Additional Medtronic Perspective - rhBMP-2

- **Integrity and patient safety are Medtronic's highest priorities, and we strongly believe that the safety profile reported to the FDA and summarized in the product label support the safe use of INFUSE® Bone Graft (rhBMP-2) for the identified indications. The articles in the Spine Journal do not question the integrity of the safety results reported by Medtronic to the FDA for product approval.**

    - Medtronic's reporting of adverse events to the FDA on rhBMP-2, which is summarized in the "Information For Use" brochure that accompanies each product sold, is not in question. Rather, the articles call into question why the researchers' data in published studies differed from the data filed by us with the FDA.
    - We strongly believe that the safety profile reported to the FDA and summarized in the product label support the safe use of rhBMp-2 for the identified indications.
    - We reported known adverse events to the FDA, in both the pre- and post-market settings and we are confident that the agency had the necessary safety information when it approved the product for use in patients.
    - In fact, the Spine Journal articles use the data Medtronic provided on RhBMP-2 as the comparative data set for their analysis of the peer-review literature.

- **In 2008 INFUSE® Bone Graft (rhBMP-2) received the Prix Galien USA 2008 Award for Best Biotechnology Product. The Prix Galien USA Awards committee of 11, including seven Nobel Laureates, recognizes the technical, scientific and clinical research skills necessary to develop innovative medicines that improve the human condition, and the award is considered the industry's highest accolade for pharmaceutical research and development.**

- **While the *Spine Journal* articles raise questions about researchers' conclusions in their published peer-reviewed literature, the articles do not raise questions about the data Medtronic submitted to the FDA in the approval process or the information available to physicians today through the instructions for use brochure attached to each product sold.**

    - Through the peer review process, clinical investigators study and publish articles arising from clinical trials that are of interest to them, including development of their own methodology, which is often not comparable to the original data filed with the FDA for PMA approval.

- We believe that the peer-review process issues raised in this edition of the Spine Journal deserve further review and analysis, and we are committed to working with the Journal editors and other academics to evaluate any actions we should take that are within a manufacturer's control.
- The theoretical potential for the emergence of diseases associated with growth biologics, such as cancer, is something Medtronic takes seriously and has motivated us to develop a formal surveillance program.

- **Medtronic has led the industry in reforms designed to eliminate or mitigate conflicts of interest. We have implemented a number of important reforms under the review and guidance of an expert outside advisor to provide additional objective information to patients and caregivers. Going forward, we will continue to investigate questions surrounding researchers' potential conflicts of interest, refine our policies as warranted, and strive to lead the industry in ethical and transparent business practices.**

    - In recent years, Medtronic has implemented policies placing restrictions on participation of royalty earners in clinical studies.
    - We have broadened our clinical program significantly, and follow rigorous OMA processes.
    - We were one of the first companies voluntarily to disclose payments to physicians on our company website.

- **Medtronic is committed to ongoing study of the safety and efficacy of rhBMP-2, especially within applications not covered by FDA labeling.**

    - We are currently working with the FDA to establish a post-market surveillance (PMS) network to better understand real-world use, including a broad range of safety signals and early detection of other rare events.
    - We are also investing millions of dollars in several new studies in large segments where physician-directed use is prevalent.

- **Medtronic intends to work proactively with the FDA to satisfy any safety questions or concerns and to determine whether any communications with stakeholders are appropriate at this time.**