2011

USP 34
NF 29

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Volume 1

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USP 34–NF 29

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2011

USP 34

THE UNITED STATES PHARMACOPEIA

NF 29

Volume 1

THE NATIONAL FORMULARY

By authority of the United States Pharmacopeial Convention
Prepared by the Council of Experts and its Expert Committees

Official from May 1, 2011

The designation on the cover of this publication, "USP NF 2011," is for ease of identification only. The publication contains two separate compendia: *The United States Pharmacopeia*, Thirty-Fourth Revision, and *The National Formulary*, Twenty-Ninth Edition.

THE UNITED STATES PHARMACOPEIAL CONVENTION
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SIX-MONTH IMPLEMENTATION GUIDELINE

The *United States Pharmacopeia–National Formulary* and its supplements become official **six months** after being released to the public. The *USP–NF*, which is released on November 1 of each year, becomes official on May 1 of the following year.

This six-month implementation timing gives users more time to bring their methods and procedures into compliance with new and revised *USP–NF* requirements.

The table below describes the new official dates. The 2010 *USP 33–NF 28 Reissue,* and the supplements and *Interim Revision Announcements (IRAs)* to that edition, will be official until May 1, 2011, at which time the *USP 34–NF 29* becomes official.

Publication	Release Date	Official Date	Official Until
USP 34–NF 29	Nov. 1, 2010	May 1, 2011	May 1, 2012 (except as superseded by supplements, *IRAs,* and *Revision Bulletins*)
First Supplement to the USP 34–NF 29	February 1, 2011	August 1, 2011	May 1, 2012 (except as superseded by *Second Supplement, IRAs,* and *Revision Bulletins*)
Second Supplement to the USP 34–NF 29	June 1, 2011	December 1, 2011	May 1, 2012 (except as superseded by *IRAs* and *Revision Bulletins*)
USP 35–NF 30	Nov. 1, 2011	May 1, 2012	May 1, 2013 (except as superseded by supplements, *IRAs,* and *Revision Bulletins*)

IRAs will continue to become official on the first day of the second month of the *Pharmacopeial Forum (PF)* issue in which they are published as final. For instance, *IRAs* published as final in the May–June *PF* (issue 3) will become official on June 1. This table gives the details of the *IRAs* that will apply to *USP 33–NF 28 Reissue* and *USP 34–NF 29.*

IRA	Release Date	Official Date	Revises
Jan. 1, 2011 *IRA, PF* 37(1)	Jan. 1, 2011	Feb. 1, 2011	*USP 33–NF 28 Reissue* and its supplements
Mar. 1, 2011 *IRA, PF* 37(2)	Mar. 1, 2011	April 1, 2011	*USP 33–NF 28 Reissue* and its supplements
May 1, 2011 *IRA, PF* 37(3)	May 1, 2011	June 1, 2011	*USP 33–NF 28 Reissue* and its supplements
July 1, 2011 *IRA, PF* 37(4)	July 1, 2011	Aug. 1, 2011	*USP 33–NF 28 Reissue* and its supplements
Sept. 1, 2011 *IRA, PF* 37(5)	Sept. 1, 2011	Oct. 1, 2011	*USP 34–NF 29* and its supplements
Nov. 1, 2011 *IRA, PF* 37(6)	Nov. 1, 2011	Dec. 1, 2011	*USP 34–NF 29* and its supplements
Jan. 1, 2011 *IRA, PF* 38(1)	Jan. 1, 2012	Feb. 1, 2012	*USP 34–NF 29* and its supplements
Mar. 1, 2011 *IRA, PF* 38(2)	Mar. 1, 2012	April 1, 2012	*USP 34–NF 29* and its supplements

Revision Bulletins published on the USP website will become official on the date specificed on the *Revision Bulletin*

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transparent graticule reference circles is used to size white and transparent particles, while dark particles are sized by using the outer diameter of the black opaque graticule reference circles.

In performing the *Microscopic Particle Count Test,* do not attempt to size or enumerate amorphous, semiliquid, or otherwise morphologically indistinct materials that have the appearance of a stain or discoloration on the membrane filter. These materials show little or no surface relief and present a gelatinous or film-like appearance. In such cases, the interpretation of enumeration may be aided by testing a sample of the solution by the *Light Obscuration Particle Count Test*.

Evaluation

For preparations supplied in containers with a nominal volume of more than 100 mL, apply the criteria of *Test 2.A*.

For preparations supplied in containers with a nominal volume of less than 100 mL, apply the criteria of *Test 2.B*.

For preparations supplied in containers with a nominal volume of 100 mL, apply the criteria of *Test 2.B*. [NOTE—*Test 2.A* is used in the *Japanese Pharmacopeia*.]

Test 2.A *(Solutions for parenteral infusion or solutions for injection supplied in containers with a nominal content of more than 100 mL)*—The preparation complies with the test if the average number of particles present in the units tested does not exceed 12 per mL equal to or greater than 10 µm and does not exceed 2 per mL equal to or greater than 25 µm.

Test 2.B *(Solutions for parenteral infusion or solutions for injection supplied in containers with a nominal content of less than 100 mL)*—The preparation complies with the test if the average number of particles present in the units tested does not exceed 3000 per container equal to or greater than 10 µm and does not exceed 300 per container equal to or greater than 25 µm.

⟨789⟩ PARTICULATE MATTER IN OPHTHALMIC SOLUTIONS

Particulate matter consists of mobile, randomly sourced, extraneous substances, other than gas bubbles, that cannot be quantitated by chemical analysis because of the small amount of material they represent and because of their heterogeneous composition. Ophthalmic solutions should be essentially free from particles that can be observed on visual inspection. The tests described herein are physical tests performed for the purpose of enumerating extraneous particles within specific size ranges.

Every ophthalmic solution for which the monograph includes a test for *Particulate matter* is subject to the particulate matter limits set forth for the test being applied, unless otherwise specified in the individual monograph. When higher limits are appropriate, they will be specified in the individual monograph. Ophthalmic preparations that are suspensions, emulsions, or gels are exempt from these requirements, as are medical devices. Refer to the specific monograph when a question of test applicability occurs.

Light obscuration and microscopic procedures for the determination of particulate matter in ophthalmic solutions are identical to those for injections; therefore, where appropriate, *Particulate Matter in Injections* ⟨788⟩ is cross-referenced. This chapter provides a test approach in two stages. The ophthalmic solution is first tested by the light obscuration procedure (stage 1). If it fails to meet the prescribed limits, it must pass the microscopic procedure (stage 2) with its own set of test limits. Where for technical reasons the ophthalmic solution cannot be tested by light obscuration, microscopic testing may be used exclusively. Documentation is required, demonstrating that the light obscuration procedure is incapable of testing the ophthalmic solution or that it produces invalid results.

It is expected that most articles will meet the requirements on the basis of the light obscuration test alone; however, it may be necessary to test some articles by the light obscuration test followed by the microscopic test to reach a conclusion on conformance to requirements. Any product that is not a pure solution having a clarity and a viscosity approximating those of water may provide erroneous data when analyzed by the light obscuration counting method. Such materials may be analyzed by the microscopic counting method. In some instances, the viscosity of a material to be tested may be sufficiently high so as to preclude its analysis by either test method. In this event, a quantitative dilution with an appropriate diluent may be made to decrease viscosity, as necessary, to allow the analysis to be performed.

In the tests described below, the results obtained by examining a discrete unit or group of units for particulate matter cannot be extrapolated with certainty to other units that remain untested. Thus, sampling plans based on known operational factors must be developed if valid inferences are to be drawn from observed data to characterize the level of particulate matter in a large group of units. Sampling plans need to be based on consideration of product volume, particle numbers historically found to be present in comparison to limits, particle size distribution of particles present, and variability of particle counts between units.

LIGHT OBSCURATION PARTICLE COUNT TEST

This test applies to ophthalmic solutions, including solutions constituted from sterile solids, for which a test for *Particulate matter* is specified in the individual monograph. The test counts suspended particles that are solid or liquid.

Test Apparatus, Instrument Standardization, Test Environment, Test Procedure, and Calculations—Proceed as directed for *Light Obscuration Particle Count Test* under *Particulate Matter in Injections* ⟨788⟩.

Interpretation—The ophthalmic solution meets the requirements of the test if the average number of particles present in the units tested does not exceed the appropriate value listed in *Table 1*. If the average number of particles exceeds the limit, test the article by the *Microscopic Particle Count Test*.

Table 1. Light Obscuration Test Particle Count

	Diameter	
	≥ 10 µm	≥ 25 µm
Number of particles	50 per mL	5 per mL

MICROSCOPIC PARTICLE COUNT TEST

Some articles cannot be tested meaningfully by light obscuration. In such cases, individual monographs clearly specify that only a microscopic particle count is to be performed. The microscopic particle count test enumerates subvisible, essentially solid, particulate matter in ophthalmic solutions, after collection on a microporous membrane filter. Some ophthalmic solutions, such as solutions that do not filter readily because of their high viscosity, may be exempted from analysis using the microscopic test.

When performing the microscopic test, do not attempt to size or enumerate amorphous, semiliquid, or otherwise morphologically indistinct materials that have the appearance of a stain or discoloration on the membrane surface. These

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