

only required tests in the proposed rule, but establishments may choose to perform inprocess tests and tests on ingredients in order to prevent waiting until final product testing to discover defects.

iv. *Costs per test.* We estimated the costs per test partly with published prices of independent laboratories as posted on the Internet (Refs. E50 and E51), and partly from our conversations with FDA and industry experts on testing. We found that testing costs vary according to frequency and complexity. The more frequently technicians perform tests, the lower are the costs per test. Many tests require sophisticated equipment, such as gas chromatography, high pressure liquid chromatography, distillation, extraction, various spectrophotometers, and other types of equipment. Using sophisticated equipment requires trained personnel. Even simple physical or organoleptic testing requires training or experienced personnel. The type of ingredient, compound, or product can also affect the cost because some are easily identified using routine or single step techniques and others require multiple steps or complex techniques, especially if there are similar products that can be mistaken for the products being identified. The type of defect tested for affects the cost; some defects can be found visually if they are found on the surface, but others are latent. Some tests require multiple samples or multiple steps. In addition, tests require the taking and of samples, whose cost can vary.

We assumed that \$20 per test represented a plausible lower bound. This cost represents the full cost of carrying out a test, including collecting and storing the sample, the time for training the personnel who carry out the test, and any associated records. Although some Internet testing prices for tests were as high as \$300, we assumed that with frequent testing \$150 would be a more plausible upper bound average cost. The majority of listed

prices fell into the \$20 to \$80 range, so we selected \$50 (the midpoint) as most likely. The average cost per test was about \$60.⁸

Changing our assumption about the midpoint of testing costs would change our estimate of the cost of the rule. If the cost of testing each batch is actually significantly higher, then the impact to those firms that incur the cost and to society will have been understated.

v. *The number and cost of tests:* *summary.* We estimated the number of tests required of the representative manufacturer as a weighted average of the number of tests required for vitamins and minerals and the number of tests required for all other supplements (which were mainly herbal products). We used survey responses to a question about the establishment's primary line of business for the weights used to compute the average number of tests. We dealt with multiple responses by treating all nonvitamin and nonmineral responses as other dietary supplements. The following weights, as shown below, differed by size of manufacturer:

- 24 percent of very small manufacturers produce vitamins and minerals; 76 percent produce other dietary supplements.
- 42 percent of small manufacturers produce vitamins and minerals; 58 percent produce other dietary supplements.
- 69 percent of large manufacturers produce vitamins and minerals; 31 percent produce other dietary supplements.

The annual cost of testing differed by the size of the firm, because the average number of batches produced differed. For the option calling for more strict regulation, the total costs of testing would be much higher than in the proposed rule. The unadjusted total cost of testing under the more restrictive CGMP option would be:

\$148,000 for very small establishments;
\$415,000 for small establishments;
\$263,000 for large establishments.

We estimate that the adjusted total cost for testing for the proposed regulation will be:

\$11,230 for very small establishments;
\$19,907 for small establishments;
\$7,626 for large establishments.

We found some corroboration for these estimates in a comment on the Advance Notice of Proposed Rulemaking entitled "Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Supplements" published in the **Federal Register** of February 6, 1997 (62 FR 5699 to 5709). According to the comment, the cost of testing components and final products inhouse would be at least \$650 per batch plus microbiological tests. Testing costs could be more if establishments sent samples to independent laboratories for testing or if they conducted extensive identity tests of herbal and botanical products. If we apply the \$650 to the annual number of batches per establishment, the comment implies that very small establishments would perform \$145,000 ($223 \times \650) worth of tests, small establishments would perform \$360,000 ($554 \times \650) worth of tests, and large establishments would perform \$200,000 ($309 \times \650) worth of tests. These estimates are reasonably close to our simulation estimate.

The unadjusted testing costs represent the total requirements and recommendations, not the additional costs that would be incurred in response to the proposed rule. Tests on incoming components and inprocess tests would not be required by the proposed rule. Most establishments already conduct some tests, or send samples out for testing. We, therefore, adjusted the estimated testing costs of the proposed rule to include only required tests and to account for the testing costs currently borne voluntarily by manufacturers. The survey results showed how many respondents were conducting various types of tests.

TABLE 14.—VALUES USED IN TESTING COST CALCULATIONS

Name	Value or distribution used	Source
Number of dietary ingredients per product batch	Vitamins and minerals—13; All other categories—4.	Sample from 3,000 dietary supplement labels (Ref. E46).

⁸ The average cost is higher than the most likely cost because we modeled costs with a Beta-Pert distribution that was skewed rightward (toward higher costs). The Beta distribution is part of the Bernoulli family of distributions and is closely related to the Binomial. The Binomial gives the distribution of the number of successes (s) in n trials if the probability of the success in each trial

is p. The Beta shows the distribution of the value of p when s successes occur in n trials. The Beta-Pert distribution is a Beta distribution that has been rescaled to run between values other than 0 and 1. The Beta-Pert uses a minimum, maximum, and most likely value to generate a distribution running from the minimum to the maximum, with a mean equal to (minimum + (4 × most likely) + maximum)/

6. We used the Beta-Pert distribution because we did not have a representative sample to derive the distribution, but we did have enough information to identify a plausible maximum, minimum, and most likely value. The use of the Beta-Pert, then, indicates that we do not know the shape of the probability distribution of possible testing costs, but we do have limited data.