Table 14-2 ISO 14644 Classification of Clean room Particle Limits

	Maximum concentration limits (particles per cubic meter of air) for particles ≥ the sizes per column				
ISO Classification	**0.1 μm**	**0.3 μm**	**0.5 μm**	**1 μm**	**5 μm**
1	10	–	–	–	–
2	100	10	4	–	–
3	1000	102	35	8	–
4	10,000	1020	352	83	–
5	100,000	10,200	3520	832	29
6	1000,000	102,000	35,200	8320	290
7	–	–	352,000	83,200	2930
8	–	–	3520,000	832,000	29,300
9	–	–	–	8320,000	293,000

or per cubic meter (EU grades, International Standards Organization classifications). Flow of equipment, materials, and personnel need to move from lower classified environments to the higher classifications (Fig. 12-2). Since ISO classifications are given, even though air is the topic of the next chapter, Table 14-2 provides the ISO classification (ISO 14644) (1) of clean room particulate limits that the Food and Drug Administration adheres to, replacing the old Federal Standard 209 (A, B, C, D, and E) series of clean room classifications (Class 100, 10000, etc.). Chapter 21 (Table 21-1) contains more information about air and microbial classifications of clean rooms according to FDA and European Union standards.

The extra requirements for the aseptic area are designed to provide an environment where a sterile fluid (liquid or dispersed system) or powder may be exposed to the environment for a brief period during subdivision from a bulk container to individual-dose containers without becoming contaminated. Contaminants such as dust, lint, other particles, and microorganisms normally are found floating in the air, lying on counters and other surfaces, on clothing and body surfaces of personnel, in the exhaled breath of personnel, and deposited on the floor. The design and control of an aseptic area is directed toward reducing the presence of these contaminants so that they are no longer a hazard to aseptic filling.

Although the aseptic area must be adjacent to support areas so that an efficient flow of components may be achieved, barriers must be provided to minimize ingress of contaminants to the critical aseptic area. This includes separation of personnel from critical product filling, stoppering, and capping. Such barriers may consist of a variety of forms, including sealed walls, manual or automatic doors, airlock pass throughs, ports of various types, hard plexiglas barriers, plastic curtains, and the like (Figs. 14-1 and 14-2).

FLOW PLAN

In general, the components for a sterile product flow either from the warehouse, after release, to the compounding area, as for ingredients of the formula, or to the materials support area, as for containers and equipment. After proper processing in these areas, the components flow into the security of the aseptic area for filling of the product in appropriate containers. From there the product passes into the quarantine and packaging area where it is held until all necessary tests have been performed. If the product is to be sterilized in its final container, its passage normally is interrupted after leaving the aseptic area for subject to the sterilization process. After the results from all tests are known, the batch records have been reviewed, and the product has been found to comply with its release specifications, it passes to the finishing area for final inspection and final release for shipment. There sometimes are variations from this flow plan to meet the specific needs of an individual product or to conform to existing facilities. Automated operations normally have much larger capacity and convey the components from one area to another with little or no handling by operators.

The key in sterile product facility design is to ensure that movement of equipment, materials, and people is unidirectional, eliminating any crossover of clean and dirty equipment and