Certificate

PREDNISONE TABLETS

USP Catalog No.:	1559505
USP Lot No.:	R132B0

(10 mg nominal prednisone content per tablet)
FOR DISSOLUTION PERFORMANCE VERIFICATION TEST (PVT)

Period of validity: This certificate of USP Prednisone Tablets Lot R132B0 is valid through 31 December 2022.

The USP Prednisone Tablets RS is provided for use in the *Performance Verification Test* for USP Apparatus 1 and 2 with 1-Liter vessels in the USP General Test Chapter on DISSOLUTION <711> and DRUG RELEASE <724>, APPARATUS SUITABILITY. Store in a dry place. Store the tablets at controlled room temperature not exceeding 25°.

Dissolution Medium: We recommend preparing the medium as follows:
Heat a suitable amount of water, while stirring gently to about 41-45°. 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. 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 30 minutes, in each vessel, expressed as percent of the labeled amount. Use 499 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 30 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 reference standard into solution. 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. At the time of use, peel back the paper-backed lidding to remove the tablets from the blister card.

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. Transform the percent dissolved results to the natural log scale, determine the mean and variance. For assemblies with 12 or 14 positions (12 or 14 dissolution vessels), 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 or 14 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 in case of assemblies with less than 12 positions. 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 the sampling time point specified. 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 Stages** 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, the assembly has passed the PVT. Otherwise continue to Step 4. (see *note 1*).
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 1 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 Stages** 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.

In order to comply with the requirements of ASTM E29, all limit values in Table 1 are expressed with two significant figures.

Table 1: Performance Verification Test (PVT) limits (values apply only to Lot R132B0)

<table>
<tr><th rowspan="3">Apparatus</th><th rowspan="3"># of vessels</th><th colspan="2" rowspan="2">Single-Stage</th><th colspan="4">Two-Stage</th></tr>
<tr><th colspan="2">1st Stage of Two Stages</th><th colspan="2">2nd Stage of Two Stages</th></tr>
<tr><th>GM*</th><th>%CV</th><th>GM*</th><th>%CV</th><th>GM*</th><th>%CV</th></tr>
<tr><td rowspan="5">1</td><td>6</td><td rowspan="3">47-76</td><td>16</td><td>51-70</td><td rowspan="2">12</td><td rowspan="2">47-76</td><td rowspan="2">15</td></tr>
<tr><td>7</td><td>15</td><td rowspan="2">52-70</td></tr>
<tr><td>8</td><td>15</td></tr>
<tr><td>12</td><td>47-77</td><td>16</td><td colspan="4" rowspan="2">Not Applicable</td></tr>
<tr><td>14</td><td>47-76</td><td>15</td></tr>
<tr><td rowspan="5">2</td><td>6</td><td rowspan="5">27-37</td><td>8.3</td><td rowspan="3">28-35</td><td rowspan="3">6.2</td><td rowspan="3">27-37</td><td>7.7</td></tr>
<tr><td>7</td><td>8.1</td><td>7.5</td></tr>
<tr><td>8</td><td>7.9</td><td>7.4</td></tr>
<tr><td>12</td><td>8.2</td><td colspan="4" rowspan="2">Not Applicable</td></tr>
<tr><td>14</td><td>8.0</td></tr>
</table>

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

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

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

Run 2: $x_{n+1}, x_{n+2}, \ldots, x_{2n}$ 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, 14:

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

Note 1:
There are circumstances when the %CV after the first stage equals or exceeds the value in the **Futility Factor** table (without rounding), then it is impossible to meet the %CV criterion after the second stage. The lab can stop after the first stage (run). However, after any adjustments to equipment, test procedure, and so on, the PVT must be restarted with a new first run.

Futility Factor
(%CV at or above value given, second stage testing will not produce passing result)

Apparatus	No. of Vessels		
	6	**7**	**8**
1	21	21	21
2	11	11	10

LABEL TEXT

Quality Assurance

Certificate Version History

Version Number	Date	Reasons for Change
00	**30-JUL-2021**	First issue
01	**18-MAR-2022**	The Valid Use Date (VUD) has been extended from 30 June 2022 to 30 September 2022.
02	**26-JUL-2022**	The Valid Use Date (VUD) has been extended from 30 September 2022 to 31 December 2022.

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