How Low Can You Go?

A look at the sensitivity of currently available package integrity test methods may help you prepare for the findings of an ongoing Michigan State University School of Packaging study on package defect size.

by Daphne Allen
Editor

As a Michigan State University School of Packaging research team looks for the smallest threat to sterility, *PMP News* looks at the sensitivity of today's test methods.

Led by assistant professor Laura Bix, PhD, MSU School of Packaging aims to answer this long-standing question: What is the smallest hole that will cause a breach of sterility in sterile medical packaging? Researchers are now preparing to identify whether a 10-µm-sized or a 100-µm-sized hole results in significant ingress of microorganisms through normal Brownian motion or pressure differentials that mimic an altitude of 8000 feet. This study originally started out as a task-group study within the medical device packaging technical committee of The Institute of Packaging Professionals (IoPP) in 2002. Under IoPP member Bix, MSU researchers have managed the project.

Research is planned to take place in two phases. Phase I consists of two experiments. Experiment 1 involves testing trays with nonporous lidstock (LFK-002 paper/PE/foil/PE/HSC) using a new methodology for whole-package microbial-challenge testing. Results from this work are expected to be complete in May 2007.

The results of a preliminary run of Experiment 1 were reported to IoPP's Medical Device Packaging Technical Committee in November 2004, and these results gave the researchers confidence that the method worked, so they have begun Experiment 2. Experiment 2 will explore the effect pressure differentials across the sterile barrier have on the penetration of microbes into the packaging. Rigid PETG trays sealed with LKF-002 paper/PE/foil/PE/HSC lids will be exposed to an environment in which microbes are aerosolized into the air space above the package. The completion date for Experiment 2 is on or about August 15, 2006. Phase I results should dictate future research for Phase II.

Can it be done? Does it matter? Is

BUBBLE IMMERSION

Potential Sensitivity: 250 µm for the internal pressurization method.

Industry Perspective: Donald Barcan, Donbar Industries (Long Valley, NJ), explains that this test is done either by "pressurizing the package (internal pressurization) while the package is suspended underwater in an open tank or by suspending the package underwater and applying a vacuum above the water." He adds that this method "is also very useful when looking for gross integrity defects other than seal defects."

VISUAL INSPECTION

Potential Sensitivity: 75 µm

Industry Perspective: "Visual inspection is the process most often used to detect package-integrity defects," says Barcan. "The main reason for its widespread use is convenience and low cost. However, the major drawback is that this test is qualitative in nature and is operator dependent."

Equipment available: While Barcan says that "no special equipment is required outside of good eyesight, adequate lighting, and perhaps a magnifying glass, specialized equipment is available. The Viú (Visual Inspection Unit) from Van der Stähl Scientific Inc. uses polychromatic side lighting along with a 3× magnification for pouch viewing. Barcan says he has also "used polarized light to readily find holes of this magnitude."

DYE TESTING

Potential Sensitivity: 50 µm

Industry Perspective: Barcan calls this the "the second most popular seal-defect test method." He adds: "Many companies, including mine, use dye to verify package defects outside the seal area though it is important to note that the ASTM standard is only for seal defects." However, it is messy, and, "for porous packaging materials, the test has to be conducted quickly, otherwise the dye will permeate the package walls and make channel identification difficult or impossible," says Barcan. "There are coatings available to seal the permeable web and thereby increase the test time. This can greatly improve the seal area test sensitivity for porous packages."

Equipment available: Required equipment is inexpensive.

ASTM Standard	Test Type	Package	Hole Size	Channel Size	Leak Rate
D3078-02	Bubble emission	Flexibles	—	—	10^{-6} Pa m^3/s
F1886-98(2004)	Visual seal inspection	Seals	—	75 µm (0.003 in.)	
F1929-98(2004)	Dye penetration of porous packaging	Seals	—	—	50 µm (0.002 in.)
F2095-01	Pressure decay for nonporous packaging with and without restraining plates	Seals or pinholes	—	—	10^{-5} Pa m^3/s
F2096-04	Internal pressurization bubble test	Pouches or trays	250 µm (0.010 in.)	250 µm (0.010 in.)	—
F2227-02	CO_2 tracer gas	Nonlidded trays	50 µm (0.002 in.)		—
F2228-02	CO_2 tracer gas	Porous lidded trays and pouches	50 µm (0.002 in.)	100 µm (0.004 in.)	—
F2338-04	Vacuum decay	Nonlidded trays or cups	50 µm (0.002 in.)		—
		Porous lidded trays and pouches	100 µm (0.004 in.)	125 µm (0.005 in.)	—
F2391-05	Helium tracer gas	Nonporous rigid and flexible	—	—	10^{-2} Pa m^3/s to 10^{-11} Pa m^3/s

Table I. A summary sheet taken from the scope of each test method. The scope and precision and bias sections of each method should be reviewed carefully for applicability to a given package and according to expected results. *PMP News* would like to thank Hal Miller, ASTM Committee F02 Chairman, and of PACE Solutions LLC, for his assistance in compilation. ASTM International standards are copyrighted by ASTM International, 100 Barr Harbor Dr., West Conshohocken, PA 19428-2959. Copies of the complete standards may be purchased from ASTM International (www.astm.org).

the approach realistic? These are questions that come to mind, along with this practical one: Will it change medical package integrity testing?

"If there is no significant microbial ingress detected at the 100-µm level, this is good news," says Hal Miller of PACE Solutions LLC. "Most every integrity test method out there can detect this level of sensitivity. However, if there is significant ingress at this level and none at the 10-µm level, then more work needs to be done to hone in on the optimum level."

Bix acknowledges that test-method sensitivity depends upon the package and the material. "You can detect breaches in nonporous packages to much lower levels than you can when they are within packages with a porous component," she says.

Adds Ondrea Kassarjian, who as a student was a part of Bix's research team and now works for Lansmont Corp. (Monterey, CA): "Other variables that determine whether a particular breach presents a threat include package thickness; pressure gradients, whether there is a tortuous path through the material, such as with Tyvek; whether contaminants are airborne or liquid; and the life span of the contaminating organism. After all, even if it can get in, how long can it live without a host?"

Furthers Darrell R. Morrow, PhD, and Jeffrey Morrow-Lucas of Leak Detection Associates Inc. (Blackwood, NJ), "It is very important to distinguish between the type of fluid carrier [gas

PRESSURE OR VACUUM DECAY:

Potential Sensitivity: 25 µm

Industry Perspective: "This is my favorite test method for impermeable packages because of its sensitivity, being quantitative, and being less operator dependent," says Barcan. "The major drawback when compared with other test methods is that this method will not show you the location of the defect but rather evaluate the total package leak rate. In practice, however, most companies will use this test method to determine if the package has a defect and follow it up with other tests to pinpoint the exact location of the leak."

Equipment available: The TME Worker from T.M. Electronics, VeriCon from PTI—Packaging Technologies & Inspection (Tuckahoe, NY), and Qualitek and Qualipak systems from Uson L.P. (Houston). Coatings, such as the new one developed by Barcan called WholeSeal, can convert permeable materials to impermeable ones, enabling users to test permeable packages with these methods.

ULTRASOUND

Potential Sensitivity: 25 µm

Industry Perspective: According to Packaging Technologies & Inspection, which offers the Seal-Scan noncontact airborne ultrasound testing unit, "ultrasound is transmitted and reflected at the transition from one medium to the next. The greater the acoustic difference between media (most evident at a gas-to-solid transition), the more sound is reflected and the less sound transmitted through."

Adds Barcan: "Ultrasound uses high-frequency sound waves to detect differences in density. A change in density occurs when a normally sealed material has a discontinuity or unsealed area. The two most significant processes use either water coupling of the ultrasound transducer to the test package or air. There is no ASTM test method for this technology at this time."

Equipment available: Seal-Scan and Seal-Sensor systems, which utilize noncontact airborne ultrasound technology, from PTI—Packaging Technologies & Inspection; C-SAM D-9000 from Sonoscan Inc. (Elk Grove, IL) for C-mode scanning acoustic ultrasound.

(air) or liquid (typically, aqueous)] involved in a given microbial transport situation. A given material and/or sealed package is challenged to a far greater extent by liquid-borne microbial moieties than by gas/air-borne moieties," they explain.

Given these realities, Bix says that her team isn't looking for a "black-or-white" answer. And even if her team does identify a hole size, it won't necessarily end the debate—or her research. "We may come up with a small hole size—but it doesn't consider [the effects of] secondary packaging or tertiary packaging" on sterility, she explains.

Still, identifying the "critical hole size" is the million-dollar question, says Kassarjian. "Some people are interested in the truth, while others are scared. Test equipment providers are trying to increase their sensitivities. And what if material suppliers find out that their materials aren't performing as they should be?"

Stephen Franks, executive vice president, T.M. Electronics (Boylston, MA), is confident that testing equipment will keep pace with the research. "No matter what hole size is determined, if determined, to allow contamination in a medical package, then the instrument manufacturers will find a method to detect this hole size. At this point, if 100 µm were the size, then an operator could see it, and almost any instrument can find it. However, the caveat as

always is that porous materials make the job harder."

"It is hard to find a universal test method that will find all defects: channels, pinholes, and other defects," says Kassarjian.

With all this in mind, we offer some industry perspective on physical test methods as they stand today to help you identify how sensitive your method is. We have also included a table on method sensitivity as described by ASTM standards.

We acknowledge that this article may not offer a complete analysis for each test method. We also acknowledge that these stated sensitivities are potential ones and cannot be guaranteed for every testing program or for all test equipment. Finally, we realize that a discussion of test sensitivity is not a discussion of testing unit quality. According to some industry experts, commonly used testing equipment often finds defects at 100-µm sizes, and this may be sufficient. ■

TRACER GAS

Potential Sensitivity: submicron levels

Industry Perspective: "Based on helium leak-rate studies by Lee Kirsch of the College of Pharmacy, University of Iowa, a single leak with a rate $<3x10^{-6}$ cm^3 at/sec is sufficient to stop aqueous-borne microbes from entering a package. The results of the study by Kirsch indicated that, conservatively speaking, the nominal hole size, below which aqueous-borne microbes are filtered out, is ~0.2 microns. In the case of a porous packaging material with all holes or pores <0.2 µm, any gas, including helium, would pass through at an extremely high rate (>1 cm^3 at/sec), many decades above the microbial barrier pass/fail criterion of $<3\times10^{-6}$ cm^3 at/sec. Consequently, it is all but impossible to measure the actual seal quality of any porous package; at least in the context of determining whether the seal quality meets, or surpasses, the requisite value of $<3\times10^{-6}$ cm^3 at/sec. For nonporous packages, helium leak-rate testing, per test method ASTM F2391-05, currently offers the best opportunity to determine the quality level for sealed packages."

Equipment Available: SIMS 1284+ Helium Leak Detection unit from Leak Detection Associates Inc. (Blackwood, NJ), Pac Guard Model 400 from Mocon Inc. (Minneapolis), and systems from Helium Leak Testing Inc. (Northridge, CA).