Table 22-6 Size of Particles of Varying Probability Levels[a]

Particle concentration	Particle size (μm) 50% chance	Particle size (μm) 100% chance
USP limit 50 particles/mL[b]	18.82	51.45
USP limit 5 particles/mL[c]	19.96	54.88
1 mL ampul, 1 particle	20.07	55.21
2 mL ampul, 1 particle	20.08	55.25
5 mL ampul, l particle	20.09	55.28
10 mL ampul, 1 particle	20.10	55.29
20 mL ampul, 1 particle	20.10	55.29
50 mL vial, 1 particle	20.10	55.29
1 L large volume, 1 particle	20.10	55.29

[a]Arcsine $P_1 = 0.33689252 + 0.02231515$ size $+ 0.000035$ size versus concentration -0.00008694 concentration.
[b]Not more than 50 particles/mL equal to or larger than 10 μm.
[c]Not more than 5 particles/mL equal to or larger than 10 μm.
Source: From Ref. 6.

It is not only the size, but also, and probably more importantly, the number of large particles injected into man intravenously that is considered dangerous. Thus, official standards have been enforced for maximum allowable numbers of certain-sized particles in parenteral solutions.

At least one attempt has been made to quantify the size and concentration of particles that can be detected by the unaided eye (6). Five-milliliter ampuls containing 10 to 500 particles per mL of particle sizes between 5 and 40 μm (using polystyrene beads) were inspected by 17 inspectors in a standard booth. Based on a multiple linear analysis model that calculated the probability of rejecting an ampul as a function of particle size and concentration, sizes of particles detected at various concentration levels at 50% and 100% probability of rejection rates were predicted. These data are reproduced in Table 22-6. The authors concluded that a 50% probability of rejection rate be achieved with 20 μm particles in sample solutions in order for potential inspectors to be qualified for in-line inspection. However, it is interesting to note that a minimum particle size of 55 μm was required for all inspectors to reject all solutions containing this size of particle.

Good attitude and concentration cannot be overemphasized. One of the major limitations of human inspection for particulate matter is reduced efficiency of the individual because of a lack of concentration. This can easily occur if the inspector suffers from extreme worry or other distraction resulting from outside personal pressures. Obviously, emotional stability is an important criterion in selecting inspectors.

Fatigue also becomes a major limitation of human inspection. Personnel should be provided appropriate relief from the inspection function by rotating jobs and allowing for rest periods.

Formal training programs must precede the acceptance of an individual as a qualified inspector. The training program should include samples of both acceptable and unacceptable product containers that must be distinguished by the trainee. During the training period, all units inspected by the trainee should be reinspected by qualified inspectors to ensure the quality of the inspection and the development of the trainee. After the inspector has passed his/her training period, performance tests should be done at random intervals to ensure that quality standards are being maintained. Personal experience plus some older literature reports (not cited) supports the logical conclusion that the more training and experience an inspector accumulates, the better the discrimination ability of the inspector to detect particles and other defects in finished products.

Methodology

Most inspection processes are referred to as off-line inspections, in which the inspection procedure occurs at the completion of the manufacturing, filling, and sealing process. In-line