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April 5, 2007

Andrew C. von Eschenbach, M.D.
FDA Commissioner
Division of Dockets Management (HFA-305)
Food and Drug Administration (FDA)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Dear Dr. von Eschenbach:

The American Academy of Orthopaedic Surgeons (AAOS/Academy), representing over 17,000 Board certified orthopaedic surgeons, welcomes the opportunity to comment on the open public hearing, "Sentinel Network to Promote Medical Product Safety" [Docket No. 2007N-0016]. The Academy appreciates the efforts of the FDA to facilitate the hearing in a transparent manner in which stakeholders were invited to present their perspectives in a public forum.

Stakeholders expressed an interest in collaborating with the FDA in creating a sentinel network to improve and increase the agency's abilities to enhance patient safety through a modernized post-market surveillance system. Creating such a system or systems will require extensive resources. While the Congress may appropriate funds for an improved pharmaceutical surveillance system for fiscal year 2008, the funding will need to be significant with annual appropriations for each of the three centers within the FDA. The AAOS supports the efforts of the FDA to create sentinel networks to improve and enhance patient safety. Transparency and effective communication must occur between the FDA and medical specialty societies so that we may share the most up-to-date information with our patients. The Academy will limit our comments to the following:

- The AAOS supports select federal agencies' efforts to share relevant data;
- The AAOS supports global harmonization efforts in international consensus standards development;
- The FDA must build a computerized infrastructure for the sentinel network;
- The AAOS affirms that the FDA does not regulate the practice of medicine;
- The AAOS supports unique device identification (UDI) proposed rule making;
- The AAOS clarifies the role of specialty societies;

- The AAOS supports the total product life-cycle of medical products;
- The AAOS supports the development of a tissue sentinel event network;
- The AAOS supports the efforts of the Centers for Education and Research on Therapeutics (CERTs).

THE AAOS SUPPORTS SELECT FEDERAL AGENCIES' EFFORTS TO SHARE RELEVANT DATA

The AAOS supports regulatory and legislative mandates to allow federal health partners to share data, if those agencies adhere to federal patient privacy protections. Potential agencies include the Department of Veteran's Affairs (VA), the Centers for Medicare and Medicaid Services (CMS), the Agency for Healthcare Research and Quality (AHRQ), and the Department of Defense (DoD). Currently, memorandums of understanding between these relevant agencies are outdated or non-existent. Such agreements when implemented may provide an earlier warning system with additional safety information. These memorandums of understandings are in the best interests of the American public and should proceed in a timely manner.

THE AAOS SUPPORTS GLOBAL HARMONIZATION EFFORTS IN INTERNATIONAL CONSENSUS STANDARDS DEVELOPMENT

The AAOS thanks the FDA for its leadership on global harmonization task forces and the advances in standardization accomplished over the past few years. The Academy encourages the role of international consensus standards organizations in defining nomenclature and standardization of safety data fields for case report forms used to support clinical research studies.

THE FDA MUST BUILD A COMPUTERIZED INFRASTRUCTURE FOR THE SENTINEL NETWORK

A computerized infrastructure must be developed at the FDA. Whereas the FDA operates with a largely paper-based system currently, computerized systems must be established to increase efficiency, track, search, and analyze medical product data. Many recommendations in the Prescription Drug User Fee Act IV (PDUFA) are designed to provide the FDA with sufficient resources to enhance the informatics systems and epidemiological capabilities. The Breckinridge Institute findings on the "Independent Verification and Validation of Adverse Event Reporting System (AERS) II Requirements Process"[1] are troubling with four-to-five year delays in replacing the AERS and a total estimated cost of twenty-five million dollars, rather than a few million dollars if problems within the Center for Drug Evaluation and Research were addressed earlier.

The AAOS supports the continuance of the Medical Product Surveillance Network (MedSun) to provide active medical device surveillance data. The AERS and the Manufacturer and User Facility Device Experience Database (MAUDE) generally establish early warning signals yet these passive surveillance systems do not appropriately assess the incidence, risk factors, or patterns of use of drugs and devices.

THE AAOS AFFIRMS THAT THE FDA DOES NOT REGULATE THE PRACTICE OF MEDICINE

During the stakeholders meeting, participants reinforced the need to determine if medical products were being used appropriately. The AAOS affirms that neither the federal government nor the FDA regulates the practice of medicine. Physicians may in their best medical judgment prescribe medical products for an appropriate patient in an off-label manner. The U.S. Supreme Court[2] observed that the off-label usage of medical devices is an accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine.

Clinical trials are becoming increasing more expensive to conduct with costs escalating every year. Pharmaceutical clinical trials are currently exceeding $900,000 to bring a drug to the U.S. market. Device and biological product clinical trials remain expensive and consume nearly a decade of pre-market trials under the best of circumstances. While it remains optimal to conduct a clinical trial to determine safety and effectiveness for every intended use of a medical product, it is not economically feasible for most medical products. Therefore, off-label prescribing is common practice and substantial. Depending on the specialty and practice area, the off-label use of drugs accounts for up to 85% of total prescriptions in chemotherapy and pediatrics.[3]

THE AAOS SUPPORTS UNIQUE DEVICE IDENTIFICATION (UDI) PROPOSED RULE MAKING

While the AAOS is cognizant of the FDA's regulatory authority, FDA's collaboration and communication on UDI systems with other federal agencies including but not limited to the AHRQ, the CMS, the VA, and the DoD is laudable and of great benefit to the global healthcare community. Patient safety, through better human factors design, is a critical device safety problem. Gathering more data in post-market surveillance may provide information on sub-optimal device design that could be a cause of medical errors, such as buttons on an infusion pump control pad located too closely together. Human factors engineering is a critical element in the use of medical devices. Device design is often a factor in adverse events, not just human error. By implementing a UDI system, early device problems will be captured more quickly and will prevent multiple events from occurring.

Development of a system of Unique Device Identifiers

The AAOS wholeheartedly endorses the development of a UDI system and urges the FDA to publish a proposed rule. As the U.S. is the largest manufacturer of medical devices, the implementation of such a system could and may well prove to be a global initiative. This system must be mandatory to be effective as voluntary collection is random and inefficient for all stakeholders. We strongly urge the FDA to mandate a UDI system for all medical devices to aid in patient safety, to decrease medical errors, and to decrease healthcare costs for our nation.

Hospital Interface

As with other initiatives, the UDI system will have little utility if it is not incorporated at the hospital level. Bar-codes are currently required on pharmaceutical drugs and at present are systematically used at few hospitals. Similarly, though a 2005 Joint Commission requirement, hospitals are required to track allograft tissue. The AAOS is aware that tissue processors could

identify and track tissue immediately following the Biomedical Tissue Services and Donor Referral Services recalls. However, hospitals did not immediately notify surgeons (and patients) due to lengthy hospital chart abstractions. Most hospitals track their recalls manually by a lengthy chart review. Some hospitals manage their own bar-coding systems and synchronize their data with manufacturers, distributors or others in the supply chain. This additional layer adds the possibility of medical error, is inefficient, and expensive to maintain.

Hospitals must implement tracking and identification of drugs, devices, and biologicals on a national level to increase safety for patients. The AAOS encourages the FDA to coordinate efforts on UDI systems with the American Hospital Association and the Joint Commission.

THE AAOS CLARIFIES THE ROLE OF SPECIALTY SOCIETIES

The AAOS continues to meet with several agencies within Health and Human Services about developing a national hip and knee registry. The goals of the registry are to improve patient outcomes, decrease revision rates, and to identify early problem components. The Swedish registry decreased their revision rates by 50% by identifying best surgical practices and best-performing implants in total joint replacements.[4]

By 2030, the demand for total joint replacements is estimated to increase dramatically. Primary total knee replacements are projected to rise by 673% to 3.48 million by 2030. Primary hip replacements are expected to increase by 174% to 572,000 in 2030.[5] Costs of total, partial and revision hip replacement amounted to $12.01 billion dollars in 2003, while total and revision knee replacement cost $12.85 billion dollars in 2003.[6]

The Comptroller General, the Honorable David M. Walker of the U.S., in his 2006 fiscal wake-up tour presentation, "Saving Our Future Requires Tough Choices Today," stated that from 2005-2030 in constant dollars, Medicaid spending is predicted to increase 166% while Medicare spending is anticipated to increase 331%. Healthcare was our nation's top tax expenditure in 2005 at a cost of 118.4 billion dollars. The Comptroller General also stated that the current U.S. fiscal policy is unsustainable.[7]

Nonetheless, costs to develop a national total hip and knee joint replacement registry if accomplished by a private entity are projected at nearly 40 million dollars. Annual expenses to maintain the collection and analysis of data are estimated at several million dollars per annum. As the AAOS is a non-profit entity, it is not feasible for the AAOS or any other private entity to assume the totality of the registry costs. While we fully support the development of such a registry, the AAOS hopes to leverage an agreement with federal entities and hospitals. The Academy believes that a national total joint replacement registry will ultimately lead to better patient care.

THE AAOS SUPPORTS THE TOTAL PRODUCT LIFECYCLE OF MEDICAL PRODUCTS

In fiscal year 2001, the Director of the Center for Devices and Radiological Health, David W. Feigal, MD, MPH, introduced the concept of the total product life cycle to the center. As the FDA is the only agency that has access to pre-market clinical data, it is imperative for the FDA

to link to post-market data by creating a system that accommodates the total lifecycle of the medical product. The three centers undoubtedly will require differing product collection fields. In addition, as medical science continues to validate genetic knowledge and the subsequent implementation of appropriate medical applications, the sentinel network must accommodate this new information.

THE AAOS SUPPORTS THE DEVELOPMENT OF A TISSUE SENTINEL EVENT NETWORK

The Transplant Transmission Sentinel Network (TTSN) formed following the 2005 Centers for Disease Control and Prevention (CDC) sponsored workshop to prevent organ and tissue allograft transmitted infections. AAOS Fellow, Michael Joyce, MD is representing the AAOS, and is co-chair of the advisory group. A goal of the TTSN is to set up an electronic sentinel network for detecting, communicating, tracking, and preventing the transmission of infections from allograft donors to recipients. The network will ensure more definitive and rapid tissue recalls and allow the hospitals to promptly identify recipients, check inventory, and eliminate the oversight of a piece recalled tissue being implanted. Other partners in this network include the CDC, FDA, Health Resources and Services Administration (HRSA), Joint Commission, American Association of Tissue Banks, American Orthopaedic Society for Sports Medicine, CMS, United Network for Organ Sharing, Association of Organ Procurement Organizations (AOPO), and additional organizations. The Academy wholeheartedly endorses the development and implementation of this real-time tissue network and may work to secure its funding.

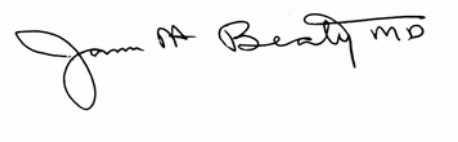
THE AAOS SUPPORTS THE EFFORTS OF THE CERTS

The AAOS supports the continued efforts of the CERTs as mandated by the Food and Drug Administration Modernization Act (FDAMA). A large body of knowledge is accumulating from the research conducted by the CERTs on the optimal use of drugs, biological products, and medical devices. Journal articles developed from CERTs research are of significant benefit to the medical community.

CONCLUSION

Public and private sectors must work together to provide a safe environment for patients. The AAOS appreciates the FDA's willingness to seek perspectives on the development of sentinel networks for medical products and to seek input from professional medical associations. The Academy looks forward to working with the FDA on future efforts to increase patient safety.

Sincerely,



James H. Beaty, M.D.
President
American Academy of Orthopaedic Surgeons

[1] Breckinridge Institute. Independent Verification and Validation of Adverse Event Reporting System (AERS) II Requirements Process, November 2006, http://finance.senate.gov/press/Bpress/2007press/prb030707a.pdf
[2] *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350 (2001)
[3] Jong, WT, Vulto A, deHoog, M, Schimmel, KJ, Tibboel, D, van den Anker, JN. Unapproved and off label use of drugs in a children's hospital. *N Eng J Med* 2000;343:1125.
[4] Malchau, H et al, 2002, The Swedish Total Hip Replacement Register, *J. Bone Joint Surg. Am.*, 84:2-20, 2002
[5] Ong. KL, Mowat, FS, Chan N, Lau E, Halpern MT, Kurtz, SM, May 2006, Early burden of revision hip and knee arthroplasty in Medicare enrollees, *Clin Orthop Relat Res*, 446:22-8.
[6] Frankowski, J. Patient Demographics: Information about orthopaedic patients and conditions http://www.aaos.org/Research/stats/patientstats.asp
[7] Walker, DM, Aug. 2006, Saving Our Future requires Tough Choices Today, *US Government Accountability Office*, http://www.gao.gov/ GAO-06-1084CG.