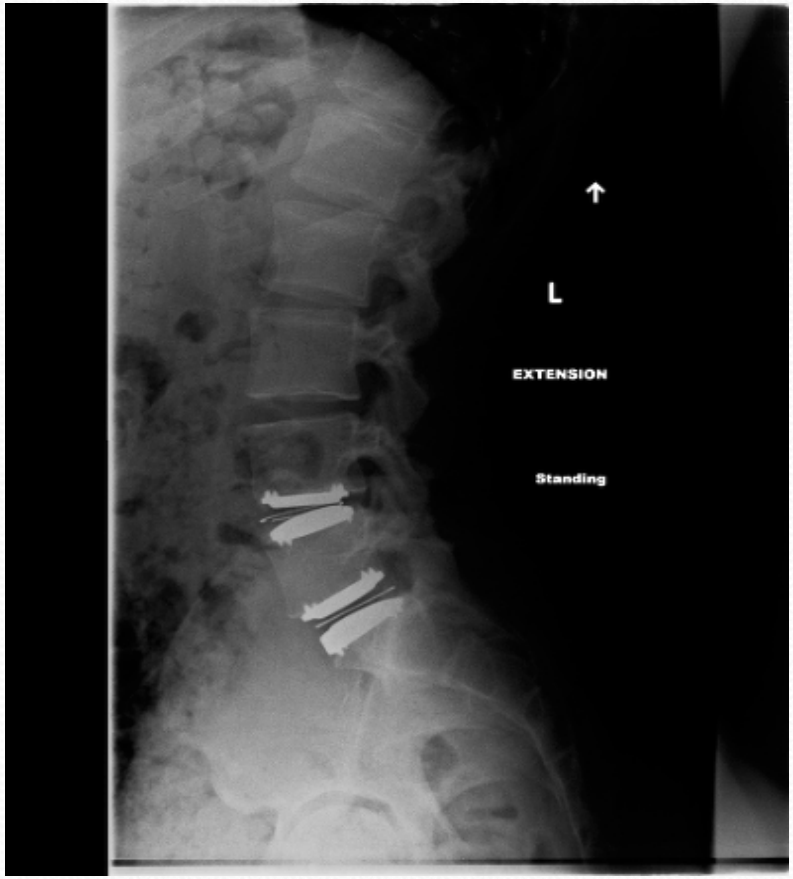
Industry Influence

The Story of the Charite

Charles Rosen, MD
President, Association for Ethics in Spine Surgery
Clinical Professor of Orthopaedic Surgery
University of California, Irvine,
School of Medicine

Charite Artificial Disc Replacement (ADR)



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The Charite study

(and Swiss cheese)

- First 26% of patients excluded
- Control group has a 60% failure rate
- 2/3 ‘s of patients at end of study on daily narcotics
- Intended motion is not measured as an endpoint of success.
- Motion itself not normal
- FDA engineer criticizes testing as ‘inadequate’
- 24 months total time and 204 patients

Association for Ethics in Spine Surgery

Marketing

Journals

Medical societies

Internet announcements

Association for Ethics in Spine Surgery

THE WALL STREET JOURNAL

June 7, 2005

Back Fire:

J&J's New Device For Spine Surgery Raises Questions

Artificial Disk Aims to Help Body's Natural Movement; Some See Risk if It Slips
'Big Money Riding on This'

By RHONDA L. RUNDLE and SCOTT HENSLEY
Staff Reporters of THE WALL STREET JOURNAL

It sounds like an excellent answer for persistent back pain: an artificial disk, placed between the bones of the spine, that helps the body move naturally. After decades of research by doctors, **Johnson & Johnson** became the first to market an artificial disk in the U.S. last October, and surgeons are flocking to a J&J training center in Cincinnati to learn how to implant it.

Now a vigorous debate has emerged among doctors about the durability of the J&J device and its effectiveness compared with older "fusion" surgery, in which the bones of the spine are fused together. Some surgeons are predicting that a wave of patients will suffer complications over the next 10 to 15 years and need to have the device, called Charité, removed. That's particularly worrisome because the surgery to take it out can be dangerous -- more so, they say, than the repairs when fusion surgery goes wrong.

J&J says malfunctions are rare. About 5% of Charité patients need a new operation to fix problems, in line with older surgeries, says Richard Toselli, vice president for research and development at J&J's DePuy Spine subsidiary. He says in most cases repair surgery doesn't involve big risks.

"I had back pain and now severe back pain with nerve pain down both legs. I can't hardly stand it. It's everyday."

"I am very depressed and need to keep my job and family but it gets harder each day."

" I basically stay in bed at least 22 hours a day."

" Nurse came into the waiting room and Dr. _____ really just wishes that you would go away."

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" I was the second person in the U.S. to have the procedure.....received coverage ... on national news stations. After experiencing complications, Dr._____ immediately discontinued all press coverage. Today completely bedridden."

"No doctor in this state will see me ... All of them told me that I had to go back to the one that did the surgery."

"Another happy day forthcoming. Hope Anastasia will only wish for death less than 4 times today."

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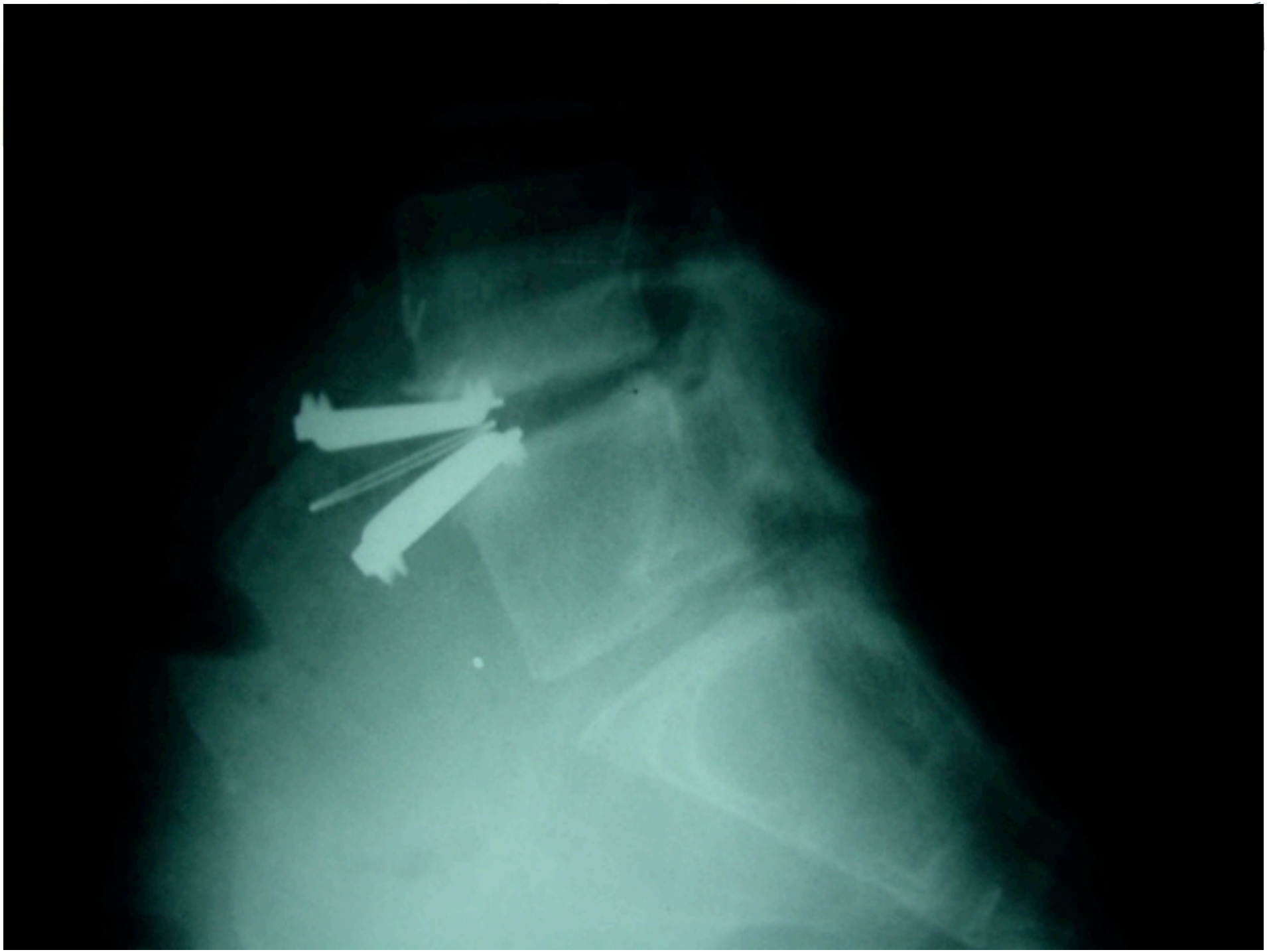


The Potential Biomechanical Etiology for Lumbar Disc Replacement Failures:

A Review of 24 Patients and The Rationale for Revision

Orthopaedic Biomechanics Laboratory

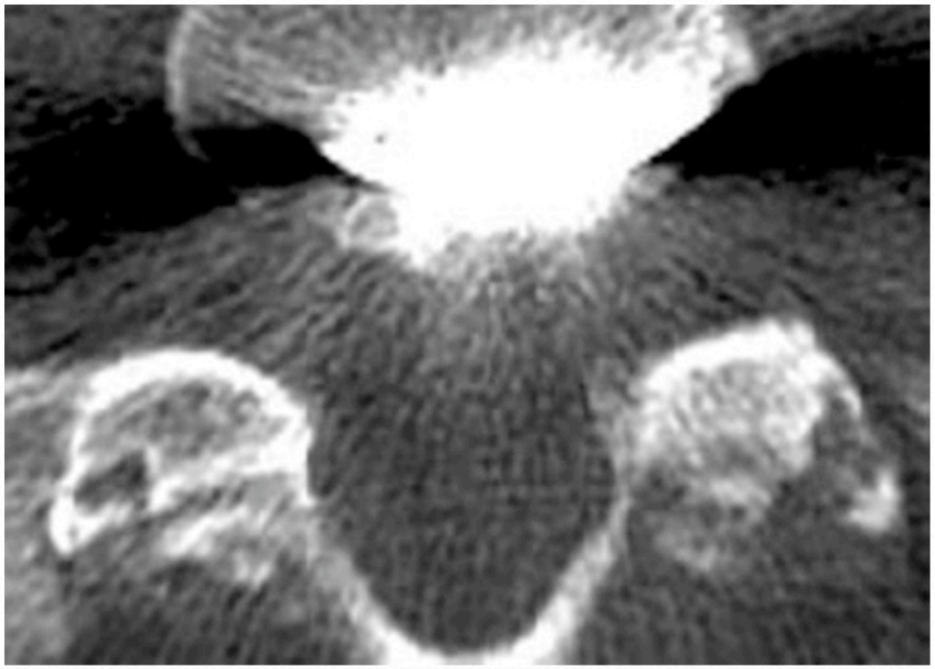
University of California, Irvine

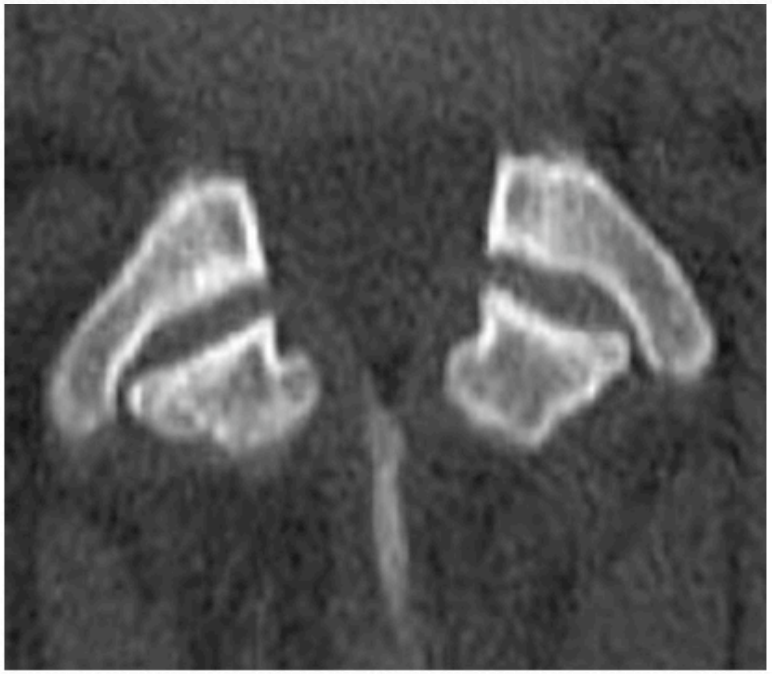
VA Long Beach HealthCare System

Charles Rosen, MD,

Douglas Kiester, MD

Thay Q Lee, PhD





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How did this happen?

The study gave the impression of being

INDEPENDENT VALIDATION

But, was NOT

Five Year Results of the Prospective Randomized Multicenter FDA IDE ProDisc®-L Clinical Trial

Rick Delamarter, MD1, Jack Zigler, MD2, Jeffrey M. Spivey, MD3,

Raymond Linovitz, MD4, Guy O. Danielson, III, MD5, Thomas Haider, MD6,

Frank P. Cammisa, Jr., MD7, James Zucherman, MD8,

Richard A. Balderston, MD9, Scott Kitchell, MD10, Kevin Foley, MD11,

Robert Watkins, MD12, David Bradford, MD13, James Yue, MD14,

Hansen Yuan, MD15, Harry Herkowitz, MD16, John A. Bendo, MD3,

Timothy Peppers, MD17, Barton Sachs, MD18, Federico P. Girardi, MD7,

Michael A Kropf, MD19, Jeffrey A. Goldstein, MD3

Financial Ties Are Cited as Issue in Spine Study

By Reed Abelson

New York Times : January 30, 2008

- The confidential documents show that Dr. --------invested at least $25,000 in Viscogliosi Brothers fund to finance Spine Solutions.
- “Most of the 11 other Prodisc investor-surgeons who were asked to comment also declined.”
- “The way the Prodisc was tested and approved provides a stark example of conflicts of interest among clinical researchers — conflicts that are seldom evident to doctors and patients trying to weigh the value of a new device or drug.”

J Neurosurg (Spine 2) 1:143–154, 2004

Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charité intervertebral disc

Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004

FRED H. GEISLER, M.D., PH.D., SCOTT L. BLUMENTHAL, M.D., RICHARD D. GUYER, M.D., PAUL C. MCAFEE, M.D., JOHN J. REGAN, M.D., J. PATRICK JOHNSON, M.D., AND BRADFORD MULLIN, M.D.

Illinois Neuro-Spine Center at Rush-Copley Medical Center, Aurora, Illinois; Texas Back Institute, Plano, Texas; Spine and Scoliosis Center at St. Joseph's Medical Center, Towson, Maryland; Cedars-Sinai Institute for Spinal Disorders, Los Angeles, California; and Mount Carmel East Hospital, Columbus, Ohio

“Disclosures”

American Academy of Orthopaedic Surgeons

- Do you or a member of your immediate family serve on any Board of Directors, as an owner, officer, or on a relevant committee of any health care organization (e.g., hospital, surgery center, medical and/or orthopaedic professional society)? Y/N
- *If yes, please list organization and position held.*
- Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication? Y/N *If yes, please list publication, publisher and position.*
- Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device? Y/N *If yes, please list company(ies).*
- Within the past 12 months, have you served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company? Y/N *If yes, please list company(ies).*
- Are you or a member of your immediate family a paid or unpaid consultant for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
- *Paid: Y/N —If yes, please list company(ies).*
- *Unpaid: Y/N—If yes, please list company(ies).*
- Do you personally or, to the best of your knowledge, does your department receive research or institutional support from any publisher? Y/N *If yes, please list company(ies).*
- Do you personally or, to the best of your knowledge, does your department receive research or institutional support from any pharmaceutical, biomaterial or orthopaedic device or equipment company or supplier? Y/N *If yes, please list company(ies).*
- Do you or a member of your immediate family receive stock or stock options from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds)? Y/N *If yes, please list company(ies).*
- Do you or a member of your family receive any other financial/material support from any medical and/or orthopaedic publisher? Y/N *If yes, please list company(ies).*
- Do you or a member of your family receive any other financial/material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier? Y/N *If yes, please list company(ies).*

North American Spine Society-NASS

- **NONE:**
  less than $250 per year.
- **MINOR**:
  $250 up to $10,000 total support (from all sources combined) per year, or less than or equal to 5% company ownership if value of ownership is less than or equal to $10,000.
- **MAJOR**:
  more than $10,000 total support (all sour
  combined) per year, or more than 5%
  company ownership.

UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

WEDNESDAY, JUNE 2, 2004

PANEL MEMBERS PRESENT:

MICHAEL J. YASZEMSKI, M.D., Ph.D., Chairperson, Mayo Clinic Graduate, School of Medicine
JANET L. SCUDIERO, M.S., Acting Executive
MAUREEN A. FINNEGAN, M.D

JOHN S. KIRKPATRICK, M.D
of Alabama, School of Medicine
SANJIV S. NAIDU, M.D., Ph.D., Voting Member,
Pennsylvania State College of Medicine
SALLY L. MAHER, ESQ., Industry Representative, Smith
and Nephew Endoscopy
KLEIA LUCKNER, J.D., M.S.N., Consumer Representative,
The Toledo Hospital
MARCUS P. BESSER, Ph.D., Deputized Voting Member,
Thomas Jefferson University
BRENT A. BLUMENSTEIN, Ph.D., Deputized Voting Member,
TriArc Consulting
FERNANDO G. DIAZ, M.D., Ph.D., Deputized Voting
Member, Detroit Medical Center
CHOLL W. KIM, M.D., Ph.D.,
University of California, San Diego
JAY D. MABREY, M.D., Deputized
University of Texas, Health Science Center
CELIA WITTEN, M.D., Ph.D., FDA Division Director,
General Restorative & Neurological Devices

American Academy of Orthopaedic Surgeons

Mark Melkerson
Deputy Director, DGRND
Food and Drug Administration
HFZ-140 Room 350D
9200 Corporate Boulevard
Rockville, MD 20850

Dear Mr. Melkerson:

The Orthopaedic Device Forum has completed a draft guidance on "'Preclinical and Clinical Trial Design for Cervical and Lumbar Disc ReplacementS ystems." Members of the Farum and the ad hoc group are pleased to assist the FDA in drafting proposed guidance documents that pertain to the practice of orthopaedic surgery so that they reflect current orthopaedic thought and practice.

The disc ad hoc group chairman sought out members who were non-conflicted. Two members were allowed to participate with conflicts of interest but their experience and expertise was deemed necessary to provide guidance to the development of the draft document. Appropriate disclosures were vetted with the entire ad hoc disc subcommittee.

We thank the FDA for receiving the submission of this draft guidance document. The Orthopaedic Device Forum will continue to assist the FDA in scientific matters of mutual interest. Thank you.

Sincerely,

John Kirkpatrick, MD
Chair, Disc Ad Hoc Subcommittee

Bernard N. Stuberg, MD
Chair, Orthopaedic Device Forum
Guidance doc from AAOS

Bill Christianson'
Bryan Cunningham M.Sc.*
Brian Doherty, PbD.
Lisa Ferrara, Ph.D.c
Jove Graham
Seth Greenwald D.Phil.
James Kang, M.D.
John Kirkpatrick, M.D
Jack Lemons, Ph.D.
Ensor Transfeldt, M.D.
David A. Wong, M.D.,MSc, FRCS(C)
Mike Yaszemski, M.D., Ph.D.

Association for Ethics in Spine Surgery

Association for Ethics in Spine Surgery (AESS)

is born

Who are AESS members ?

Board certified spine surgeons –
orthopedic, neurosurgical, osteopathic

Affiliate physicians in spine care –
Rehabilitation, pain management

Affiliate health care providers in spine care –
Physical and occupational therapy

ALL sign affidavits that they do not accept any money from industry.

What does AESS do ?

AESS Supports:

FULL disclosure

The Sunshine Act. Senators Grassley and Kohl.

Independent validation

Evidence based medicine (EBM)

Association for Ethics in Spine Surgery

AESS Supports:

Evidence Based Medicine

Level I	Randomized, controlled clinical trials
Level II	Prospective non-randomized, comparative studies
Level III	Retrospective comparative or case controlled studies
Level IV	Case series
Level V	Expert opinion

AESS Opposes:

Guidance for Industry and FDA Staff
Preparation and Review of Investigational Device Exemption Applications (IDEs) for Total Artificial Discs

Document issued on: April 11, 2008

21 CFR 860.7(c)(2) identifies the following sources of valid scientific evidence:

- well-controlled investigations
- **partially controlled studies**
- studies and objective **trials without matched controls**
- well documented **case histories** conducted by qualified experts
- **reports of significant human experience**
- with a marketed device from which it can be
- fairly and responsibly be determined by
- qualified experts that there is assurance of the safety and effectiveness of a device under its

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Zindrick et al, Spine 2008 "An Evidence Based Medicine Approach in Determining Factors That May Affect Outcome in Lumbar Total Disc Replacement."

"...conclusions are mainly drawn from lower level, least reliable evidence."

"..the majority ...addressing question of outcome...are level IV."

AESS Opposes:

ADVAMED SUGGESTED CHANGES:

- ...payments should be reported at the recipient level only... no obligation of companies
- require reporting only of the specifically enumerated types of payments
- consulting arrangement.... disclosed only after a product is approved ...by the FDA..

Association for Ethics in Spine Surgery

What will AESS do in the future?

Provide one central website with ALL physician financial disclosures required under Sunshine Act

EthicalSpineSurgeon.org

Host the FIRST ever conference with complete disclosure

(here !)

Association for Ethics in Spine Surgery

EthicalDoctor.org

Industry Relation Guidelines

- Develop Guidelines that can be used at Universities around the country to define appropriate disclosures
  - protect patients
  - increase playing field
  - decrease massive product competition (level expenditures on ineffective treatment)
  - support evidence based medicine (not industry directed)

Association for Ethics in Spine Surgery

Thank you.