

SIMILARITY AND DIFFERENCE FACTORS

As confirmation of acceptance of each formulation of the test product, difference (f_1) and similarity (f_2) factors [113] should be determined by performing the requisite dissolution rate testing on 12 units of each according to the FDA's Guidance on Dissolution Testing of Immediate Release Solid Oral Dosage Forms [114].

The difference factor (f_1) is a measurement of the relative error between the two curves, whereas the similarity factor is a measurement of the similarity in the percent dissolution between the two curves. If the f_1 values range between 0 and 15 and f_2 values range between 50 and 100, the dissolution curves being compared are considered similar or equivalent. The closer f_1 and f_2 are to 0 and 100, respectively, the better the comparability of the curves.

These factors can be determined using the following formulas:

$$f_1 = \left\{ \frac{\left[\sum |R_t - T_t| \right]}{\sum R_t} 100 \right\}$$

$$f_2 = 50 \log \left\{ \left[1 + \frac{1}{n} \sum w_t (R_t - T_t)^2 \right]^{-0.5} 100 \right\}$$

where f = fit factor, R_t = reference assay at time t (percent dissolved), T_t = test assay at time t (percent dissolved), n = number of sample points, w_t = weighting at time t (optional), and \sum = summation from $t = 1$ to $t = n$.

In the example above, it was noted that the dissolution profile depicted in Figure 4.12 for a formula with increased lubricant levels represented the formulation of choice. Calculated f_1 and f_2 values for this formulation relative to Brand Lots 1, 2, and 3 indicate that the test product is equivalent in vitro to only Brand Lot 2. The table below is a summary of all the calculated f_1 and f_2 values.

	Brand Lot 1 vs. Test ^a	Brand Lot 2 vs. Test ^a	Brand Lot 3 vs. Test ^a
f_1	39.8	4.6	14.4
f_2	30.5	72.8	42.2

^a Test formulation—increased lubricant, depicted in Figure 4.12 (target hardness 6–10 kp).

REFERENCES

1. Stowell GW, Whittle RR. Form A of fluoxetine hydrochloride. The present invention provides novel processes for the preparation of Form A of fluoxetine hydrochloride. U.S. Patent 6,313,350, November 6, 2001.