ments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve USP Paclitaxel Impurity Mixture RS in acetonitrile, sonicating if necessary, to obtain a solution having a known concentration of about 1 mg per mL.

Standard solution—Dissolve an accurately weighed quantity of USP Paclitaxel RS in acetonitrile, sonicating if necessary, to obtain a solution having a known concentration of about 1 mg per mL.

Test solution—Transfer about 10 mg of Paclitaxel, accurately weighed, to a 10-mL volumetric flask. Dissolve in and dilute with acetonitrile to volume, sonicating if necessary, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 227-nm detector and a 4.6-mm × 15-cm column that contains 3-µm packing L1. The flow rate is about 1.2 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–28	100	0	isocratic
28–33	100→98	0→2	linear gradient
33–58	98→10	2→90	linear gradient
58–60	10	90	isocratic
60–63	10→100	90→0	linear gradient
63–70	100	0	isocratic

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between paclitaxel and benzyl analog is not less than 1.8. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%. [NOTE—For the purpose of peak identification, the approximate relative retention times are given in *Table 3*. The relative retention times are measured versus Paclitaxel.]

Table 3

Name	Relative Retention Time	Limit (%)
Propyl analog[1]	0.54	0.2
Cephalomannine (Paclitaxel related compound A)	0.76	0.5
sec-Butyl analog[2]	0.81	0.2
n-Butyl analog[3]	0.89	0.1
Benzyl analog	1.10	0.4
Baccatin VI	1.23	0.2
Pentyl analog[4]	1.31	0.2
7-Epipaclitaxel	1.51	0.4

[1] The following chemical name is assigned to the related compound Propyl analog: Baccatin III 13-ester with (2*R*,3*S*)-3-butanoylamino-2-hydroxy-3-phenylpropanoic acid.

[2] The following chemical name is assigned to the related compound *sec*-Butyl analog: Baccatin III 13-ester with (2*R*,3*S*)-2-hydroxy-3-(2-methylbutanoylamino)-3-phenylpropanoic acid.

[3] The following chemical name is assigned to the related compound *n*-Butyl analog: Baccatin III 13-ester with (2*S*,3*S*)-2-hydroxy-3-(pentanoylamino)-3-phenylpropanoic acid.

[4] The following chemical name is assigned to the related compound Pentyl analog: Baccatin III 13-ester with (2*R*,3*S*)-3-(hexanoylamino)-2-hydroxy-3-phenylpropanoic acid.

Procedure—Inject a volume (about 12 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the areas for all the peaks. Calculate the percentage of each impurity in the portion of Paclitaxel taken by the formula:

$$100(r_i / r_U)$$

in which r_i is the response of each individual impurity; and r_U is the sum of the areas of all the peaks obtained from the *Test solution*. In addition to not exceeding the limits for paclitaxel related impurities in *Table 3,* not more than 0.1% of any other single impurity is found; and not more than 2.0% of total impurities is found.

Assay—

Diluent—Prepare a mixture of methanol and acetic acid (200:1).

Mobile phase—Prepare a filtered and degassed mixture of water and acetonitrile (11:9). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve, using sonication if necessary, an accurately weighed quantity of USP Paclitaxel RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 1 mg per mL.

Assay preparation—Transfer about 10 mg of Paclitaxel, accurately weighed, to a 10-mL volumetric flask. Dissolve in *Diluent,* using sonication if necessary, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 227-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L43. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is between 0.7 and 1.3; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of $C_{47}H_{51}NO_{14}$ in the portion of Paclitaxel taken by the formula:

$$10C(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Paclitaxel RS in the *Standard preparation;* and r_U and r_S are the peak responses for paclitaxel obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Paclitaxel Injection

» Paclitaxel Injection is a sterile, stabilized solution of Paclitaxel, suitable for dilution for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of paclitaxel ($C_{47}H_{51}NO_{14}$).

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I glass, at controlled room temperature.

Labeling—Label it to indicate that it is to be diluted with a suitable parenteral vehicle prior to intravenous infusion.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
USP Paclitaxel RS
USP Paclitaxel Related Compound B RS
10-Deacetyl-7-epipaclitaxel.

Identification—

A: The retention time of the major peak in the chromatogram of the *Test solution* corresponds to that in the chromato-

gram of the *Standard solution*, as obtained in the test for *Limit of degradation products*.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.67 USP Endotoxin Unit per mg of paclitaxel.

pH ⟨791⟩: between 3.0 and 7.0, in a solution (1 in 10).

Limit of degradation products—

Solution A—Prepare a filtered and degassed mixture of water and acetonitrile (3:2).

Solution B—Use filtered and degassed acetonitrile.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Dissolve accurately weighed quantities of USP Paclitaxel RS and USP Paclitaxel Related Compound B RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, to obtain solutions having known concentrations of about 1.2 mg per mL and 0.006 mg per mL, respectively.

Test solution—Quantitatively dilute an accurately measured volume of Injection with acetonitrile to obtain a solution containing about 1.2 mg of paclitaxel per mL, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 227-nm detector and a 4.6-mm × 15-cm column that contains 3-µm packing L1. The flow rate is about 1.2 mL per minute. The column temperature is maintained at 35°. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–26	100	0	isocratic
26–66	100→17	0→83	linear gradient
66–67	17→100	83→0	linear gradient
67–75	100	0	isocratic

Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between paclitaxel related compound B and paclitaxel is not less than 1.2; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas of the analyte peaks. Calculate the percentage of each degradation product in the volume of Injection taken by the formula:

$$100(C_S / C_U)(r_i / r_S)$$

in which C_S is the concentration, in mg per mL, of USP Paclitaxel Related Compound B RS in the *Standard solution;* C_U is the concentration, in mg per mL, of paclitaxel in the *Test solution*, based on the labeled amount of paclitaxel per mL of Injection; r_i is the peak area for each degradation product obtained from the *Test solution;* and r_S is the peak area for paclitaxel related compound B obtained from the *Standard solution*. In addition to not exceeding the limits stated in *Table 1*, not more than 0.1% of any other paclitaxel degradation product is found; and not more than 2.0% of total paclitaxel degradation products is found.

Table 1.

Relative Retention Time	Name	Limit (%)
0.19	Baccatin III	0.8
0.21	Ethyl ester side chain	0.4
0.50	10-Deacetylpaclitaxel	0.8
0.95	10-Deacetyl-7-epipaclitaxel (paclitaxel related compound B)	0.5
1.40	7-Epipaclitaxel	0.6

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Diluent—Transfer 200 µL of glacial acetic acid to a 1-liter volumetric flask containing about 500 mL of methanol, mix, and dilute with methanol to volume.

Mobile phase—Prepare a filtered and degassed mixture of water and acetonitrile (11:9). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Paclitaxel RS in *Diluent* to obtain a solution having a known concentration of about 0.6 mg per mL.

Assay preparation—Quantitatively dilute an accurately measured volume of Injection with *Diluent* to obtain a solution containing about 0.6 mg of paclitaxel per mL.

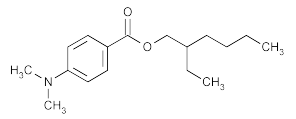
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 227-nm detector and a 4.0-mm × 25-cm column that contains 5-µm packing L43. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the retention time of the paclitaxel peak is between 6.0 and 10.0 minutes; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the paclitaxel peaks. Calculate the quantity, in mg, of paclitaxel ($C_{47}H_{51}NO_{14}$) in each mL of the Injection taken by the formula:

$$(L/D)C(r_U / r_S)$$

in which L is the labeled quantity, in mg, of paclitaxel in each mL of Injection; D is the concentration, in mg per mL, of paclitaxel in the *Assay preparation*, based on the labeled quantity; C is the concentration, in mg per mL, of USP Paclitaxel RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Padimate O



$C_{17}H_{27}NO_2$ 277.40

Benzoic acid, 4-(dimethylamino)-, 2-ethylhexyl ester.

2-Ethylhexyl *p*-(dimethylamino)benzoate [21245-02-3].

» Padimate O contains not less than 97.0 percent and not more than 103.8 percent of $C_{17}H_{27}NO_2$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Padimate O RS