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⟨671⟩ CONTAINERS—PERFORMANCE TESTING

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INTRODUCTION

It is the purpose of this chapter to provide standards for the functional properties of packaging systems used for solid oral dosage forms (SODFs) and liquid oral dosage forms (LODFs). The tests in this chapter may be applied to ▲packaging systems for▲ (USP 1-Dec-2020) other dosage forms with the appropriate justification. ▲These▲ (USP 1-Dec-2020) tests ▲▲ (USP 1-Dec-2020) determine the moisture vapor transmission rate (MVTR) i.e., water vapor permeation rate, for plastic packaging systems for manufacturers, packagers, and repackagers (*Table 1*). This chapter also includes a classification system that allows pharmacists and institutional repackagers to select appropriate containers to repackage SODFs and LODFs. Definitions that apply to this classification system are provided in *Packaging and Storage Requirements ⟨659⟩*.

▲Guidance on the application of these methods to determine the MVTR and the use of MVTR data to support the demonstration of the equivalence of plastic packaging systems when repackaging SODFs is contained in *The Application of Moisture Vapor Transmission Rates for Solid Oral Dosage Forms in Plastic Packaging Systems ⟨1671⟩*. Definitions of a blister, blister card, barrier blister types, moisture vapor transmission rate, and test specimen are contained in *⟨1671⟩, Glossary*.

The chapter also contains a method for the determination of spectral transmission of plastic containers.▲ (USP 1-Dec-2020)

Table 1. Moisture Vapor Transmission Test Methods for ▲Plastic▲ (USP 1-Dec-2020) Packaging Systems

Section	Moisture Vapor Transmission for ▲Plastic▲ (USP 1-Dec-2020) Packaging Systems	Classification System for ▲Plastic▲ (USP 1-Dec-2020) Packaging Systems		
Subsection	▲Desiccant Method (*Methods 1*, *2*, and *3*) Water Method (*Method 4*)▲ (USP 1-Dec-2020)	Classification Based on Desiccant Method ▲for SODF (*Methods 5*, *6*, and *7*)▲ (USP 1-Dec-2020)		Classification Based on Water Method ▲for LODF (*Method 8*)▲ (USP 1-Dec-2020)
Application	Multiple-unit containers ▲▲ (USP 1-Dec-2020) and single-unit or unit-dose containers	Multiple-unit containers ▲▲ (USP 1-Dec-2020)	Single-unit and unit-dose containers ▲▲ (USP 1-Dec-2020)	Multiple- ▲▲ (USP 1-Dec-2020) unit containers
Users	Manufacturers, ▲Packagers Repackagers▲ (USP 1-Dec-2020)	Manufacturers Packagers Repackagers Pharmacies	Manufacturers Packagers Repackagers Pharmacies	Manufacturers Packagers Repackagers Pharmacies

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MOISTURE VAPOR TRANSMISSION FOR ▲PLASTIC▲ (USP 1-DEC-2020) PACKAGING SYSTEMS

Introduction

The purpose of the moisture vapor transmission test method, which is based upon American Society for Testing and Materials (ASTM) method D7709,[1] is to obtain reliable and specific MVTRs that can be used to distinguish barrier performance of packaging systems used for regulated articles by manufacturers, packagers, and repackagers. This test method will establish a value that represents the MVTR of the container–closure system being evaluated. There may be additional packaging systems where the test methods in this section could be applied; however, any deviation should be described. If other methods are used to measure MVTR, these methods should be described in sufficient detail to justify their use.

Desiccant Methods for Packaging Systems ▲▲ (USP 1-Dec-2020)

This section describes moisture vapor transmission test methods for multiple-unit containers (see *Method 1*), high-barrier ▲and ultra-high barrier▲ (USP 1-Dec-2020) single-unit and unit-dose containers (see *Method 2*), and low-barrier single-unit and unit-dose containers (see *Method 3*). ▲▲ (USP 1-Dec-2020)

These methods include the following:

- A specific moisture vapor transmission value for a container rather than a classification
- Sufficient sensitivity and precision to allow differentiation among moisture barrier performance for containers
- Conditions used for testing packaging systems that are the same as those used for accelerated stability testing of the primary packaging of regulated articles [typically 40°/75% relative humidity (RH)]

EQUIPMENT

The following equipment should be used to complete the test method:

- A balance for weighing the test specimens that has sufficient capacity to weigh the test specimens throughout the period of the test. ▲▲ (USP 1-Dec-2020) The balance must have sensitivity adequate to measure small differences in weight from one time point to the next. The weighing uncertainty must be less than 5% of the weight gain from one time point to the next. The weighing uncertainty is typically three times the balance resolution/sensitivity. As an example, a balance with a resolution of 0.1 mg is acceptable for packaging systems whose weight gain per time interval is more than or equal to 6 mg [(0.1 × 3)/5%], which is 60 times the balance sensitivity.
- A chamber capable of maintaining 40 ± 2° and 75 ± 5% RH. Other chamber conditions can be used, ▲but should be noted in the report,▲ (USP 1-Dec-2020) as long as the balance sensitivity is adequate to measure small weight differences from one time point to the next time point.

DESICCANT

Method 1: The desiccant is anhydrous calcium chloride in granular form. Other desiccants, such as a molecular sieve or silica gel, may be suitable. If anhydrous calcium chloride is used, pre-dry at 215 ± 5° for 7¼±¼ h to ensure that any hexahydrate present is fully converted to

the anhydrate. Cool the desiccant in a desiccator for at least 2 h before use. [NOTE—It has been shown[2] that anhydrous calcium chloride may contain calcium hexahydrate, which loses water only when the temperature reaches 200°.]

Methods 2 and 3: ▲USP Desiccant, Small RS; USP Desiccant, Medium RS; and USP Desiccant, Large RS. The Reference Standards for desiccants are molecular sieves molded in a form to fit the size and shape of the blister cavity used. These desiccants should be at or near their original values when stored in their original and unopened containers, and thus drying should not be required. Prior to use, if the average weight of 10 tablets exceeds the weight specified on the USP certificate by more than 3%, drying shall be performed. Dry at 250 ± 5° for 1–2 h and cool in a desiccator for at least 2 h before use. Store desiccant in a tightly closed container in the driest conditions possible after being removed from original container.▲ (USP 1-Dec-2020)

PROCEDURE

Method 1: Use 15 multiple-unit containers and 15 closures representative of the system to be tested. Prepare the test specimens by filling each multiple-unit container to two-thirds ▲of its nominal volume▲ (USP 1-Dec-2020) with desiccant and then, for screw-type closures, applying the closure using the torque that is within the range of tightness specified in *Table 2*. For other closure types, apply the closure according to the intended method. ▲If the intended use of the container shall have an impervious seal, then▲ (USP 1-Dec-2020) ensure that a proper seal has been made with the intended membrane to the land area of the bottle ▲opening.▲ (USP 1-Dec-2020) Identify each multiple-unit container with indelible ink. Do not use a label. If there is a need to increase the precision of the method, the user can test the system without the closure as long as an impervious seal remains on the container. If desired, weigh each multiple-unit container at ambient temperature and RH. Record this weight for time 0, but do not use it in the calculation of permeation. Place all containers in the test chamber (40°/75% RH) within 1 h of weighing. Weigh all multiple-unit containers at time intervals of 7 days ± 1 h. Weigh the multiple-unit containers at 7, 14, 21, 28, and 35 days to get ▲five▲ (USP 1-Dec-2020) steady-state data points. (The time interval from time 0 to day 7 is the period of equilibration.) Prior to weighing at each time interval, equilibrate the containers for about 30 min at the weighing temperature and RH. Limit the time out of the chamber to less than 2 h. Record the weights in an appropriate manner for later computation of the regression line.

Table 2. Torque Applicable to Screw-Type Container

Closure Diameter[a] (millimeters)	Suggested Tightness Range with Manually Applied Torque[b] (inch-pounds)	Suggested Tightness Range with Manually Applied Torque[b] (Newton-meters)
8	5	0.56
10	6	0.68
13	8	0.90
15	5–9	0.56–1.02
18	7–10	0.79–1.13
20	8–12	0.90–1.36
22	9–14	1.02–1.58
24	10–18	1.13–2.03
28	12–21	1.36–2.37
30	13–23	1.47–2.60
33	15–25	1.69–2.82
38	17–26	1.92–2.94
43	17–27	1.92–3.05
48	19–30	2.15–3.39
53	21–36	2.37–4.07
58	23–40	2.60–4.52

Closure Diameter[a] (millimeters)	Suggested Tightness Range with Manually Applied Torque[b] (inch-pounds)	Suggested Tightness Range with Manually Applied Torque[b] (Newton-meters)
63	25–43	2.82–4.86
66	26–45	2.94–5.08
70	28–50	3.16–5.65
83	32–65	3.62–7.35
86	40–65	4.52–7.35
89	40–70	4.52–7.91
100	45–70	5.09–7.91
110	45–70	5.09–7.91
120	55–95	6.22–10.74
132	60–95	6.78–10.74

[a] The torque designated for the next larger closure diameter is to be applied in testing containers having a closure diameter intermediate to the diameters listed.

[b] A suitable apparatus is available from SecurePak, *www.secure-pak.com*. An MRA model of a spring torque tester with indicators on both the removal and application sides is available in the following ranges: 1) 0–25 inch-pounds, read in 1-inch-pound increments; 2) 0–50 inch-pounds, read in 2-inch-pound increments; and 3) 0–100 inch-pounds, read in 5-inch-pound increments.

Method 2: Use 10 test units for this method. Provide a minimum of 10 blister cavities for each test unit. If the ▲blister▲ (USP 1-Dec-2020) card contains fewer than 10 cavities, bundle the cards to form a ▲▲ (USP 1-Dec-2020) test unit of at least 10 cavities. This is required to provide sufficient weight gain at each time interval. Fill with predried desiccant, and seal the blisters on equipment that is capable of correctly filling and sealing the blister. The desiccant should fill the cavity. The total weight of the desiccant must be sufficient to meet the quantity required to avoid partial saturation of the *Desiccant* before completion of the test. Fill the blisters in a low-humidity atmosphere (as low as possible, but not greater than 50% RH). Do not expose the desiccants to room humidity for more than 30 min before sealing. Identify each test specimen with indelible ink; do not use a label. ▲▲ (USP 1-Dec-2020) It should be noted that bundling of the blisters during storage can impact air flow and correspondingly increase data variability.

Weigh each test unit at ambient temperature and RH. Record this weight for time 0. Place all test units in the test chamber (40°/75% RH) within 1 h of weighing. Weigh all test units at time intervals of 7 days ± 1 h. Weigh the test units at 7, 14, 21, 28, and 35 days to get five steady-state data points. (The time interval from time 0 to day 7 is the period of equilibration.) Prior to weighing at each time interval, equilibrate the containers for 30 ± 5 min at the controlled weighing temperature and RH. Limit the time out of the chamber to less than 2 h. Record the weights in an appropriate manner for later computation of the regression line.

Ultra-high barrier blisters may not show the full measure of precision and sensitivity this method can provide. For ultra-high barrier blisters, test units should have more than 10 cavities, but NMT 30 cavities. Examples are foil–foil blisters or very small blisters formed from other materials. An alternative approach is to double or triple the length of weighing intervals to achieve at least a 6-mg weight gain per time interval by the test specimen.

Method 3: Prepare the test units as directed in *Method 2*. Place all test units in the test chamber (40°/75% RH) within 1 h of weighing. Weigh the test units at the end of 2 days (48 ± 1 h). At this time, the difference in weight (the weight gain) is divided by the number of blister ▲cavities▲ (USP 1-Dec-2020) and days (2) in each test unit and this is taken as the MVTR in mg/day/▲cavity.▲ (USP 1-Dec-2020) The number of blisters tested depends on the barrier characteristics of the material, the size of the blister, and the sensitivity of the balance used in the test. For this method, the requirement of five consecutive weighings is waived because the desiccant quickly becomes saturated when packed in a low-barrier package and stored at 40°/75% RH. [NOTE—For low-barrier single-unit and unit-dose containers, the weight gain after the second day displays a curvilinear profile typical of approaching saturation of the desiccant. To obtain five weighings within 2 days is not viable and is likely to increase variability. *Methods 2* and *3* may require that the blister cards be bundled in multiples to achieve periodic weight gains of sufficient magnitude to use the balance sensitivity; when bundled, these cards or test specimens are called test units. The weight gain in each weighing period must be 20 times the sensitivity of the balance, and the balance sensitivity is three times the balance precision. In other words, the minimal weight gain per time interval should be at least 60 times the balance precision.]

CALCULATIONS

Methods 1 and 2: Perform the regression analysis for each test unit (see *Regression equation*). Typically, the initial data point (at day 0) is not included in fitting the regression line. The slope of the regression line is the MVTR of each test unit. For *Method 1*, the slope is the MVTR

for the corresponding multiple-unit container. For *Method 2*, the MVTR of each blister cavity is calculated by dividing the slope by the number of cavities in each test unit.

Method 3: Calculate the weight gain in mg/day/▲cavity▲ (USP 1-Dec-2020) from day 0 to day 2 using the 10 test units (see *Calculations*). The MVTR of each blister ▲cavity▲ (USP 1-Dec-2020) is calculated by dividing the weight gain by 2 (for 2 days) and the number of ▲blister cavities▲ (USP 1-Dec-2020) in each test unit.

Regression equation:

$$W = I + MT$$

Calculations:

$$Slope\left(M\right) = \sum_{i=1}^{N}\left[\left(W_i - \overline{W}\right)\left(T_i - \overline{T}\right)\right] / \sum_{i=1}^{N}\left(T_i - \overline{T}\right)^2$$

$$\text{Intercept } (I) = \overline{W} - M\overline{T}$$

W = measured weight (mg)

I = regression line intercept (point where regression line intersects the vertical axis)

M = regression line slope

T = time point

N = number of data points (each point consists of a weight and a time)

$\overline{W}$ = overall weight mean

$\overline{T}$ = overall time point mean

$$\sum_{i=1}^{N}\left[\left(W_i - \overline{W}\right)\left(T_i - \overline{T}\right)\right]$$

equals the sum of cross-products (for example, for each of the N data points, subtract the overall weight mean from the measured weight and the overall time point mean from the time point and multiply the two differences to get a cross-product, then sum all N cross-products).

$$\sum_{i-1}^{N}\left(T - \overline{T}\right)^2$$

equals the sum of squared deviations (for example, for each of the N data points, subtract the overall time point mean from the time point and square the difference, then use the sum of all N squared differences).

RESULTS

Method 1: Report the MVTR as the average value, in mg/day/container, and the standard deviation of the 15 slopes. Properly describe the container–closure system tested ▲(e.g., material, size, shape, and color).▲ (USP 1-Dec-2020)

Method 2: Report the MVTR as the average value, in mg/day/cavity, and the standard deviation of the 10 test unit slopes. Properly describe the container–closure system tested ▲(e.g., material, size, shape, and color).▲ (USP 1-Dec-2020)

Method 3: Report the MVTR as the average value from day 0 to day 2, in mg/day/▲cavity,▲ (USP 1-Dec-2020) and the standard deviation of the 10 test unit slopes. Properly describe the container–closure system tested ▲(e.g., material, size, shape, and color).

Water Method for Packaging Systems

This section describes moisture vapor transmission test methods (see *Method 4*) for low-barrier, high-barrier, and ultra-high barrier single-unit and unit-dose containers.

Method 4 includes the following:

- A specific moisture vapor transmission value for a packaging system rather than a classification.
- Sufficient sensitivity and precision to allow differentiation among moisture barrier performance for plastic blister packaging systems.
- Inverse environmental conditions (40°/25% RH) from those that are used for the desiccant method and stability testing of the primary packaging of regulated articles (40°/75% RH). These inverse conditions achieve the same pressure difference when water is used in place of desiccant.
- MVTR determination is based upon weight loss instead of weight gain.

EQUIPMENT

The following equipment should be used to complete the test method:

- A humidity-controlled glove box capable of maintaining relative humidity at 25% ± 5%.
- A balance for weighing the test specimens that has sufficient capacity to weigh the test specimens throughout the period of the test. The balance must have sensitivity adequate to measure small differences in weight from one time point to the next. The weighing uncertainty must be less than 5% of the weight gain from one time point to the next. The weighing uncertainty is typically three times

the balance resolution/sensitivity. As an example, a balance with a resolution of 0.1 mg is acceptable for packaging systems whose weight gain per time interval is more than or equal to 6 mg [(0.1 × 3)/5%], which is 60 times the balance sensitivity.

- A chamber capable of maintaining 40 ± 2°/25% ± 5% RH.

AMOUNT OF WATER FOR TEST CONTAINERS

For blisters, approximately 10–100 mg of water per blister cavity (about 1–10 drops), depending upon expected MVTR, is adequate for all blister types at 40°/25% RH. As an example, consider the preparation of a low-barrier MVTR package, e.g., a polyvinyl chloride (PVC) water-filled blister. The expected MVTR is about 1.5 mg water/(day × cavity) at 40° and a 75% RH vapor–pressure difference. The initial amount of water required to create 100% RH at 40° in this blister (approximately 0.5 cc volume) is 0.025 mg, on the basis of absolute humidity. For a typical MVTR study of a low-barrier blister, 7 days are allowed for equilibration, followed by a study period of 28 days for obtaining 3–5 weight determinations. This is a total exposure time, or permeation time, of 35 days. According to the *Water-based method equation*, a minimum of 52.5 mg of water is needed.

Water-based method equation: 1.5 mg water/(day × cavity) × 35 days + 0.025 mg = 52.5 mg water/cavity

The recommended amount of water for this blister system is about 100 mg per cavity. The water-based method equation can be used to determine the minimum amount of water for all blister types, and this amount should then be multiplied by a factor between 2 and 3 to achieve an excess.

PROCEDURE

Method 4: Use 10 test units for this method. Provide a minimum of 10 blister cavities for each test unit. If the blister card contains fewer than 10 cavities, bundle the cards to form a test unit of at least 10 cavities. This is required to provide sufficient weight loss at each time interval.

Fill blister cavities with a sufficient quantity of water. Care should be taken to insure the cavities are not overfilled and that water does not end up on the seal area.

Identify each test specimen with indelible ink; do not use a label. High-barrier plastic blister cards may be bundled to increase weight loss between weight determinations. Low-barrier plastic blister cards do not need to be bundled, regardless of the number of cavities per card. For bundled test units, it should be noted that bundling of the blisters during testing can impact air flow and correspondingly increase data variability.

Place test units in the humidity-controlled glove box at 25% RH for 60 min. Remove test units from the glove box and record initial weight to nearest 0.1 mg and time. Place all test units in the test chamber (40°/25% RH) and weigh at time intervals of 7 days ± 1 h. Weigh the test units at 7, 14, 21, 28, and 35 days to get five steady-state data points. Additional time points can be added to provide for laboratory operations and higher barrier blisters. At each time point, place the test units in the humidity-controlled glove box and allow to equilibrate for 60 min, then weigh, and record the time. After weighing, samples are placed back into the test chamber. [Note—It is imperative that the weighing order of test units be consistent among all time point weight determinations.]

Ultra-high barrier blisters may not show the full measure of precision and sensitivity this method can provide. For ultra-high barrier blisters, test units should have more than 10 cavities, but NMT 30 cavities. Examples are foil–foil blisters or very small blisters formed from other materials. An alternative approach is to double or triple the length of weighing intervals to achieve at least a 6-mg weight gain per time interval by the test specimen.

All test units should be inspected for the presence of water at each time point. Opaque and cold-form foil blisters should be opened at the conclusion of the test to insure the presence of water in each cavity since visual inspection is not possible.

CALCULATIONS

Method 4: Perform the linear regression analysis for each test unit by following the *Calculations* in *Methods 1 and 2* in *Desiccant Methods for Packaging Systems*, except the slope in *Water Method for Packaging Systems* is negative because of the moisture egresses and weight loss with time in the water method. The MVTR of each blister cavity is calculated by dividing the absolute value of the slope by the number of cavities in each test unit.

RESULTS

Method 4: Report the MVTR as the average value, in mg/day/cavity, and the standard deviation of the 10 test unit slopes. Properly describe the container–closure system tested.▲ (USP 1-Dec-2020)

Change to read:

CLASSIFICATION SYSTEM FOR PLASTIC PACKAGING SYSTEMS

Introduction

A classification system is included to provide methods that allow pharmacists and institutional repackagers to select appropriate containers for repackaging. Repackaging is the act of taking a finished drug product from the container in which it was distributed by the original manufacturer and placing it into a different container without further manipulation of the drug. The classification system provided can also be used by the drug product manufacturer for testing packaging systems that have had the primary seal broached.

Classification Based on Desiccant Method ▲for Solid Oral Dosage Forms▲ (USP 1-Dec-2020)

This section describes the methods for assigning the classification for multiple-unit containers (*Method* ▲*5*),▲ (USP 1-Dec-2020) multiple-unit containers with induction seals (*Method* ▲*6*),▲ (USP 1-Dec-2020) and single-unit and unit-dose containers (*Method* ▲*7*)▲ (USP 1-Dec-2020) used by pharmacists and institutional repackagers.

DESICCANT

Methods ▲5 and 6:▲ (USP 1-Dec-2020) Place a quantity of 4- to 8-mesh, anhydrous calcium chloride[3] in a shallow container, taking care to exclude any fine powder, dry at 215 ± 5° for 7¼±¼ h, and cool in a desiccator ▲for at least 2 h before use.▲ (USP 1-Dec-2020) [NOTE—It has been shown[2] that anhydrous calcium chloride may contain calcium hexahydrate, which loses water only when the temperature reaches 200°.]

Method ▲7: Use USP Desiccant, Small RS; USP Desiccant, Medium RS; or USP Desiccant, Large RS. The USP Reference Standards for desiccants are molecular sieves molded in a form to fit the size and shape of the blister cavity used. These desiccants should be at or near their original values when stored in their original and unopened containers, and thus drying should not be required. Prior to use, if the average weight of 10 tablets exceeds the weight specified on the USP certificate by more than 3%, drying shall be performed. Dry at 250 ± 5° for 1–2 h, and cool in a desiccator for at least 2 h before use. Store desiccant in a tightly closed container in the driest conditions possible after being removed from original container.▲ (USP 1-Dec-2020)

PROCEDURE

Method ▲5:▲ (USP 1-Dec-2020) Select 12 containers of a uniform size and type. Clean the sealing surfaces with a lint-free cloth, and close and open each container 30 times within the range of tightness specified in *Table 2*. Add desiccant to 10 of the containers, designated "test containers", filling each to within 13 mm of the closure if the container volume is 20 mL or more, or filling each to two-thirds of ▲its nominal volume▲ (USP 1-Dec-2020) if the container volume is less than 20 mL. If the interior of the container is more than 63 mm in depth, an inert filler or spacer ▲(e.g., glass beads)▲ (USP 1-Dec-2020) may be placed in the bottom to minimize the total weight of the container and desiccant; the layer of desiccant in such a container must be NLT 5 cm in depth. Close each container immediately after adding desiccant, and apply the torque designated in *Table 2* when closing screw-capped containers. To each of the remaining two containers, designated "controls", add a sufficient number of glass beads to attain a weight approximately equal to that of each of the test containers, and close, applying the torque designated in *Table 2* when closing screw-capped containers. Record the weight of the individual containers to the nearest 0.1 mg if the container volume is less than 20 mL, to the nearest milligram if the container volume is 20 mL or more but less than 200 mL, or to the nearest centigram (10 mg) if the container volume is 200 mL or more, and store at 75 ± 3% RH and a temperature of 23 ± 2°. [NOTE—A saturated system of 35 g of sodium chloride with each 100 mL of water placed in the bottom of a desiccator maintains the specified humidity. Other methods may be employed to maintain these conditions.] After 336 ± 1 h (14 days), record the weight of the individual containers in the same manner. Completely fill 5 empty containers of the same size and type as that of the containers under test with water or a noncompressible, free-flowing solid, such as well-tamped fine glass beads, to the level indicated by the closure surface when in place. Transfer the contents of each to a graduated cylinder, and determine the average container volume, in milliliters.

Method ▲6:▲ (USP 1-Dec-2020) Proceed as directed under *Method* ▲*5*,▲ (USP 1-Dec-2020) except fit containers with impervious seals obtained by heat-sealing the bottles with an aluminum foil–polyethylene laminate or other suitable seal. If there is a need to increase the precision of the method, the user can test the system without the closure as long as an impervious seal remains on the container. Keeping the cap on causes variation and the absorption of water by the cap liner is not part of the moisture permeation.

Method ▲7:▲ (USP 1-Dec-2020) Use this procedure for packs (e.g., punch-out cards) and blister cards that incorporate one or more separately sealed unit-dose containers or blisters. Seal a sufficient number of packs, such that NLT 4 packs and a total of NLT 10 unit-dose containers or blisters filled with 1 pellet in each unit are tested. Seal a corresponding number of empty packs, each pack containing the same number of unit-dose containers or blisters as used in the test packs, to provide the controls. Store all of the containers at 75 ± 3% RH and at a temperature of 23 ± 2°. [NOTE—A saturated system of 35 g of sodium chloride with each 100 mL of water placed in the bottom of a desiccator maintains the specified humidity. Other methods may be employed to maintain these conditions.] After 24 h, and at each multiple thereof (see *Classification*), remove the packs from the chamber, and allow them to equilibrate for about 45 min. Record the weights of the individual packs, and return them to the chamber. Weigh the control packs as a unit, and divide the total weight by the number of control packs to obtain the average empty pack weight. [NOTE—If any indicating pellets turn pink during the procedure, or if the average pellet weight increase in any pack exceeds 10%, terminate the test, and regard only earlier determinations as valid.] The test and control containers are weighed after every 24 h and after suitable test intervals for the final weighings. W_F and C_F are as follows: 24 h for Class D, 48 h for Class C, 7 days for Class B, and NLT 28 days for Class A.

CALCULATIONS

Methods ▲5 and 6:▲ (USP 1-Dec-2020) Calculate the rate of moisture vapor transmission, in mg/day/L:

$$(1000/14V)[(T_F - T_I) - (C_F - C_I)]$$

V = volume of the container (mL)

T_F = final weight of each test container (mg)

T_I = initial weight of each test container (mg)

C_F = average final weight of the two controls (mg)

C_I = average initial weight of the two controls (mg)

Method ▲7:▲ (USP 1-Dec-2020) Calculate, to two significant figures, the average rate of moisture vapor transmission, in mg/day, for each unit-dose container or blister in each pack taken:

$$[1/(N \times X)][(W_F - W_I) - (C_F - C_I)]$$

N = number of days expired in the test period (beginning after the initial 24-h equilibration period)

X = number of separately sealed units per pack

W_F = final weight of each test pack (mg)

W_I = initial weight of each test pack (mg)

C_F = final weight of the control packs (mg)

C_I = initial weight of the control packs (mg)

▲CLASSIFICATION▲ (USP 1-Dec-2020)

Method ▲5:▲ (USP 1-Dec-2020) Packaging systems are ▲classified as▲ (USP 1-Dec-2020) "tight" if NMT 1 of the 10 test containers exceeds 100 mg/day/L in moisture vapor transmission, and none exceeds 200 mg/day/L. Packaging systems are ▲classified as▲ (USP 1-Dec-2020) "well-closed" if NMT 1 of the 10 test containers exceeds 2000 mg/day/L in moisture vapor transmission, and none exceeds 3000 mg/day/L.

Method ▲6:▲ (USP 1-Dec-2020) Packaging systems are classified as ▲"tight"▲ (USP 1-Dec-2020) if the moisture vapor transmission exceeds 10 mg/day/L in NMT 1 of the 10 test containers, and none exceeds 25 mg/day/L.

Method ▲7:▲ (USP 1-Dec-2020) Class A: No pack tested exceeds 0.5 mg/day/unit in average blister MVTR; Class B: No pack tested exceeds 5 mg/day/unit in average blister MVTR; Class C: No pack tested exceeds 20 mg/day/unit in average blister MVTR; and Class D: None of the packs tested meet any of the above average blister MVTR requirements.

Classification Based on Water Method ▲for Liquid Oral Dosage Forms▲ (USP 1-Dec-2020)

The following procedure and classification scheme ▲(*Method 8*)▲ (USP 1-Dec-2020) is provided to ▲classify multiple-unit containers as "tight" for liquid oral dosage forms.▲ (USP 1-Dec-2020)

[NOTE—Determine the weights of individual container–closure systems (bottle; inner seal, if used; and closure), both as tare weights and fill weights, to the nearest 0.1 mg if the bottle capacity is less than 200 mL, to the nearest milligram if the bottle capacity is 200 mL or more but less than 1000 mL, or to the nearest ▲0.1 g▲ (USP 1-Dec-2020) if the bottle capacity is 1000 mL or more.]

PROCEDURE

▲Method 8:▲ (USP 1-Dec-2020) Select 12 bottles of a uniform size and type, and clean the sealing surfaces with a lint-free cloth. Fit each bottle with a seal, closure liner (if applicable), and closure. Number each container–closure system, and record the tare weight.

Remove the closures and, using a pipet, fill 10 bottles with water to the fill capacity. Fill two containers with glass beads, to the same weight as the filled test containers. If using screw closures, apply a torque that is within the range specified in *Table 2*, and store the sealed containers at a temperature of 25 ± 2° and 40 ± 2% RH. After 336 ± 1 h (14 days), record the weight of the individual containers, and calculate the water weight loss rate, in %/year, for each bottle taken:

$$\frac{[(W_{1i} - W_T) - (W_{14i} - W_T) - (W_{C1} - W_{C14})]}{(W_{1i} - W_T) \times 14} \times 365 \times 100$$

W_{1i} = initial weight of each individual bottle (i) (mg)

W_T = tare weight (mg)

W_{14i} = weight of each individual bottle (i) at 14 days (mg)

W_{C1} = initial weight of the control container at day 1 (mg)

W_{C14} = weight of the control container at 14 days (mg)

▲CLASSIFICATION

Method 8:▲ (USP 1-Dec-2020) The packaging systems are classified as "tight" ▲if NMT 1 of the 10 test containers exceeds 2.5%/year percentage of water weight loss and does not exceed 5.0%/year in any of them.▲ (USP 1-Dec-2020)

Change to read:

SPECTRAL TRANSMISSION ▲FOR LIGHT-RESISTANT PACKAGING COMPONENTS OR SYSTEMS

A packaging component or system intended to provide protection from light or offered as a light-resistant container meets the requirements for *Spectral Transmission for Light-Resistant Packaging Components or Systems*, where such protection or resistance is by virtue of the specific properties of the material of which the plastic component or system is composed, including any coating. A clear and colorless or a translucent packaging system that has light protection by means of an opaque enclosure by application of a suitable coating or wrapping (see *General Notices*) is exempt from the requirements for *Spectral Transmission for Light-Resistant Packaging Components or Systems*.▲ (USP 1-Dec-2020)

Apparatus

▲If the suitability of the packaging system is demonstrated through stability testing, spectral transmission testing is not required; otherwise, use a UV-visible spectrophotometer of suitable sensitivity and accuracy (see ⟨857⟩), adapted for measuring the amount of light transmitted by plastic materials used for pharmaceutical containers.▲ (USP 1-Dec-2020)

Procedure

Select a section representing the average ▲▲ (USP 1-Dec-2020) thickness. Cut a circular section from ▲the packaging component or system,▲ (USP 1-Dec-2020) and trim as necessary to get a segment convenient for mounting in the spectrophotometer. After cutting, wash and dry the specimen, taking care to avoid scratching the surfaces. If the specimen is too small to cover the opening in the specimen holder, mask the uncovered portion of the opening with opaque paper or masking tape, provided that the length of the specimen is greater than that of the slit in the spectrophotometer. Immediately before mounting in the specimen holder, wipe the specimen with lens tissue. Mount the specimen with the aid of a tacky wax, or by other convenient means, taking care to avoid leaving fingerprints or other marks on the surfaces through which light must pass. Place the section in the spectrophotometer with its cylindrical axis parallel to the plane of the slit and approximately centered with respect to the slit. When properly placed, the light beam is normal to the surface of the section and reflection losses are at a minimum.

Continuously measure the transmittance of the section with reference to air in the spectral region of interest with a recording instrument or at intervals of about 20 nm with a manual instrument, in the region of 290–450 nm.

▲Acceptance Criteria▲ (USP 1-Dec-2020)

The observed spectral transmission does not exceed the limits given in *Table 3* for ▲plastic components and systems▲ (USP 1-Dec-2020) for parenteral use. The observed spectral transmission for plastic containers for products intended for oral or topical administration does not exceed 10% at any wavelength in the range of 290–450 nm.

Table 3. ▲Spectral Transmission Limits for Plastic Packaging Components or Systems▲ (USP 1-Dec-2020)

Nominal Size (mL)	Maximum Percentage of Spectral Transmission at Any Wavelength Between 290 and 450 nm
1	▲25▲ (USP 1-Dec-2020)
2	▲20▲ (USP 1-Dec-2020)
5	▲15▲ (USP 1-Dec-2020)
10	▲13▲ (USP 1-Dec-2020)
20	▲12▲ (USP 1-Dec-2020)
▲50▲ (USP 1-Dec-2020)	▲10▲ (USP 1-Dec-2020)
▲>▲ (USP 1-Dec-2020) 50	▲10▲ (USP 1-Dec-2020)

Delete the following:

▲GLOSSARY

Blister:
Formed, lidded, and sealed plastic or foil dome that contains the capsule or tablet (usually a single unit or unit dose).

Low-barrier blister:
Blisters made from low-barrier materials, formed and sealed so that the moisture vapor transmission rate when tested at 40°/75% RH is greater than 1.0 mg/cavity/day.

High-barrier blister:
Blisters made from high-barrier material, formed and sealed so that the moisture vapor transmission rate when tested at 40°/75% RH is less than 1.0 mg/cavity/day.

Ultra-high barrier blister:
Blisters made from ultra-high barrier material, formed and sealed so that the moisture vapor transmission rate when tested at 40°/75% RH is less than 0.01 mg/cavity/day.

Blister card:
A contiguous group of blisters formed and sealed with lid in place. The number of blisters per card commonly ranges from 1 to 10 but may be more. The blister card may sometimes be referred to as a packaging system.

Cavity:
Formed, lidded, and sealed plastic or foil dome (see *Blister*).

Moisture vapor transmission rate:
The steady-state moisture vapor transmission (in unit time) through a packaging system, under specific conditions of temperature and humidity. These test methods use gravimetric measurement to determine the rate of weight gain as a result of moisture vapor transmission into the packaging system and subsequent uptake by a desiccant enclosed within the packaging system.

Test specimen (or specimen)**:**
For multiple-unit containers, the bottle is the test specimen, and for single-unit or unit-dose containers, the blister card containing multiple blister cavities is the test specimen. For blisters, more than 1 card (or specimen) may be grouped into a test unit for conducting the test.

Test unit:
For multiple-unit containers, the bottle is the test unit as well as being the test specimen, and for single-unit or unit-dose containers, the test unit is a group of test specimens (blister cards) processed together for temperature and humidity exposure and for weighing at each time point. The purpose of the test unit for single-unit or unit-dose containers is to gain the advantage of additive weight gain resulting from more blister cavities than are present on a single card. The test unit, when applied to bottles, is used to maintain naming congruence among test methods 1, 2, and 3.

▲ (USP 1-Dec-2020)

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[1] ASTM D7709. *Standard Test Methods for Measuring Water Vapor Transmission Rate (WVTR) of Pharmaceutical Bottles and Blisters* published by ASTM International, 100 Barr Harbor Drive, P.O. Box C700, West Conshohocken, PA 19428-2959.

[2] Chen Y, Li Y. Determination of water vapor transmission rate (WVTR) of HDPE bottles for pharmaceutical products. *Int J Pharm*. 2008;358(1-2):137–143.

[3] Suitable 4- to 8-mesh, anhydrous calcium chloride is available from VWR International.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
<671> CONTAINERS--PERFORMANCE TESTING	Desmond G. Hunt Principal Scientific Liaison	GCPD2020 General Chapters - Packaging and Distribution

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