Figure 27-2 Membrane filtration sterility test device. *Source*: Courtesy of Millipore Corporation.

The USP and EP tests require a minimum volume of sample per container volume to be transferred to a minimum volume of each culture medium (Table 27-1). The sample volume must be a sufficient representation of the entire container volume and the volume of medium must be sufficient to promote and expedite microbial growth, if present. Adequate mixing between the sample inoculum and the culture medium must take place to maximize interaction and facilitate microbial growth.

Membrane Filtration Method

The membrane filtration (MF) sterility test became official in the 18th edition of the USP in 1970. It has since become the more popular and widely used method over the DT method and, when feasible for pharmacopeial articles, should be preferred.

The successful employment of this technique requires more skill and knowledge than that required for the DT method. Five basic steps are involved in the use of the MF sterility-test method:

1. The filter unit (Fig. 27-2) must be properly assembled and sterilized prior to use.
2. The contents of the prescribed number of units are transferred to the filter assembly under strict aseptic conditions.
3. The contents are filtered with the aid of a vacuum or pressure differential system.
4. The appropriate type and volume of culture media is added to the canister.
5. The canister is incubated according to the medium used.

A suitable membrane filter unit consists of an assembly that facilitates the aseptic handling of the test articles and allows the processed membrane to be removed aseptically for transfer to appropriate media or an assembly where sterile media can be added to the sealed filter and the membrane incubated in situ. A membrane suitable for sterility testing has a rating of 0.45 μm, and a diameter of approximately 47 mm. These membranes have hydrophobic edges or low product- binding characteristics that minimize inhibitory product residue, and it is this residue that interferes with requirements of the validation test for bacteriostasis and fungistasis. For products that do not contain inhibitory substances, membranes without hydrophobic edges can be used, but wet them prior to testing.