

Food and Drug Administration, HHS

§ 446.150a

a=Horizontal distance from point of ascent to a point of a maximum peak height; and
b=Horizontal distance from the point of maximum peak height to point of descent.

The asymmetry factor (*A_s*) is satisfactory if it is not less than 1.4 and not more than 2.0

(B) *Efficiency of the column.* From the number of theoretical plates (*n*) calculated as described in §436.216(c)(2) of this chapter calculate the reduced plate height (*h_r*) as follows:

$$h_r = \frac{(L)(10,000)}{(n)(d_p)}$$

where:

L=Length of the column in centimeters;
n=number of theoretical plates; and
d_p=Average diameter of the particles in analytical column packing in micrometers.

The absolute efficiency (*h_a*) is satisfactory if it is not more than 37.5 for the doxycycline peak.

(C) The resolution (*R*) between peaks for doxycycline and epi-doxycycline is satisfactory if it is not less than 1.5.

(D) *Coefficient of variation (relative standard deviation).* The coefficient of variation (*S_R* in percent) of 5 replicate injections is satisfactory if it is not more than 2.0 percent.

(E) *Capacity factor (k').* Calculate the capacity factor (*k'*) for doxycycline as follows:

$$k' = \frac{t_r - t_o}{t_o}$$

where:

t_r=Retention time of doxycycline in minutes; and
t_o=Column dead time in minutes, which is estimated from the following equation:

$$t_o = \frac{(3.1416)(D^2)(L)(0.75)}{4F}$$

where:

D=Column diameter in centimeters;
L=Column length in centimeters;
0.75=Average total column porosity; and
F=Flow rate in milliliters per minute.

The capacity factor (*k'*) for doxycycline is satisfactory if it is not less than 1.5 and not more than 2.5. If the system suitability requirements have been

met, then proceed as described in §436.216(b) of this chapter. Alternate chromatographic conditions are acceptable provided reproducibility and resolution are comparable to the system described. However, the sample preparation described in paragraph (b)(1)(ii)(B) of this section should not be changed.

(iv) *Calculations.* Calculate the doxycycline content as follows:

$$\text{Milligrams of doxycycline per capsule} = \frac{A_u \times P_s \times d}{A_s \times 1,000 \times n}$$

where:

A_u=Area of the doxycycline peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);
A_s=Area of the doxycycline peak in the chromatogram of the working standard;
P_s=Doxycycline activity in the doxycycline working standard solution in micrograms per milliliter;
d=Dilution factor of the sample; and
n=Number of capsules in the sample assayed.

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

(3) *Dissolution.* Proceed as directed in §436.215 of this chapter. The quantity *Q* (the amount of doxycycline dissolved) is 85 percent at 60 minutes.

(4) *Identity.* The high-pressure liquid chromatogram of the sample determined in paragraph (b)(1) of this section compares qualitatively to that of the doxycycline working standard.

[55 FR 6637, Feb. 26, 1990]

§ 446.150 Methacycline hydrochloride oral dosage forms.

§ 446.150a Methacycline hydrochloride capsules.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Methacycline hydrochloride capsules are composed of methacycline hydrochloride and one or more suitable and harmless lubricants and diluents enclosed in a gelatin capsule. Each capsule contains methacycline hydrochloride equivalent to either 70 milligrams of methacycline, 140 milligrams of methacycline, or 280 milligrams of methacycline. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of methacycline that