U.S. Pharmacopeia
The Standard of Quality℠

USP Certificate

USP PREDNISONE TABLETS RS
Lot P1I300
(10 mg nominal prednisone content per tablet)

FOR DISSOLUTION PERFORMANCE VERIFICATION TEST (PVT)

Period of validity: This certificate of USP Prednisone Tablets Lot P1I300 is valid through Feb 29, 2012.

The USP Prednisone Tablets RS is provided for use in the *Performance Verification Test* for USP Apparatus 1 and 2 in the USP General Test Chapters on DISSOLUTION <711>. Do not expose the tablets to excessive humidity. Store the tablets at 15° to 25°.

Dissolution Medium: We recommend preparing the medium as follows:

Heat a suitable amount of water, while stirring gently, to about 45°. Filter under vacuum through a 0.45-µm-porosity filter into a suitable filtering flask equipped with a stirring device. Seal the flask and continue to apply vacuum while stirring for an additional five minutes. Measured vacuum should be less than 100 mbar. Other deaeration techniques validated for 37° may be used. The temperature of the *Dissolution medium* should not fall below 37° prior to the initiation of the test.

Procedure [See DISSOLUTION <711> in the current USP]**:** Determine the quantity of prednisone, $C_{21}H_{26}O_5$, dissolved at thirty minutes, in each vessel, expressed as percent of the labeled amount. Use 498.0 g of *Dissolution Medium* (which corresponds to 500 mL), where possible the medium should not be stirred prior to the initiation of the test for the purpose of equilibration, and conduct the test at 37°. Operate each apparatus at 50- rpm speed. Withdraw an aliquot of sample solution at thirty minutes and filter immediately. Measure the amount of prednisone dissolved from filtered portions of the sample aliquots at 242 nm in comparison with a solution of known concentration of USP Prednisone Reference Standard.

Notes: An amount of alcohol not to exceed 5% of the total volume of the standard solution may be used to bring the prednisone standard into solution prior to dilution with *Dissolution medium*. The filtering method must not cause adsorptive loss of drug. Bias introduced by automated methods is to be avoided. If equipment is dedicated for use with only one apparatus (basket or paddle), then performance verification is only required for that apparatus.

Test Interpretation: Laboratory can choose either of the test schemes listed below.

Single-Stage Test

The following are step-by-step instructions for the single-Stage test.

1. For each position in the assembly, test one USP Prednisone Tablets RS, and record the percent dissolved at the sampling time point specified for that apparatus. For assemblies with 12 positions (12 dissolution vessels), transform the percent dissolved results to the natural log scale, determine the mean and variance, and no further testing is required.
2. For assemblies with fewer than 12 positions, repeat Step 1 with an additional set of tablets. Again after transforming the percent dissolved results to the natural log scale, determine the mean and variance.
3. Calculate the average of the two means and of the two variances obtained in Steps 1 and 2. (Use the results from Step 1 alone for assemblies that have 12 positions.)

4. Convert the results of Step 3 to a geometric mean (GM) and percent coefficient of variation (%CV). See calculation example below for more detail.
5. Compare the results of Step 4 to the **Single-Stage** acceptance ranges in table 1. The GM must not fall outside the limits, and the %CV must not be greater than the limit. If both meet the criteria, the assembly has passed the PVT.

Optional Two-Stage Test

A laboratory may choose to implement the PVT as a Two-Stage test. The Two-Stage test is a statistically valid means of allowing the possibility of stopping the test at the first stage with a penalty. The following are step-by-step instructions for the two-stage test.

1. For each position in the assembly, test one USP Prednisone tablets RS, and record the percent dissolved at each sampling time point specified for that apparatus. After transforming the percent dissolved results to the natural log scale, determine the mean and variance.
2. Convert the results of Step 1 to a GM and %CV, and compare to the **1st Stage of Two-Stage** acceptance ranges in table 1. The GM must not fall outside the limits, and the %CV must not be greater than the limit. For calculation of the GM and %CV, see calculation example for more detail.
3. If results of Step 2 satisfy both acceptance criteria, stop; the assembly has passed the PVT. Otherwise continue to Step 4.
4. Repeat Step 1 with an additional set of tablets and after transforming the percent dissolved results to the natural log scale determine the mean and variance for the data obtained at this step.
5. Average the two means and two variances obtained in Steps 2 and 4.
6. Convert the results of Step 5 to a geometric mean (GM) and percent coefficient of variation (%CV). For calculation of the GM and %CV, see calculation example for more detail.
7. Compare the results of Step 6 to the **2nd Stage of Two-Stage** acceptance ranges in Table 1. The GM must not fall outside the limits, and the %CV must not be greater than the limit. If both meet the acceptance criteria, the assembly has passed the PVT.

Table 1. Performance Verification Test (PVT) limits (values apply only to Lot P1I300)

Apparatus	# of vessels (n)	Single-Stage		Two-Stage			
				1st Stage of Two-Stage		2nd Stage of Two-Stage	
		GM*	%CV	GM*	%CV	GM*	%CV
1	6	56 - 75	10	60- 71	7.7	56 - 75	10
	7						9.8
	8						9.7
	12			na			
2	6	25- 41	6.8	27 - 38	5.1	25- 41	6.7
	7		6.7				6.6
	8		6.5				6.4
	12		6.7	na			

* Percent of the labeled amount of prednisone dissolved at 30 minutes at 50-rpm

Calculation example (expressed as Microsoft Excel® worksheet functions):

Run 1: $x_1, x_2, ..., x_n$ in natural log scale: Ln x_1, Ln x_2, …, Ln x_n

Run 2: $x_{n+1}, x_{n+2}, ..., x_{2n}$ in natural log scale: Ln x_{n+1}, Ln x_{n+2}, …, Ln x_{2n}

1st Stage of Two-Stage for n=6, 7, 8 and Single-Stage for n=12:

GM1 = exp(average (Ln x_1:Ln x_n))

%CV1 = 100*sqrt(exp(var(Ln x_1:Ln x_n)) −1)

Single-Stage or 2nd Stage of Two-Stage for n=6, 7, 8:

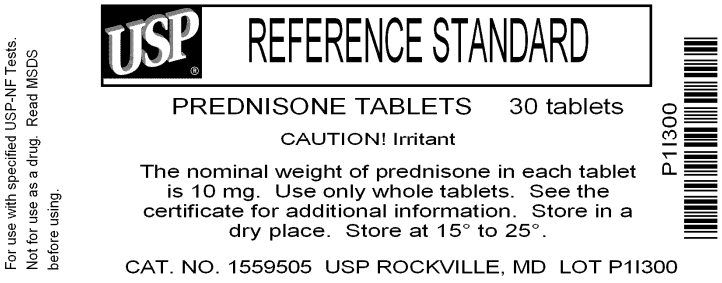
GM = exp(average (average (Ln x_1:Ln x_n), average (Ln x_{n+1}:Ln x_{2n}))) = exp(average (Ln x_1:Ln x_{2n}))

%CV= 100*sqrt(exp(average(var(Ln x_1:*Ln* x_n), var(Ln x_{n+1}:Ln x_{2n}))−1)

exp: exponential (e^x) var: variance sqrt: square root *: multiply 100: conversion factor to percentage

A webtool that can be used to perform the calculation is available on USP's Website (www.USP.org)

LABEL TEXT



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QA Director

Calculation Value

Unless otherwise stated on the Reference Standard label, a value of 100.0% should be used in USP or NF compendial applications for which the use of this Reference Standard is intended. Please refer to the specific Reference Standard label for further information.

Expiration

Current lots are identified in the Official USP Reference Standards catalog. In some cases, the previous lot may still be considered official. If so, it is identified in the column marked "Previous Lot/Valid Use Date." Ordinarily, the previous lot is carried in official status for about one year after the current lot enters distribution.

It is the responsibility of each user to determine that this lot is current when used. To ensure up-to-date information, USP publishes the Official USP Reference Standards Catalog, which contains official lot designations. This information is also available on the USP web site, at www.usp.org, as well as in the bimonthly subscription publication, *Pharmacopeial Forum*.

Instructions for Use

Follow the instructions in the appropriate USP or NF Monographs and General Requirements for Tests and Assays of the current *USP–NF*. In the event that instructions on the label of this lot differ from those found in the current *USP–NF,* those on the label supersede any instructions listed in Chapter <11>.

Non-Monograph Use

The suitability of this Reference Standard for use in non-compendial applications is solely the responsibility of the user.
