

# Title

## DEFINITION

[Drug] Transdermal System contains NLT [\_.\_]% and NMT [\_.\_]% of CmHn\_p

## IDENTIFICATION

- **A. INFRARED ABSORPTION <197K>** [or <197M> or <197F>]

**or**

### INFRARED ABSORPTION <197S>

**Analytical wavelength:** {if more than a single wavelength, use **Wavelength range** as the subsection head}

**Cell:** {if other than 0.1-mm cell is used}

**Standard solution:** [ ] (g/mL in [solvent])

**Sample solution:** [ ] (g/mL in [solvent])

- **B. Ultraviolet Absorption <197U>**

**Analytical wavelength:** {if more than a single wavelength, use **Wavelength range** as the subsection head}

**Sample solution:** [ ] (g/mL in [solvent {if water, no need to state; in General Notices}])

**Acceptance criteria:** Absorptivities, calculated on the [dried][anhydrous] basis, do not differ by more than \_0%.

**Ratio:** Ax/Ay, [ ]-[ ]

- **C. Thin-Layer Chromatographic Identification Test <201>**

**Adsorbent:**

**Standard solution:** [ ] (g/mL in [solvent])

**Sample solution:** [ ] (g/mL in [solvent])

**Application volume:** [ ] (L)

**Developing solvent system:**

**Spray reagent:**

**Analysis**

- **D.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the **Assay**.
- **E.** A solution of [ ] μg/mL (or mg/mL) meets the requirements of the [flame] test[s] for [sodium, calcium, etc.] [<191>].

## ASSAY {Chromatographic Assay}

### PROCEDURE

**Mobile phase:** Solvent 1, solvent 2, and solvent 3 ([ ]:[ ]:[ ]). {Solvents should be in the order of Organic:Aqueous. If more than one organic constituent, then list them in the order of prevalence.}

**System suitability solution:** [ ] mg/mL of [drug {usually a USP Reference Standard}] and [ ] mg/mL of related compound [ ] in {if water, no need to state; per General Notices}

**Quantitative limit solution:** [ ] mg/mL of USP [ ] RS in [ ]

**or**

**Quantitative limit solution:** [ ] mL/mL of *System suitability solution* in [ ]

**Standard solution:** [ ] mg/mL of USP [ ] RS in [ ]

**Sample solution:** equivalent to [ ] mg/mL of [ ], from [Transdermal System] in [ ]

### Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

**Mode:** LC or GC

**Detector:** [detector type] [ ] nm

**Column:** [ ]-mm × [ ]-cm; packing L[ ]

**Temperature:** [ ]° **or** [See the temperature program table.](#)

**Flow rate:** [ ] mL/min

**Injection size:** [ ] μL

**Injection type:** {for GC}

### System suitability

**Sample:** *System suitability solution* and *Standard solution* [sometimes *Internal standard solution*]

**Suitability requirements**

**Resolution:** NLT [ ] between \_\_\_ and \_\_\_

**Column efficiency:** NLT [ ] theoretical plates

**Tailing factor:** NMT [ ]

**Relative standard deviation:** NMT \_\_\_% for [{number of}] replicate injections]

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of [drug] in the portion of [ ] taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times F \times 100$$

$r_U$  = peak response from the *Sample solution*

$r_S$  = peak response from the *Standard solution*

$C_S$  = concentration of the *Standard solution* (mg/mL)

$C_U$  = nominal concentration of the *Sample solution* (mg/mL)

$F$  = any monograph correction factor when a value is provided, such as a unit conversion

**Acceptance criteria:** [\_\_\_]%-[\_\_\_]% on the [ ] basis

**ASSAY {Titration Assay}**

• PROCEDURE

**Sample solution:**

**Titrimetric system**

(See *Titrimetry* <541>.)

**Mode:** Direct titration or residual titration

**Titrant:**

**Back-titrant:**

**Endpoint detection:** Potentiometric, colorimetric, or coulometric

**Analysis**

**Samples:**

Each mL of [ ] N titrant is equivalent to [\_\_\_] mg of [ ] {insert Drug chemical formula}.

Or

Calculate the percentage of the [drug substance] in the portion taken {equations for titrations are not needed if "Each mL [ ] N titrant is equivalent to [\_\_\_] mg of ..." is written into the text}:

$$\text{Result} = [(V - B) \times N \times F \times 100] / [TN \times W \times (100 - A)/100]$$

$V$  = sample titrant volume (mL)

$B$  = blank titrant volume (mL)

$N$  = titrant normality {units}

$F$  = equivalence factor (mg sample/mL of TN)

$TN$  = theoretical normality

$W$  = sample weight (mg)

$A$  = assay correction for LOD

**Acceptance Criteria:** [\_\_\_]%-[\_\_\_]% on the [ ] basis

**ASSAY {Microbiological Assay}**

• PROCEDURE

**Sample solution:** {Describe as required. Use template for the HPLC Assay above, but specify the appropriate buffer as directed in *Antibiotics—Microbial Assays* <81>.}

**Analysis:** Proceed as directed for [ ] under *Antibiotics—Microbial Assays* <81>. Use a volume of *Assay Preparation* diluted quantitatively to yield a *Sample solution* having a concentration assumed to be equal to the median dose level of the Standard.

**OTHER COMPONENTS** {may not be in all monographs; included in those monographs that have *Content of... tests*}

- **CONTENT OF [ ]**: [NLT \_\_\_\_%] [between \_\_% and \_\_%]
- **CONTENT OF CHLORIDE**: [NLT \_\_\_\_%] [\_\_%– \_\_%]
- **NITROGEN DETERMINATION, Method [I] [II] <461>**: [Proceed as directed, starting with \_\_\_\_ [m]g of [drug]: [NLT \_\_\_\_%] [Between \_\_% and \_\_%, ] is found.]

**PERFORMANCE TESTS**

- **DRUG RELEASE <724>**: {If the monograph has more than one test, be sure that it is noted in the *Labeling* section, except for Test 1, and use the following text: If the product complies with this test, the labeling indicates that it meets *USP Dissolution/Drug release Test [x].*}

**Test [1]**

**Medium**: [\_\_\_\_]; [\_\_] mL

**Apparatus [5][6][7]**: [ ] [rpm] [cycles/min]{Necessary description of the test system should be provided, including how the Transdermal System is held in place during testing. For Apparatus 7, provide the size of the solution container and indicate the sample holder that is used}

**Times**: [ ], [ ], [ ] h

**Analysis**: {Described if different from that in the chapter.} Determine the amount of [C<sub>x</sub>H<sub>x</sub>\_\_\_\_O<sub>x</sub>] released by using the following procedure. {Directions similar to those in the *Dissolution test.*}

**Tolerances**: The amount of C<sub>x</sub>H<sub>x</sub>\_\_\_\_ O<sub>x</sub> released, expressed as [µg/h/cm<sup>2</sup>] [a percentage of the labeled amount absorbed in vivo], at the times specified, conforms to Acceptance Table 1 below for transdermal drug delivery systems.

Time (h)	Amount Dissolved (Release Rate)
—	
—	
—	

- **UNIFORMITY OF DOSAGE UNITS <905>**: Meet the requirements for [*Weight Variation*][*Content Uniformity*]  
**OR**
- **UNIFORMITY OF DOSAGE UNITS <905>**: Meet the requirements for *Weight Variation* with respect to [amoxicillin] and for *Content Uniformity* with respect to [clavulanic acid]

**IMPURITIES**

**Inorganic Impurities**

- **RESIDUE ON IGNITION <281>**: NMT [ ]%
- **CHLORIDE AND SULFATE, Chloride <221>**: A [ ]-g portion shows no more chloride than corresponds to [ ] mL of 0.020 N hydrochloric acid ([ ]%).
- **CHLORIDE AND SULFATE, Sulfate <221>**: A [ ]-g portion shows no more sulfate than corresponds to [ ] mL of 0.020 N sulfuric acid ([ ]%).
- **SELENIUM <291>**: [\_.\_\_%].[\_.\_\_%], a \_\_-mg specimen mixed with \_\_ mg of magnesium oxide being used.]
- **ARSENIC, Method [ ] <211>**: [ ] ppm
- **LEAD <251>**: [ ] ppm
- **HEAVY METALS, Method [I] [II] <231>**: [ ] ppm

**Organic Impurities** {include only degradation products and product specific impurities}

• **PROCEDURE 1**

**Mobile phase**: Solvent 1, solvent 2, and solvent 3 ([ ]:[ ]:[ ])

**System suitability solution**: [ ] mg/mL of [drug {usually a USP Reference Standard}] and [ ] mg/mL of related compound [ ] in [ ]

**Quantitative limit solution**: [ ] mg/mL of USP [ ] RS in [ ]

**or**

**Quantitative limit solution**: [ ] mL/mL of *System suitability solution* in [ ]

**Standard solution**: [ ] mg/mL of USP [ ] RS in [ ]

**Sample solution:** equivalent to [ ] mg /mL of [ ], from [Transdermal System] in [ ]

**Chromatographic system**

(See *Chromatography* <621>, *System Suitability*.)

**Mode:** LC or GC

**Detector:** [detector type] [ ] nm

**Column:** [ ]-mm × [ ]-cm; packing L[ ]

**Temperature:** [ ]° or See the temperature program table [for GC].

**Flow rate:** [ ] mL/min

**Injection size:** [ ] μL

**Injection type:** [for GC]

**System suitability**

**Sample:** *System suitability solution* or *Standard solution*

**Suitability requirements**

**Resolution:** NLT [ ] between \_\_\_ and \_\_\_

**Column efficiency:** NLT [ ] theoretical plates

**Tailing factor:** NMT [ ]

**Relative standard deviation:** NMT \_\_\_.%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of [limited substance] in the portion of [Drug] taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$  = peak response of [limited substance] from the *Sample solution*

$r_S$  = peak response from the *Standard solution*

$C_S$  = concentration of the *Standard solution* (mg/mL)

$C_U$  = concentration of the *Sample solution* (mg/mL)

**Acceptance criteria**

**Individual impurities:** See *Impurity Table 1*. {Create an impurity table if there are more than three named impurities. A table will be numbered "1", even if only 1 impurity table is in the document.}

**Total impurities:** NMT [ ]%

**Impurity Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
[Drug] related compound ___ <sup>a</sup>	—	—	[.]
{All identified impurities should be listed. If possible, provide a short name for an impurity when no USP Reference standard is available, for example: [Drug] Z-isomer, <sup>b</sup> [Drug] Butyl analog, <sup>c</sup> [Drug] 3-ketone. <sup>d</sup> Give full chemical names as footnotes.}	—	{two decimal places if less than 1.0; one decimal place if more than 1.0}	[.]
[Drug]	1.0	1.0	—
Any other individual, unidentified impurity	—	1.0	[.]

<sup>a</sup> Chemical name.

<sup>b</sup> Chemical name.

<sup>c</sup> Chemical name.

<sup>d</sup> Chemical name.

or

**Solution A:** Solvent 1, solvent 2, and solvent 3 ([ ]:[ ]:[ ]). Adjust with [ ] to a pH of [ ].

**Solution B:** Solvent 1, solvent 2, and solvent 3 ([ ]:[ ]:[ ]). Adjust with [ ] to a pH of [ ].

**Mobile phase:** See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	A1	B1
T1	A1	B1

T2	A2	B2
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#### Example of GC Temperature program table

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	6
40	30	80	14
80	30	200	3

#### Chromatographic system

(See *Chromatography <621>*, *System Suitability*.)

**Mode:** LC or GC

**Detector:** [detector type] [ ] nm

**Column:** [ ]-mm × [ ]-cm; packing L[ ]

**Temperature:** [ ]° or [See the temperature program table](#) {for GC}.

**Flow rate:** [ ] mL/min

**Injection size:** [ ] (L

**Injection type:** {for GC}

#### System suitability

**Sample:** System suitability solution or Standard solution

#### Suitability requirements

**Resolution:** NLT [ . ] between \_\_\_ and \_\_\_

**Column efficiency:** NLT [ ] theoretical plates

**Tailing factor:** NMT [ ]

**Relative standard deviation:** [ ], NMT [ . ]%

#### Analysis

**Samples:** Standard solution and Sample solution

Calculate the percentage of [limited substance] in the portion of [Drug] taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$  = peak response of [limited substance] from the *Sample solution*

$r_S$  = peak response from the *Standard solution*

$C_S$  = concentration of the *Standard solution* (mg/mL)

$C_U$  = concentration of the *Sample solution* (mg/mL)

#### Acceptance criteria

**Individual impurities:** See *Impurity Table 1*. {The table will be numbered with "1", even if only one table.}

**Total impurities:** NMT [ ]%

**Impurity Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT %
[Drug] related compound <sup>a</sup>	—	—	[ . ]
{All identified impurities should be listed. If possible, provide a short name for an impurity when no USP Reference standard is available, for example: [Drug] Z-isomer, <sup>b</sup> [Drug] Butyl analog, <sup>c</sup> [Drug] 3-ketone. <sup>d</sup> Give full chemical names as footnotes.}	—	{two decimal places if less than 1.0; one decimal place if more than 1.0}	[ . ]
[Drug]	1.0	1.0	—
Any other individual, unidentified impurity	—	1.0	[ . ]

<sup>a</sup> Chemical name.

<sup>b</sup> Chemical name.

<sup>c</sup> Chemical name.

<sup>d</sup> Chemical name.

## IMPURITIES {TLC Impurities procedure}

Organic Impurities

### • [Test]

**Standard solution:**

**Sample solution:**

**Adsorbent:** {e.g., 0.25-mm layer of chromatographic silica gel mixture. We have to specify it here but not in the ID test. Chapter <201> mentions it, but <621> does not.}

**Application volume:** [ ]  $\mu$ L

**Developing solvent system:** Solvent 1, Solvent 2, and Solvent 3 ([ ]:[ ]:[ ])

**Spray reagent:**

**Analysis:** Proceed as directed for *Chromatography* <621>, *Thin-Layer Chromatography*.

[Spray the plate with \_\_\_\_\_. Examine the plate under [short-wavelength UV light] [and then under] [long-wavelength UV light].

{When listing several spots on a TLC plate, cite in the order of increasing  $R_F$  value.}

{When stating a quantitative result, indicate:}

Any spot obtained from [ ], except for the principal spot, is not more intense than the spot of the *Standard solution* [ ]: NMT 0.\_% of any individual impurity is found.

## SPECIFIC TESTS

### • MICROBIAL ENUMERATION TESTS <61>

and/or

- **TESTS FOR SPECIFIED MICROORGANISMS <62>:** [Drug] meets the requirements of the tests for the absence of [*Salmonella* species] [*Escherichia coli*] [*Staphylococcus aureus*] [*Pseudomonas aeruginosa*].

or

The total aerobic microbial count does not exceed [ ] cfu/g (or mL), and the total combined molds and yeasts count does not exceed [ ] cfu/g (or mL). [The total aerobic microbial count is less than [ ] cfu/g (or mL).]

- **SPECIFIC GRAVITY <841>:** [ ]-[ ] [at °]
- **MELTING RANGE OR TEMPERATURE, [Class \_\_\_\_] <741>:** [ ]°-[ ]°
- **SPECIFIC ROTATION <781S>:** [+]-[-] [ ]° to [+]-[-] [ ]°  
**Sample solution:** [ ] mg/mL in [ ]
- **OPTICAL ROTATION, Angular Rotation <781A>:** [+]-[-] [ ]° to [+]-[-] [ ]°  
**Sample solution:** [ ] mg/mL in [ ]
- **CRYSTALLINITY <695>:** Meets the requirements
- **REFRACTIVE INDEX <831>:** [ ]-[ ] [at °]
- **ACIDITY:** [Dissolve \_\_ mg in \_\_ mL of \_\_\_\_]. [To \_\_ mL of \_\_\_\_], add [ ] of [ ] TS, and titrate with [ ] [to a \_\_\_\_ color]: NMT [ mL] of [\_.] N sodium hydroxide is required [to produce a \_\_\_\_ color] [for neutralization] [to produce a color change].
- **pH <791>:** [ ]-[ ] , [in a solution (\_\_\_\_ in \_\_\_\_)]
- **LOSS ON DRYING <731>:** Dry a sample [in a vacuum] [at a pressure not exceeding \_\_ mm of mercury] at [ ]° for [ ] h: it loses NMT .\_% of its weight.
- **LOSS ON IGNITION <733>:** When ignited at [ ] ([for \_ h] [to constant weight]), it loses [NMT .\_%][ .\_% - .\_%] of its weight.
- **WATER DETERMINATION, Method [I]/[II] <921>:** [\_.]%-[\_.]%
- **OTHER REQUIREMENTS:** It meets the requirements of the test for [ ] under [ ]. [Where the following language is used, please see the example of Indocyanine Green: Where the label states that the drug substance is sterile, it meets the requirements for *Sterility Tests* <71> and *Labeling* under *Injections* <1>. Where the label states that [Drug] must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements under *Bacterial Endotoxins Test* <85>.]

## ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in [well-closed] [tight] [light-resistant] containers [ ], and store at \_\_\_\_].

- **LABELING:** There should be no changes from the classic monograph. {Example: Label the article to indicate whether it is the anhydrous form or the hemihydrate form, and label it to indicate with which impurity procedures it complies.}
- **USP REFERENCE STANDARDS <11>** {ALPHABETICAL ORDER}
  - USP [Drug] RS
  - USP [Drug] Related Compound [ \_\_\_ ] RS