

US Bone-Growth Studies Under Fire for Alleged Bias

By Kerry Sheridan | AFP – Tue, Jun 28, 2011

A US medical journal on Tuesday published a scathing critique of industry-funded studies on spine research, alleging that they failed to report adverse events to the journals that publish them.

The review study came days after the Senate Finance Committee launched an inquiry into whether doctors being paid by device giant Medtronic failed to report serious side effects from the bone-growth agent Infuse in clinical studies.

The product was introduced in 2002 to help bones heal after spinal surgery and has been used in about 500,000 patients. Since its arrival on the market, it has also been linked to some cases of cancer, male sterility, throat swelling and leg pain.

A Loyola University spokesman told AFP that some doctors in the spinal community believe that a "small number, fewer than five" fatalities may have resulted from its use, though no published data points to any deaths.

The review article co-authored by three US-based doctors in *The Spine Journal* says that in 13 trials involving 780 patients, "industry-funded researchers did not report a single adverse event involving Medtronic's Infuse Bone Graft."

Meanwhile, the authors of "nearly all the trials had financial ties with the manufacturer, with investigators earning as much as \$26 million per study," the journal reported.

The product brings in about \$900 million in annual revenues for Medtronic, according to US media.

In 2008, the US Food and Drug Administration issued a public health notice about "life-threatening complications" associated with the product, also known as recombinant human Bone Morphogenetic Protein (rhBMP), when used in the upper or cervical spine.

"FDA has received at least 38 reports of complications during the last four years with the use of rhBMP in cervical spine fusion," the agency said at the time.

"These complications were associated with swelling of neck and throat tissue, which resulted in compression of the airway and/or neurological structures in the neck. Some reports describe difficulty swallowing, breathing or speaking."

Last week, Senator Max Baucus, who chairs the Senate Finance Committee, and senior member Chuck Grassley sent a letter to Medtronic asking it to "produce documents related to its controversial bone growth product Infuse."

The senators "raised concerns over recent media reports that indicate medical researchers in charge of Infuse clinical trials may have been aware of and failed to report evidence that the product may cause sterility in men and potentially harmful bone growth," the panel said on its website.

"The letter also notes many of these investigators had substantial financial ties to the device manufacturer."

Medtronic said it had received the senators' inquiry and "intend(s) to respond," but noted that the side-effects mentioned are already included in its FDA-approved product labeling.

"Patient safety is of the utmost important to Medtronic," the company statement said.

"Accordingly, we provide PMA (pre-market approval) clinical study adverse event data to the FDA irrespective of any financial relationship between the company and the clinical investigator or study author."

The doctors' editorial in The Spine Journal said that the potential dangers of the drug -- noted by the FDA years after its approval -- were never mentioned in early industry-backed studies.

"Serious potential problems, such as the association of rhBMP-2 with sterility or cancer risks, which were prominently discussed in Food and Drug Administration documents and hearings, did not receive one line of discussion in the industry-sponsored publication of those trials," they wrote.

"It harms patients to have biased and corrupted research published. It harms patients to have unaccountable special interests permeate medical research.

"We all must do a better job going forward," the editorial concluded.

The review study was authored by Eugene Carragee of Stanford University, Eric Hurwitz of the University of Hawaii and Bradley Weiner of The Methodist Hospital in Houston, Texas.

The editorial was signed by Carragee, Weiner, Alexander Ghanayem of Loyola University, David Rothman of Columbia University and Christopher Bono of Brigham and Women's Hospital in Boston, Massachusetts.