the volume is 10 mL or more, 3 containers if the nominal volume is more than 3 mL and less than 10 mL, or 5 containers if the nominal volume is 3 mL or less. If necessary, fit the containers with the accessories required for their use (needle, piston, syringe) and transfer the entire contents of each container without emptying the needle into a dry tared beaker by slowly and constantly depressing the piston. Determine the volume, in mL, calculated as the mass, in g, divided by the density.

The volume measured for each of the containers is NLT the nominal volume.

Large-Volume Intravenous Solutions

For intravenous solutions, select 1 container. Transfer the contents into a dry measuring cylinder of such a capacity that the volume to be determined occupies at least 40% of the nominal volume of the cylinder. Measure the volume transferred.

The volume is NLT the nominal volume.

Other Chapters of Interest

<659> *Packaging and Storage Requirements*

- Referenced in MaPP 5019.2
- Required for all articles in USP-NF based on General Notices 10.10
- Recently revised with portions becoming official as of Dec 1, 2025
- Provides packaging and storage condition definitions as well as additional information
  - **Multiple-dose container** (also referred to as Multi-dose)**:** A *Container–closure system* that holds a sterile medication for parenteral administration (injection or infusion) that has met antimicrobial effectiveness testing requirements, or is excluded from such testing requirements by FDA regulation. A *Multiple-dose container* is intended to contain more than one dose of a drug product. When space permits, a *Multiple-dose container* is labeled as such. *Multiple-dose containers* are generally expected to contain 30 mL or less of medications. The beyond-use date for an opened or entered (e.g., needle-punctured) *Multiple-dose container* is 28 days unless otherwise specified by the manufacturer on the label. An example of a *Multiple-dose container* is a vial.
- Includes specific section on Injection Packaging

<7> *Labeling*

- Includes definitions and standards
- Required for all articles in USP-NF based on General Notices 10.20
- Key sections:
  - **LABELS AND LABELING FOR INJECTABLE PRODUCTS**
    - Defines information to be included on label
  - **Quantity and Total Volume for Injectable Drug Products Packaged in Single- and Multiple-Dose Containers**
  - For injectable drug products greater than 1 mL (single- or multiple-dose) L
    - the quantity per total volume followed by (quantity/mL).
  - For containers that hold a volume of less than 1 mL,
    - Quantity per fraction of a milliliter
    - For containers with 1 mL, the strength should be expressed as quantity/mL

The following example formats are acceptable:

1. For containers less than 1 mL: 12.5 mg/0.625 mL
2. For containers equal to 1 mL: 5 mg/mL (not 5 mg/1 mL)
3. For containers greater than 1 mL:

Example 1: 500 mg/10 mL

(50 mg/mL)

Example 2: 25,000 Units/5 mL

(5,000 Units/mL)

New Complex Injectables Chapters in Development

- <1154> *Liposomal Drug Products*
  - Published in PF 48 (6) and PF 50 (6), received extensive industry feedback
  - Now published in USP-NF, with official date of April 1, 2026
- <1155> *Iron Colloidal Products – Characterization Methods*
  - Published in PF 51 (6) on Nov 1, 2025
  - Open for comment through Jan 31, 2026
- <1156> *LG Polymer Microparticle Drug Products – Characterization Methods*
  - Published in PF 51 (6) on Nov 1, 2025
  - Open for comment through Jan 31, 2026
- <1157> *Drug – Device Combination Products*
  - New chapter in development
  - First draft is complete, being reviewed by FDA

Charting a Path Forward

Current Challenges

- Existing USP framework is primarily focused on small molecules
- Biologics present some unique challenges with respect to dose content and uniformity, including:
  - Heterogeneous biologics
  - High concentration drug products
  - Potency-based dosing
  - Lyophilized products needing reconstitution
  - Sample limitations due to sample size requirements and destructive testing (especially for cell and gene therapies)
  - Impact of container closure (silicone oil, adsorption)

Modernizing Dose Content and Uniformity for Biologics

- Existing framework
  - USP chapters establish foundational expectations
  - FDA guidance documents and MaPP 5019.1 and 5019.2 provide specific guidance for biologics
- Future goals
  - Establish flexible CU frameworks for biologics that address limitations
  - Expand use of science- and risk-based approaches
  - Harmonize strategies to support manufacturing, testing, and regulatory alignment
- Potential mechanisms
  - Modernize USP <905>
  - Develop new chapters
    - Could include informational (>1000) and/or procedural (<1000) chapters

Thank You

Empowering a healthy tomorrow