What has been described relates to traditional buildings with permanent walls and ceilings typically made of plasterboard dry wall build upon concrete slab floors, then covered with special finishes that give smoothness, cleanability, and durability to the facility. As will be discussed, a more modern approach is the use of modules where the walls are constructed from laminated clean room material mounted on anodized aluminum tracks or attached to joined aluminum extrusions that form the stud and cross members of the room.

CLEAN ROOM CLASSIFIED AREAS

Because of the extremely high standards of cleanliness and purity that must be met by sterile products, it has become standard practice to prescribe specifications for the environments in which these products are manufactured, that is, clean rooms. Because so many sterile products are manufactured at one site for global distribution, air quality standards in aseptic processing areas must meet both United States and European requirements. European standards differ from United States standards in the following ways:

1. Use Grade classifications (A, B, C, and D) rather than Class X (100, 1000, 100,000, etc.).
2. Use particle and microbial limits per cubic meter rather than per cubic foot.
3. Require particle measurements at 5 μm in addition to 0.5 μm in Grade A and B areas.
4. Differentiate area cleanliness dynamically and "at rest" (Grade B).

Air quality is discussed in chapters 13 and 15.

Clean room design traditionally has Class 100 rooms adjacent to Class 100,000 rooms. Regulatory authorities have raised great concerns about this significant change in air quality from critical to controlled areas. It is now preferable to have an area classified from Class 1000 to Class 10,000 in a buffer area between a Class 100 and Class 100,000 area monitored and controlled. Precautions also must be taken to prevent deposition of particles or other contaminants on clean containers and equipment until they have been properly boxed or wrapped preparatory to sterilization and depyrogenation.

COMPOUNDING AREA

In this area the product is prepared, formulated from a "recipe". Although it is not essential that this area be aseptic (unless aseptic formulation using presterilized components/ingredients is to be accomplished), control of microorganisms and particulates should be more stringent than in the materials support area. For example, means may need to be provided to control dust generated from weighing and compounding operations. Cabinets and counters should, preferably, be constructed of stainless steel. They should fit snugly to walls and other furniture so that there are no catch areas where dirt can accumulate. The ceiling, walls, and floor should be similar to those for the materials support area.

ASEPTIC AREA

The aseptic area requires construction features designed for maximum microbial and particulate control. The ceiling, walls, and floor must be sealed so that they may be washed and sanitized with a disinfectant, as needed. All counters should be constructed of stainless steel and hung from the wall so that there are no legs to accumulate dirt where they rest on the floor. All light fixtures, utility service lines, and ventilation fixtures should be recessed in the walls or ceiling to eliminate ledges, joints, and other locations for the accumulation of dust and dirt. As much as possible, tanks containing the compounded product should remain outside the aseptic filling area, and the product fed into the area (Fig. 14-1) through hose lines. Proper sanitization is required if the tanks must be moved in. Large mechanical equipment that is located in the aseptic area should be housed as completely as possible within a stainless steel cabinet to seal the operating parts and their dirt-producing tendencies from the aseptic environment. Further, all such equipment parts should be located below the filling line. Mechanical parts that will contact the parenteral product should be demountable so that they can be cleaned and sterilized.

Comparison of differences in requirements of critical areas and controlled areas for aseptic processing operations is given in Table 14-5. Note that the definition of a classified area includes several criteria besides the number of particles of per cubic foot or meter.