**Table 27-7** Probability of Accepting a Batch as Sterile Assuming the Contamination Rate to be Constant at 0.1%

| Sterility-test sample size | Batch size | | |
|---|---|---|---|
| | 1000 | 2000 | 5000 |
| 10 | 0.99 | 0.99 | 0.99 |
| 20 | 0.98 | 0.98 | 0.98 |
| 50 | 0.95 | 0.95 | 0.95 |

fungistatic tests. Where the DT test is employed, the initial transfer test is required to incubate for 14 days for EP, but only 7 days for the USP test.

## LIMITATIONS OF THE STERILITY TEST

The USP referee sterility test suffers from at least three limitations:

1. The invariant uncertainty that the small sample used in the test reliably represents the whole lot
2. The inability of the culture media and incubation conditions to promote the growth of any and all potential microbial contaminants
3. The unavoidable problem of occasional accidental contamination of the sterility-test samples.

### The Problem of Sampling and Statistical Representation

The probability of accepting lots having a given percent contamination is related to the sterility-test sample size rather than to batch size (Ref. 1 and all references therein). For example, if a batch is 0.1% contaminated (one nonsterile unit in 1000 units) and 10 units are sampled for a sterility test, the probability of finding one of those 10 samples to be the one contaminated unit in 1000 is not significantly different if the batch size were 1000, 2000, or 5000. Increasing the sample size from 10 to 20 to 50 units per batch, however, affects the probability of accepting the batch as sterile to a more significant degree than does the increase in batch size, assuming that the increase in batch size does not increase the level of contamination. This phenomenon is depicted in Table 27-7. The probability rate does not change as the batch size is increased, but does change as the sample size is increased. Of course, a key factor is that the contamination rate remains at 0.1% as the batch size increases. This, in reality, may not be true, especially for aseptically filled products. Hence, if the contamination rate increases with batch size, the probability of acceptance decreases for the same sample size.

The relationship of probability of accepting loss of varying degrees of contamination to sample size is given in Table 27-8. Three details may be learned assuming the data in Table 27-8 to be real: (*i*) as the sample size is increased, the probability of accepting the lot as sterile is decreased; (*ii*) at low levels of contamination, for example, 0.1%, the odds of ever finding that one contaminated sample in 1000 units are so small that one must face the fact that lots are

**Table 27-8** Relationship of Probabilities of Accepting Lots of Varying Assumed Degrees of Contamination to Sample Size

| Number of samples tested (n) | Probability of accepting the lot as a function of assumed contamination rate from 0.1 to 20 percent | | | | | |
|---|---|---|---|---|---|---|
| | 0.1 | 1 | 5 | 10 | 15 | 20 |
| 10 | 0.99 | 0.91 | 0.60 | 0.35 | 0.20 | 0.11 |
| 20 | 0.98 | 0.82 | 0.36 | 0.12 | 0.04 | 0.01 |
| 30 | 0.95 | 0.61 | 0.08 | 0.01 | | |
| 100 | 0.91 | 0.37 | 0.01 | | | |
| 300 | 0.74 | 0.05 | | | | |
| 500 | 0.61 | 0.01 | | | | |