With their array of gels, pastes, and putties, demineralized bone matrix (DBM) products are a confusing area. What questions can your OR team ask to help make good product choices? OR Manager talked with experts who outlined issues to consider. Suggested questions to ask companies are in the sidebar on page 15.

First, some background. Products with DBM are manufactured from donor cortical bone that has been processed to remove minerals and expose factors that can stimulate bone growth. The result is a powder that may have both osteoinductive and osteoconductive properties. DBM is often combined with carriers such as a polymer or gelatin and molded into a paste, gel, or other form that can be more easily applied and retained in the surgical site.

More than 30 DBM products are listed in a 2010 review of bone-graft substitutes by the American Academy of Orthopaedic Surgeons.

Not the same as BMP products

It’s important to note that DBM products, though they have growth factors including bone morphogenic proteins (BMP), are not the same as BMP products, which contain a highly concentrated form of one genetically engineered BMP.

DBM products derived solely from allograft bone are regulated as human tissue by the Food and Drug Administration (FDA). DBM products that include carriers are regulated as medical devices and must have a 510(k) clearance or premarket approval.

Inducing new bone growth

Perhaps the most confusing issue with DBM products is the extent of their osteoinductivity or ability to induce new bone growth. Companies use different methods to test their DBMs for osteoinductivity, and the results are difficult to compare.

Two general types of tests are used, an animal model using mice or rats and laboratory tests such as the alkaline phosphatase assay (ALP), which measure enzymes produced by bone-growing cells. The animal model entails implanting DBM in muscle tissue of mice or rats and measuring the resulting bone growth.

Consensus lacking

Currently, consensus is lacking on a standard test method and measurement of results. An American Society for Testing and Materials (ASTM) task force has worked for several years on a guidance for a standard test method, which the FDA has pushed for, notes Simon Bogdansky, PhD, an independent consultant to the tissue banking industry.
Recently, the task force proposed a draft guidance that would recommend use of the animal test. Whether the draft will be finalized and accepted by the industry remains to be seen, he says.

Bogdansky says most companies will say they test for osteoinductivity, but those results are difficult to analyze and compare. He says he personally is “predisposed to believe the animal test method is probably the most robust and predictive,” though not all would agree.

How do test results in animals relate to a DBM’s clinical performance in humans?

Bogdansky responds, “No one to my knowledge has ever been able to demonstrate a correlation between an animal model of bone growth and what actually happens in clinical performance—there is a bit of a leap of faith.”

Effects of tissue processing

Questions also arise about how processing affects osteoinductivity. In processing tissue, suppliers must strike a balance between eliminating pathogens and destroying growth factors and other beneficial qualities.

Companies use a variety of processing methods, including gamma and e-beam sterilization and aseptic washes, to strike this balance.

Again, there is no consensus on the effects of these methods. In addition, use of human bone introduces variables that can affect processing and the osteoinductivity of the resulting product.

Regarding the use of irradiation to sterilize tissue, Bogdansky comments, “Some products are not irradiated; others are irradiated and perform well clinically.”

He adds: “All of the manufacturers making sterile products today have long figured out what doses and conditions to use such that their product remains osteoinductive.”

When is DBM tested?

As important as the test method is when the test is performed—before bone is processed or afterward, says Joseph Lane, MD, FACS, an orthopedic surgeon who chairs the biologics committee at the Hospital for Special Surgery in New York City. He notes that sterilization by irradiation or ethylene oxide can destroy much of the osteoinductivity.

“What is ideal is an in vivo [mouse or rat] test performed at the end of production rather than at the beginning,” he says.

He also favors testing lots from every bone donor, noting there is great variability in the biological health of donated bone. Even careful donor screening may not uncover every issue with donors, such as those who have had chemotherapy or some other treatment that might affect bone quality.

“There are companies that don’t test every lot. Then you run the risk that there will be little or no activity, knowing there are some donors that just don’t have it,” Dr Lane notes.

He referred to a 2010 report in The Journal of Bone and Joint Surgery in which researchers tested 10 lots of one DBM putty and found significant variability both in BMP concentrations and in the ability of the lots to achieve spinal fusions in rats.

He suggests questioning companies closely about their donor sources. The widely publicized scandal in the Northeast in 2005, in which tissue was procured from funeral homes without consent or donor screening, illus-
trates the abuses that have occurred. (An overview of donor screening is in the October 2010 OR Manager.)

He adds that, though some may think DBM products are pretty much the same, there is evidence they differ in their ability to induce bone growth. A 2005 study by Lee et al comparing 8 DBM products found significant differences in their results for spinal fusions in rats.

**Literature is limited**

The medical literature doesn’t provide definitive guidance on DBM products, according to a review of 5 years of abstracts by ECRI Institute conducted early in 2010.

“We found about a dozen studies, only one randomized,” says David Snyder, research analyst for the institute, an independent nonprofit organization that evaluates health care technology (www.ecri.org).

The randomized trial, by Lindsey et al, reported in 2006, compared DBM to iliac crest autograft for treating long-bone fractures.

Most of the reports consist of comparative studies examining use of one DBM product used in combination with an autograft versus autograft alone in spinal fusion. There are also case series reports of DBM used for applications such as treatment of long-bone nonunions and filling of voids left by bone necrosis.

—Pat Patterson

The American Academy of Orthopaedic Surgeons (AAOS) publication, The Evolving Role of Bone Graft Substitutes, is a helpful overview of the physiology of bone grafting, bone allograft material, and the burden of proof. A chart lists commercial bone graft substitutes. Single copies are available at www.orl-inc.com/aaos_publications/

**References**


**DBM products: Facts to know**

Facts to know were outlined by Andrea Stephens, CTBS, a certified tissue bank specialist with VHA Inc:

- Confirm CPT codes for procedures the product will be used for and reimbursement implications.
- Determine the company’s return policy.
- Make sure the product is not being used off-label.
- Request a tissue validation letter from the company as well as a product insert for all DBM products.
- Be familiar with tissue regulations and standards from the FDA and Joint Commission.
- Confirm the product’s FDA status.
  —DBM products that are regulated as medical devices require FDA clearance or premarket approval.
  —Products 100% derived from human tissue are regulated as human tissue under CFR 1270 and 1271. They do not require FDA clearance.

**DBM products: Questions to ask**

Questions OR teams can ask when evaluating DBM products:

**Is the supplier accredited by the American Association of Tissue Banks (AATB)?**

This should be a minimum criterion for any tissue supplier. In an accreditation review, a tissue bank’s processes are examined to be sure they are uniform and validated, personnel are trained, and other standards are met. Accreditation offers some assurance that materials were manufactured under controlled conditions by trained people, and the products will be consistent.

**How are tissue donors screened?**

How does the company ensure donors are screened not only to prevent disease transmission but also to ensure the biological activity of the graft?

**What processing methods were used?**

Though processing methods differ, asking the company to explain its rationale can help in assessing how well supported its process is. These are some questions to ask.

- Was the DBM product irradiated or not?
- What chemicals were used?
- Why did the company choose this process?
- Can the company provide validation that the process does not harm osteoinductivity?

**Does the company perform validated testing on every lot?**

- Such testing is important because of the variability in donor tissue.
- Is the testing for osteoinductivity performed before sterilization (if used) or afterward?

**What is the product’s expiration date?**

Does that present a challenge for OR inventory management?
What data does the company have on the safety of the DBM carrier material?

Though carrier materials are considered inert, asking for safety data provides additional information.

What clinical studies has the company performed?

What studies have been performed, whether published or in-house, to show the product is efficacious? In what procedures has the product been studied?

Sources: Simon Bogdansky, PhD; Joseph Lane, MD, FACS; David Snyder.