

The Orthopaedic Device Forum:
The First Ten Years

Executive Summary:

In 1996, the Orthopaedic Device Forum (Forum) met following discussions at a technology transfer conference in 1995, where participants addressed issues with federal statutes and those emanating from Food and Drug Administration (FDA) regulatory interpretations. The mission of the Forum is to foster an environment of open communication among the scientific community, government, and related industry on orthopaedic issues of mutual interest.

In cooperation with the Orthopaedic Surgical Manufacturers Association (OSMA), the Forum has been instrumental in accomplishing orthopaedic device down classifications which have led to increased availability of those devices in the United States. The Forum drafted guidance documents that assist the FDA in providing a predictable template for device reviews. In 1997, the Forum received a Special Recognition Award from the FDA for its participation in projects that benefitted the scientific community.

The Forum produces educational seminars to assist the FDA staff and AAOS fellowship on emerging orthopaedic issues. In addition, scientific exhibits are presented to the fellowship on FDA regulatory matters.

Biologics is an area that the Forum pioneered for the development of predictable standards. Subsequently, through the Forum's involvement, the American Society for Testing and Materials (ASTM) created a division to address the standardization of tissue engineered products. Medical/surgical standards are also developed through substantial input from Forum members.

Communications efforts are ongoing with the freestanding website at <http://www.orthopaedicdeviceforum.org>. Meeting summation reports are posted three times a year and progress reports are submitted to the AAOS annually. The Forum has perennially identified orthopaedic issues at an early stage to address regulatory problems. Advocacy efforts are ongoing in providing appropriate responses to the request for comments from several Department of Health and Human Services agencies.

Members of the Forum conceived the regulatory pathway for marketing applications of antibiotic bone cement products which achieved clearance by the FDA in 2003.

Forum members have learned the following:

- Forum projects generally consume several years of effort. Projects are rarely completed within a span of one year.
- Regulatory knowledge is essential to understanding how to navigate FDA processes.
- The Forum facilitates open communication between members and government liaisons and has avoided potential legal problems.
- The Forum has minimized formal process and has remained flexible to take on new and challenging issues.
- The Forum has aided in the advancement and availability of new technologies in identifying and implementing least burdensome regulatory pathways for developing, clinically studying, and marketing of orthopaedic devices.
- The learning curve for FDA issues usually takes 3-5 years. AAOS must continue to invest resources and have a steady stream of Fellows knowledgeable in regulatory issues.
- Engineering and biologics are two completely different disciplines; different skill sets are required.
- According to the FDA white paper, "Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products," FDA guidance documents assist in bringing products to the U.S. marketplace more quickly.
- The development of international standards is increasingly important to the U.S. device marketplace to assist in bringing new technologies to patients. The AAOS must maintain a commitment to standards activities in soliciting Fellows to participate in standards activities.

▪ **Next Steps:** Priority projects may include the following:

1. Defining whether safety is more important than efficacy for orthopaedic devices and what ramifications that could have for product approval/clearance.
2. Defining mechanisms between the FDA and the CMS that could be utilized to achieve a more timely reimbursement of FDA approved/licensed products.
3. Investigating a different classification scheme for medical devices.
4. Coordinating and developing educational staff training for government personnel.
5. Developing a consortium within the orthopaedic industry to identify orthopaedic patient needs.
6. Investigating possible legislative changes to the Humanitarian Device Exemption (HDE).
7. Facilitating the international harmonization of medical devices.
8. Investigating clinical trial design issues.
9. Working with the FDA to define a threshold for failure for orthopaedic devices from their data.
10. Tort reform should be enacted to decrease medical liability issues.
11. Proposing solutions to small volume products issues.
12. Facilitating the acceptance of foreign clinical data.
13. Revisiting the concept of adverse event reporting.

****Federal employees did not contribute to any discussion or verbiage regarding any potential legislative remedies.**

Introduction:

This document has been prepared by and on behalf of the members of the Forum. It serves as an abbreviated summary of the first ten years of activity, and suggests important areas for further work. This summation is extracted from the agendas, summation reports, and other discussions that have captured the first decade of activity. It is hoped that this document will serve as a summary useful to those organizations that have supported the Forum, and will provide perspective for future Forum members and guests.

The document is organized in the following manner:

- Brief History
- Accomplishments
 - Reclassifications
 - Guidance Documents
 - Recognition
 - Educational Efforts
 - Scientific Exhibits
 - Biologics
 - Standards
 - Communication
 - Liability
 - Early Identification of Issues
 - Consensus Conferences
- What We've Learned
- Next Steps

Brief History:

In 1994, the FDA contacted the American Academy of Orthopaedic Surgeons (AAOS) to discuss problems with collecting investigational device exemption (IDE) data. Orthopaedic device manufacturers were experiencing delays in regulatory reviews for products in the U.S. market. Additionally, the timeline for down-classification of orthopaedic devices was lengthy and the process was not satisfactory for some in the orthopaedic community. Members of the AAOS and the American Orthopaedic Association (AOA) organized a conference on technology transfer in May 1995 in Chantilly, Virginia. Senior health officials, with decision-making authority, were invited and willingly participated in the "Chantilly Conference." The pedicle screw case was pending and communication between the societies and the FDA were strained as a result. In addition, Dow Corning filed for bankruptcy due to the legal costs following the withdrawal of silicone breast implants from the U.S. market. The goal of the

symposium was to clearly distinguish between problems emanating from federal statutes and those imposed by regulatory mandates. Participants were challenged to arrive at mutually acceptable solutions.

The Forum resulted from discussions held at the symposium and first convened in January 1996 to permit regularly scheduled interactions among representatives of the scientific and clinical orthopaedic community, the FDA and other governmental agencies, and representatives of industry related to musculoskeletal health and diseases. The Forum currently meets three times per year to work on mutually acceptable projects to advance the field of orthopaedics.

Members and government liaisons to the Forum represent the following organizations: AAOS, Orthopaedic Research Society (ORS), ASTM, AOA, OSMA, FDA, Center for Medicare and Medicaid Services (CMS), and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

Mission Statement

The mission of the Orthopaedic Device Forum is to foster an environment of open communication among the scientific community, government, and related industry on orthopaedic issues of mutual interest.

Accomplishments:

(Note: 2005 projected estimates of market size and units sold are provided from industry sources)

Device Reclassifications

2000

- Reclassification of shoulder joint metal/polymer/metal non-constrained or semi-constrained porous-coated uncemented prosthesis (without this reclassification a new PMA/IDE would be necessary, and fewer product types would be available in the marketplace)
- **Cementless Shoulder: \$65,000,000; 21,666 Units**

1999

- Reclassification of elbow joint metal/polymer constrained cemented prosthesis (without reclassification this product may not have remained in the marketplace)
- **Constrained Elbow: \$17,000,000; 31,000 Units**

- Reclassification of knee joint patellofemoral polymer/metal semi-constrained cemented prosthesis (without reclassification this product may not have remained in the marketplace)
- **Patello-Femoral Joint: \$28,000,000; 8,000 Units**

- Reclassification of shoulder joint metal/polymer non-constrained cemented prosthesis/semi-constrained cemented prostheses (without this reclassification a new pre-market approval (PMA)/investigational device exemption (IDE) would be necessary, and fewer product types would be available in the marketplace)
- **Cemented Shoulder: \$75,000,000; 18,750 Units**

- Reclassification of polymethylmethacrylate (PMMA) bone cement (without this reclassification a call for PMAs/IDE's would have been required)
- **PMMA Bone Cement: \$140,000,000; 2,150,000 Units**

- Reclassification of hip joint metal/polymer constrained cemented or uncemented (acetabular) prostheses (without this reclassification these products would have been removed from the market)
- **Constrained Hip: \$65,100,000; 33,384 Units**

- Reclassification of metal/polymer knee joint, uncemented

Reclassification Efforts

- 2003-2004- Reviewed and provided input on the OSMA petition for the reclassification of mobile bearing knees.
- **Mobile Bearing Knees: \$200,000,000; 44,000 Units**

- 2000- Reviewed and provided input on the reclassification petition of the OSMA metal/metal semi-constrained hip joint prosthesis submitted to FDA in September 2000.
- **Metal/Metal Hips: \$195,300,000; 39,873 Units**

Antibiotic Bone Cement

- Members of the Forum conceived the regulatory pathway for marketing applications of this combination product which achieved clearance by the FDA in 2003.
- **Antibiotic Loaded Bone Cement: \$35,000,000; 11,666 Units**

Guidance Document Development

Development of guidance documents is a critically important tool to speed products to market. Manufacturers report that the availability of guidance documents has been shown to foster development and innovation in areas of therapeutic need, to improve the chances of initial success of a marketing application, and to shorten the time it takes to get safe and effective treatments to patients.

The Forum generated the following guidance documents:

- Pre-Clinical and Clinical Design for Cervical and Lumbar Disc Replacement Systems Guidance Document
- Plasma (Thermal) Sprayed Porous-Coated Surfaces Guidance Document
- Testing Criteria for UHMWPE Guidance Document
- Clinical Trial Design for Hip Replacement Systems

Revision of Guidance Documents

- Guidance Document for Industry and CDRH staff for the Preparation of Investigational Device Exemptions and Premarket Approval Applications for Bone Growth Stimulator Devices
- Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone Or Bone Cement

Recognition/Awards

- The Forum received a Special Recognition Award from the FDA in 1997 for its participation in collaborating on projects beneficial to the scientific community.

Educational Efforts

- Presented joint arthroplasty seminar for FDA reviewers on January 23, 2004. Drs. Cuckler, Rosenberg, Maloney, Jacobs, and Berry discussed assessing outcomes and understanding the data, the impact of evolving technologies and techniques on device regulation, alternative bearing surfaces, biological concerns, and clinical assessment.
- Produced spinal seminar for FDA reviewers on September 27, 2002. Drs. Kirkpatrick, Carl, Faciszewski, Sandhu, and Anderson discussed spinal anatomy, the evolution of spinal devices, vertebroplasty/kyphoplasty, allograft and bone graft substitutes, test methods, and clinical failures.

- Initiated a NIH sponsored workshop entitled “Wear Workshop 2000” in October 2000. Members participating as faculty: Timothy Wright, PhD (Principal Investigator), Bernard Stulberg, MD, Joshua Jacobs, MD, Seth Greenwald, D. Phil (Oxon), James Panagis, MD, MPH, and Barbara Boyan, PhD.
- Developed, organized, and participated in an AAOS symposium entitled “Regulatory Aspects in Orthopaedics”, in February 1999 which included AAOS members, industry, and FDA members.
- The Forum organized a joint meeting of AAOS Biological Implants and Biomedical Engineering Committees at the May 10, 1999 meeting of the ASTM. The focus of the meeting was to educate committee membership on techniques and goals of standards writing for bioengineering and biologics, and for interaction with the FDA, to more effectively assist in the development of guidance documents for orthopaedic devices and biological products.

Scientific Exhibits

- 2005- Presented “Antibiotic-Loaded Bone Cement in Aseptic Total Joint Replacement: Whys, Wherefores & Caveats” scientific exhibit at the 2005 AAOS Annual Meeting.
- 2004- Presented two scientific exhibits at the AAOS Annual Meeting 2004: “Musculoskeletal Tissue Transplantation in Orthopaedic Surgery: Safety and Donation. What Makes Tissue Safe and Where Does it Come From?” in conjunction with the Patient Safety Committee and the American Association of Tissue Banks. Also exhibited “Antibiotic-Loaded Bone Cement in Aseptic Total Joint Replacement: Whys, Wherefores & Caveats.”
- 2003- Presented two scientific exhibits at the AAOS Annual Meeting 2003: “Musculoskeletal Tissue Transplantation in Orthopaedic Surgery: Safety and Donation. What Makes Tissue Safe and Where Does it Come From?” in conjunction with the Patient Safety Committee and the American Association of Tissue Banks and “New Polys for Old: Contribution or Caveat?”
- 2002- Presented scientific exhibit “Alternative Bearing Surfaces: The Good, Bad and Ugly” at the AAOS Annual Meeting 2002.

- 2002- Presented scientific exhibit “New Polys for Old: Contribution or Caveat?” at the AAOS Annual Meeting 2002.
- 1998- Presented scientific exhibits, “Alternative Bearing Surfaces: The Good, Bad, and the Ugly and “Limits of UHMPE Longevity: Design, Material and Clinical Factors” at the 1998 AAOS Annual Meeting.

Biologics

Tissue Workshop-The AAOS-FDA held a joint conference on tissue transplantation following the introduction of the House of Representative’s Wyden legislation in December 1993. The AAOS testified before the Subcommittee on Regulation, Business Opportunities, and Technology of the House Small Business Committee in October 1993. The AAOS, through testimony from Bernard Rineberg, MD and Henry Mankin, MD, acknowledged the standards in bone/tissue banking set by the American Association of Tissue Banks (AATB) and Massachusetts General Hospital Bone Bank. The government was concerned about the sterility of the U.S. tissue supply in the aftermath of HIV transmission in the 1980’s. Subsequently, the Center for Biologics, Evaluation and Research (CBER)/FDA issued an interim rule on tissue transplantation in 1993.

In 2003, the Forum initiated the development of a biologics subcommittee to assess biological/combination product issues. Issues may be referred to the AAOS Biological Implants committee for further review. The subcommittee has addressed the viral inactivation of demineralized bone products, bone morphogenetic proteins, and the ASTM standard for testing osteoinductivity of demineralized bone substitutes.

Standards

The Forum initiated a new effort to develop standards for tissue engineered products and biologics. This has been fostered through ASTM and subsequently, the International Standards Organization (ISO). These organizations are currently industry leaders in developing standards in these disciplines. The AAOS and the orthopaedic scientific community/industry have had substantial input into this process. The involvement of the ASTM in the Device Forum led to the development of these standards activities.

Members of the Forum have participated in the development of many medical/surgical standards, particularly with the ASTM. Compliance with FDA

recognized consensus standards assists manufacturers in bringing products to market more quickly.

In 1998, The Forum implemented a procedure where all members of the AAOS Biological Implants and Biomedical Engineering committees become members of the ASTM.

Communication Efforts

An independent website at <http://www.orthopaedicdeviceforum.org/> is updated with summation reports after every Forum meeting. Annual progress reports are posted on this site as well.

Liability Issues:

In 1998, a Forum subcommittee, chaired by Ken DeHaven, MD issued a Task Force Liability report to the AAOS Board of Directors. The subcommittee reviewed and amended the Forum's mission statement and operational principles.

In 1998, the name of the Forum officially changed from the AAOS/FDA/OSMA Device Forum to the Orthopaedic Device Forum. Representatives from NIAMS and the Arthritis Foundation were invited to become new members. Real or potential conflicts of interest disclosure are addressed at every Forum meeting.

Early Identification of Orthopaedic Issues

The Forum originally raised issues about single-use device reprocessing (SUDs). In 2001, the AAOS Washington Office held a meeting with HHS Secretary Thompson's office to discuss the provisions of the single-use device (SUD) enforcement guidance document. Subsequently, the deadline for enforcement of Class II devices was delayed. Forum members provided input into the AAOS position statement on the use of reprocessed single-use devices. AAOS/Forum members filed two comments to the FDA on reprocessed single-use devices.

The Forum has identified many such issues at early stages and referred them to the AAOS Biological Implants and Biomedical Engineering committees for further action.

Consensus Conferences

Forum members, Timothy Wright, PhD, Bernard Stulberg, MD, James Panagis, MD, MPH, and Barbara Zimmerman, MS served on the planning committee and

Dr. Wright participated as a speaker in the NIH Consensus Development Conference on Total Knee Replacement in December 2003.

Forum members, Timothy Wright, PhD, Ken De Haven, MD, Bernard Stulberg, MD, Jack Parr, PhD, James Panagis, MD, MPH, and Jack Lemons, PhD participated as faculty in the NIH Technology Assessment Conference on “Improving Implant Performance through Retrieval Information: Opportunities and Challenges” in January 2000.

Advocacy Efforts (Comments, Testimony)

2004- Forum members wrote and submitted comments to both the FDA and Health and Human Services (HHS) on the Critical Path Initiative designed to bring medical products to market more quickly. In addition, Forum members wrote and submitted comments to the FDA on barriers to pediatric device development.

2002- Forum members wrote and provided written and oral testimony for Dr. Bernard Morrey for the June 10, 2002 HHS Secretary’s Regulatory Reform Committee meeting. Forum members submitted a comment on proposed FDA regulatory reform measures to the HHS Secretary’s Committee.

2001- Forum members participated in drafting the AAOS comment to the FDA on Good Tissue Practices.

2001- Forum members gave input to the AAOS comment on the reclassification of the hip joint metal/polymer constrained cemented or uncemented prosthesis.

2000- Forum members participated in the open public FDA meeting, “Human Bone Allograft: Manipulation and Homologous Use in Spine and Other Orthopedic Reconstruction and Repair.” An AAOS comment was subsequently drafted and filed to the FDA docket.

What we’ve learned:

- Forum projects generally consume several years of effort. Projects are rarely completed within a span of one year.
- Regulatory knowledge is essential to understanding how to navigate FDA processes. Once processes are understood, “thinking out of the box” is often helpful. Physicians and staff must keep abreast of innovations in other medical specialties to find possible applicability to orthopaedic

products. Change is often incremental and is accomplished very slowly at the federal level.

- The Forum facilitates open communication between members and government liaisons and has obviated potential legal problems. The AAOS has been named in no FDA class action suits since the inception of the Forum. The AAOS has experienced better cooperation and communication with federal authorities since the inception of the Forum.
- The Forum has minimized formal process and has remained flexible to take on new and challenging issues. The Forum values a membership comprised of all relevant players within the field of orthopaedics, and benefits from the accumulated experiences of the members.
- The Forum has aided in the advancement and availability of new technologies by collaborating with clinical, industry, and regulatory representatives in identifying and implementing least burdensome regulatory pathways for developing, clinically studying, and marketing orthopaedic devices.
- Like the Relative Value Scale Update Committee (RUC), the learning curve for FDA issues takes usually 3-5 years. AAOS must continue to invest resources and have a steady stream of Fellows knowledgeable in regulatory issues that can assist the Forum in the future.
- Engineering and biologics are two completely different disciplines; different skill sets are required. Likewise, two of the centers at the FDA: the Center for Biologics Evaluation and Research (CBER) and the Center for Devices and Radiological Health (CDRH), have completely different cultures and expertise.
- According the FDA white paper, "Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products," FDA guidance documents assist in bringing products to the U.S. marketplace more quickly.
- The development of international standards is increasingly important to the U.S. device marketplace to assist in bringing new technologies to patients. The AAOS must maintain a commitment to standards activities in soliciting Fellows to participate in standards activities, as well as

providing for travel expenses to attend the American Society for Testing and Materials, Intl. and International Standards Organization meetings. The Food and Drug Administration Modernization Act of 1997 (FDAMA) allows for the recognition of standards to satisfy a premarket submission requirement, thereby speeding up the FDA device review process.

Next Steps:

The Forum has defined a list of priorities to address over the next few years. Specified priorities may or may not require a legislative solution. The Forum will continue to assist federal authorities as a think tank and sounding board in addition to actively working on device reclassifications and writing/revising FDA guidance documents. Priority projects may include:

1. Defining whether safety is more important than efficacy for orthopaedic devices. Some orthopaedists contend that safety should be of greater concern than efficacy. Additionally, some orthopaedists contend that effectiveness is only proven after ten years of implantation with some orthopaedic devices. The Forum should investigate whether more emphasis on safety could warrant less scrutiny of short-term efficacy for orthopaedic products.

2. Inter-Agency Communication:

- Defining mechanisms between the FDA and the CMS that could be utilized to achieve a more timely reimbursement of FDA approved/licensed products. The Forum should assist in developing strategies to improve the interactive communication between the two agencies.
- Translational research should be rewarded with grants coordinated by the FDA and the NIH, particularly the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Institute of Biomedical Imaging and Bioengineering (NIBIB). NIAMS should assist in the funding of translational research efforts, which can aid in product evaluation and technology assessment. This will expedite both the development and application of testing tools, which was referred to in the FDA Innovation/Stagnation document.

3. Several years ago, the AAOS proposed the following classification scheme for medical devices to include:

Class I-notification only;

Class II- 510(k) (substantial equivalence);

Class III-long term implanted devices (non-life threatening) 510(k) with/without special controls; and

Class IV- long-term implanted devices, which require premarket approval (PMA).

The Forum may investigate if the proposed classification is of interest to the orthopaedic community. This proposed classification scheme would require a legislative solution.

4. Coordinating and developing educational staff training for government personnel. Training should encompass clinical considerations for orthopaedic technologies.

5. Developing a consortium within the orthopaedic industry to identify orthopaedic patient needs.

6. Possible legislative changes to the Humanitarian Device Exemption (HDE).

7. Facilitating the international harmonization of medical devices.

8. Clinical Trial Design Issues:

Trial design, length, patient compliance, surgeon investigator compliance, and duration of government evaluation should be assessed on a continual basis to determine the least burdensome approach. Practical, reasonable endpoints for assessment should be determined. Reasonable controls should be determined at the beginning of the clinical trial. Clinical trial design and conduct is a very expensive line item for manufacturers. Clear guidelines should be developed that 1.)assist overall trial design, but are specific to length needed to establish clinical safety and short-term effectiveness; 2.)assist patient selection based on anticipated compliance; 3.)assist appropriate surgeon investigator selection based on the protocols of the clinical trial; 4.)define reasonable endpoints; 5.)include control or placebo populations and their relevance; and 6.)appreciate the role of the IRB at investigator hospitals and the impact of HIPAA regulations.

9. FDA has the largest data bank on human outcomes data. Data should be mined to determine the threshold for failure for orthopaedic devices.

10. Small volume products issues:

How does an investigator achieve statistical significance in a study if the patient population is small? What incentive do manufacturers have for developing small volume products?

11. The acceptance of foreign clinical data should be facilitated.

12. Revisiting the concept of adverse event reporting. Modify the definition of “adverse event” to eliminate broad reporting of unintended outcomes not associated with the use of the specific device. Facilitate the development of reporting guidelines and procedures to be used when adverse events are observed during off-label use of FDA-approved devices. Develop a mechanism to inform the medical community of these risks.

****Federal employees did not contribute to any discussion or verbiage regarding any potential legislative remedies.**