

transfer into a 50-milliliter volumetric flask approximately 16 milligrams of clavam-2-carboxylate authentic sample. Dilute to volume and transfer 10 milliliters into a 100-milliliter flask. Dilute to volume with water.

(b) *Preparation of sample solution.* Accurately weigh 100 milligrams of the sample into a 10-milliliter flask. Dilute to volume with water.

(iii) *System suitability requirements—*(a) *Tailing factor.* The tailing factor (*T*) for the clavulanate standard peak is satisfactory if it is not more than 1.5.

(b) *Efficiency of the column.* The efficiency of the column (*n*) is satisfactory if it is greater than 4,000 theoretical plates.

(c) *Resolution factor.* The resolution factor (*R*) between the clavulanic acid and clavam-2-carboxylic acid peaks is satisfactory if it is greater than 1.0.

(d) *Coefficient of variation (Relative standard deviation).* The coefficient of variation (*S<sub>r</sub>* in percent) is satisfactory if it is not more than 2.0 percent.

If the system suitability requirements have been met, then proceed as described in § 436.352(b) of this chapter.

(iv) *Calculations.* Calculate the percent of clavam-2-carboxylate content as follows:

$$\text{Percent clavam-2-carboxylate content} = \frac{\text{Mean sample height (or area)} \times \text{weight of standard} \times P}{\text{Mean peak height (or area) of standard} \times \text{weight of sample} \times 50}$$

where:

*P* = Percent clavam-2-carboxylic acid in the standard.

[49 FR 39674, Oct. 10, 1984, as amended at 55 FR 11584, Mar. 29, 1990]

#### § 455.15a Sterile clavulanate potassium.

(a) *Requirements for certification—*(1) *Standards of identity, strength, quality, and purity.* Clavulanate potassium is the potassium salt of *Z*-(2*R*,5*R*)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid. It is so purified and dried that:

(i) It is equivalent to not less than 755 micrograms and not more than 920 micrograms of clavulanic acid per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) Its moisture content is not more than 1.5 percent.

(v) Its pH of an aqueous solution containing 10 milligrams per milliliter is not less than 5.5 and not more than 8.0.

(vi) It gives a positive identity test.

(vii) Its [3*R*,5*S*]-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-3-carboxylic acid (clavam-2-carboxylate) content is satisfactory if it is not greater than .01 percent.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, identity, and clavam-2-carboxylate content.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research: 12 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay—*(1) *Clavulanic acid content.* Proceed as directed in § 455.15(b)(1) of this chapter.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 10 milligrams per milliliter of clavulanate potassium.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using a solution containing 10 milligrams per milliliter.

(6) *Identity.* Proceed as directed in § 436.211 of this chapter, using the sample preparation described in paragraph (b)(2) of that section.

(7) *Clavam-2-carboxylate content.* Proceed as directed in § 455.15(b)(5) of this chapter.

[50 FR 33519, Aug. 20, 1985, as amended at 54 FR 11584, Mar. 29, 1990]

#### § 455.20 Cycloserine.

(a) *Requirements for certification—*(1) *Standards of identity, strength, quality, and purity.* Cycloserine is a white to slightly yellowish compound. It has the