

A new method for measuring porous microbial barriers: Part I

The work behind ASTM International Standard Test Method F2638

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The introduction in 1997 of the European Committee for Standardization (CEN) and International Organization for Standardization (ISO) standards for packaging and materials for terminally sterilized medical devices highlighted the need for a universally recognized microbial barrier test for such materials. Both the CEN and ISO working groups decided, in the absence of a widely accepted procedure for evaluating the integrity of the sterile package {sterile barrier system [SBS]def. ISO11607-01:2006⁽¹⁾}, that the best way forward was to carry out separate tests for seal integrity, integrity of the package materials, films and the microbial barrier of the porous materials.

Although there were a number of recognized tests for evaluating seal integrity, this was not the case for determining the microbial barrier of permeable or porous materials. Tests such as ASTM International F-1608⁽²⁾, DIN 58953 Part 6 sub-clauses 2.14 and 2.15, and BS 6256 Appendix C (Methylene Blue) were all used, but not universally recognized. In addition, all of these referenced tests take a long time to perform, with results not available for as long as three to four days in some cases.

Filtration Theory

Challenges to sterile barrier systems used to protect medical devices from bacteria and viruses come in the form of aerosols of suspended particles. Microbial spores can exist as individual entities or clusters, or they can be attached to inert particles such as dust particles. Thus, the size of a particulate challenge can range from 0.002 microns for the smallest virus up to 100 microns, which is the size of the largest dust particle that can remain suspended in air for a significant length of time.

Filtration theory predicts that materials which are permeable to air and gases employ three mechanisms to remove particles from the air stream:

- **Interception.** This occurs when a filter fiber splits the air stream that a particle is following. The particle continues on its original path and collides with the fiber. Interception is therefore a constant particle removal mechanism that is a function of the material's fiber structure. It is independent of both the particle's mass and its velocity.
- **Inertial Impaction.** This occurs when a particle, as a result of its mass, deviates from the air stream flowing around a fiber and collides with it. The effectiveness of this method of capture is directly related to the mass of the particle and the speed of the air stream. The higher the velocity and the mass of the particle, the greater the chance of it colliding with a fiber.
- **Diffusion.** This is the interception of a particle with a fiber as a result of random particle movement (Brownian motion) and, for some materials, electrostatic attraction. The effectiveness of this capture mechanism is inversely related to the mass of the particle and the velocity of the air stream. The lighter the particle and the slower its velocity, the greater the chance of capture.

All three of these mechanisms are in operation at all flow rates and for all particle sizes. However, larger particles moving at higher flow rates are more likely to be trapped by inertial impaction, whereas lighter ones moving at slower speeds are more likely to be caught by diffusion.

The BTC Project

In the absence of an internationally recognized test to evaluate the microbial barrier of permeable or porous materials, a group of seven companies within the Sterile Barrier Association (SBA), previously known as ESPA (European Sterile Packaging Association), formed the Barrier Test Consortium Ltd. (BTC) in 1998 to develop a rapid, easy-to-use, microbial barrier test for porous medical packaging materials. The BTC consisted of the following companies:

- Amcor Flexibles (formerly Rexam Medical Packaging)
- Billerud (formerly Henry Cooke)
- DuPont Medical Packaging
- Kimberly-Clark
- Oliver Medical (formerly Oliver Products)
- Perfecseal, a Division of Bemis Corp.
- Westfield Medical Packaging

Members of the BTC agreed that the new test had to meet certain key requirements. Specifically, the test had to be:

- based upon established, scientifically sound filtration principles
- applicable to the range and variety of commercially available medical packaging materials (including coated and uncoated papers, nonwovens and cellulose/synthetic mixed papers)
- reliable, reproducible and rapid
- able to be correlated with a recognized microbiological barrier test method (i.e. ASTM International F1608)
- fully definable and describable and, as such, be able to support the requirement for microbial barrier performance as part of the CEN and ISO Standards for medical packaging materials

Following a call for research proposals, the project was awarded to Air Dispersions Ltd. (ADL), based in Manchester, UK. The project tasks included:

- defining the range of microbiological barrier performances of commercially available porous packaging materials
- selecting and adapting commercially available particulate filter test equipment and optimizing test conditions
- establishing physical versus microbiological barrier correlations using materials of defined construction
- confirming that the correlation applies to commercially available materials
- specifying the particulate test method for defining microbiological barrier performance

To ensure erroneous results were not obtained due to variations in commercially available materials, the initial work was to prove a correlation existed using research-quality papers designed and produced by ADL. These papers had a high degree of uniformity and a wide range of porosity.

The next phase, a blind study, utilized 16 of 30 samples submitted by BTC members. The samples represented the range of porous packaging materials commercially available at the time. The range of properties for these materials is shown in Table I.

Table I. Range of properties for 16 sample materials* used in tests conducted by ADL

Property	Unit	Range of Value
Basis weight	g/m ²	53.6-129.0
Thickness	Mm	69-541
Air permeability (Bendtsen)	mL/min	29-43,717
Mean maximum spore penetration		$1.46 \times 10^{-3} - 5.37 \times 10^1$ (0.00146 – 53.7%)

*Four of the 16 materials tested were adhesive coated.

The specialized microbiological test ⁽³⁾ used for the project was developed by ADL several years before work began on the BTC project. This test challenges the sample with standardized dispersions of microorganisms at a range of pressure differentials corresponding to overall flow rates of 0.1 to 100.0 cm³/min/cm². This range encompasses typical conditions experienced by medical packages during normal conditions of handling, distribution and storage.

The equipment used for this test was designed as a research instrument. It was highly specialized to allow for a wide operating range of flow rates. It also featured very sensitive control mechanisms for flow control, particle control, particle size and enumeration.

Porous materials are basically filters or filtration systems. To test the effectiveness of any filter, a concentration of challenge media is forced through a sample of material. The extent of microbial penetration is determined at each flow rate by measuring the concentration of air-dispersed microorganisms both upstream and downstream of the material under test.

This test measures the extent of microbial penetration at each flow rate by measuring the concentration of air-dispersed microorganisms both before and after passing through the material. For a given test organism, the extent of penetration through the test sample is strongly dependent on the flow rate. This results in a maximum penetration value being obtained at a specific flow rate for a particular organism and packaging material. Endospores of *bacillus subtilis var. niger* are typically used. The maximum penetration value is a measure of the microbial barrier performance of the packaging material.

It is important to note that although this test gives an accurate result, it is a microbiological test and takes several days to complete. In addition, this test requires a high level of technical expertise and a dedicated microbiological laboratory. Although ADL considered the test to be a good research tool, it didn't meet the criteria requirement of being rapid.

To reduce equipment cost, the particle generator, size classifier and neutralizer were replaced by an atomizer and an aerosol of polystyrene beads measuring 1.0 µm in diameter. This modification simplified the process, allowing for variable airflow capacity and a single size, synthetic particle for the test medium.

The commercially available equipment selected for the BTC project was known to fulfil these criteria very well, enabling relatively inexperienced operators to obtain reproducible results for the physical particulate barrier performance of filter media in a matter of minutes. As with the microbiological test, a maximum penetration value is obtained.

To test medical packaging materials as opposed to filter media, it was necessary to design a special sample holder to use in conjunction with the equipment. Once the sample holder mechanism was available, it was then possible to identify percentage penetration of the most penetrating particle size (maximum particle penetration) for any material using synthetic substances as the test particle.

Basis for New ASTM Method

The BTC project was successfully completed in 2000 and formed the basis of the new ASTM international standard test method F2638-07 (4). ADL was able to demonstrate correlation between results obtained using commercially available equipment for testing the physical particulate barrier performance of fibrous filter media and those generated using ADL's specialized microbiological test. ⁽³⁾ Furthermore, the relationship extends over a wide range of commercially available packaging materials including coated and uncoated paper, and coated and uncoated nonwovens (DuPont™ Tyvek® for sterile packaging). This was not unexpected because both tests measure the effectiveness of materials to act as filter media.

Part 2 of this series will discuss the development of ASTM F2638-07, as well as provide a comparison of this new microbial barrier test method vs. ASTM F1608, which is commonly called the log reduction value (LRV) test. An in-depth look at the aerosol filtration equipment required to perform the new test method will also be presented.

References

1. ISO 11607-1:2006 *Packaging for terminally sterilized medical devices Part 1: Materials, sterile barrier systems and packaging systems.*
2. ASTM International F1608-00(2004) *Standard Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method).*
3. *Microbiological Barrier Testing of Porous Medical Packaging Materials*, Alan Tallentire and Colin Sinclair at the Meeting of the Society of Plastics Engineers (Scandinavian Section), May 1994.
4. ASTM International F2638-07 *Standard Test Method for Using Aerosol Filtration for measuring the Performance of Porous Packaging Materials as a Surrogate Microbial Barrier*

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