



# **Classification Discussion: Pedicle Screw Spinal Systems (Certain Uses - Class III Indications for Use)**

***Meeting of Orthopaedic and Rehabilitation Devices Panel***

Gaithersburg, MD

May 22, 2013

# Purpose of Panel Meeting

The purpose of this panel meeting is to discuss the available scientific evidence regarding the use of thoracolumbosacral pedicle screw spinal systems for certain indications for use. The panel will be asked to make recommendations regarding regulatory classification to either reconfirm to class III (subject to PMA), or reclassify to class I or class II (subject to 510(k)), as directed by section 515(i) of the FD&C Act.

# Presentation Outline

- Introduction
- Device Description and Regulatory History
- Clinical Background and Targeted Literature Review
- OSB Systematic Literature Review
- Dynamic Stabilization Systems
- Adverse Event Analysis
- Risks to Health / Special Controls
- Summary

# FDA Review Team

## Classification Review Team

- Katherine Kavlock, Ph.D.
- Vincent J. Devlin, M.D.
- Stephanie Bechtold, B.S.

## MAUDE Search Team

- Deepa Gavini Peck, M.S.
- Akosua Atta-Mensah, B.S.

## Epidemiology Literature Review Team

### *OSB:*

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- Hui-Lee Wong, Ph.D., M.S.
- Nathan Ivey, Ph.D.

### *ODE:*

- Amy Graf, B.S.
- Brittany Ferrell, B.S.
- Colin O'Neill, MBE
- Constance Soves, Ph.D.
- James Swiger, MBE



# **INTRODUCTION DEVICE DESCRIPTION REGULATORY HISTORY**

**Katherine Kavlock, Ph.D.**

Biomedical Engineer

Anterior Spine Devices Branch

Division of Orthopedic Devices

Office of Device Evaluation

# Scope of Panel Meeting

21 CFR 888.3070(b)(2): Class III (premarket approval), when intended to provide immobilization and stabilization of spinal segments in the thoracic, lumbar, and sacral spine as an adjunct to fusion in the treatment of degenerative disc disease and spondylolisthesis other than either severe spondylolisthesis (grades 3 and 4) at L5-S1 or degenerative spondylolisthesis with objective evidence of neurologic impairment.

# Device Description

## Traditional Rigid System



## Dynamic Stabilization System



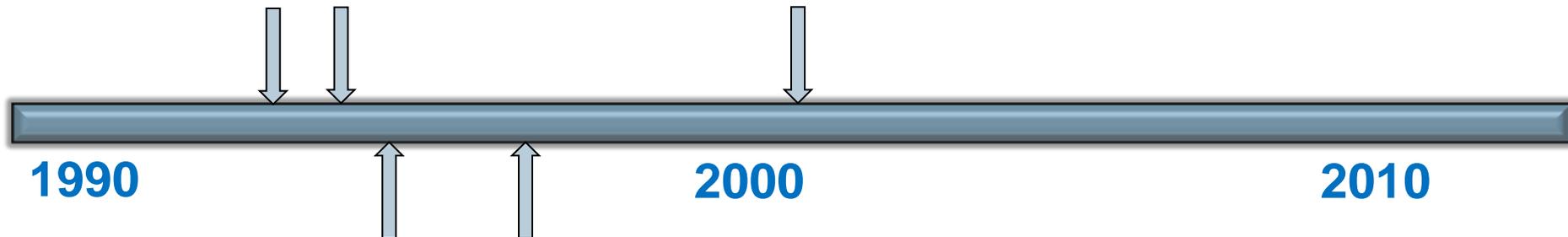
The scope of this panel meeting includes both traditional rigid systems and dynamic stabilization systems

# Regulatory History

## *Pedicle Screw Systems*

**Classification Panel Meetings for Thoracolumbosacral Pedicle Screw Systems (1993, 1994)**

**Technical Amendment Publication (2001)**



**Classification Proposed and Final Rules for Thoracolumbosacral Pedicle Screw Systems (1995, 1998)**

# Pedicle Screw Use: Pediatric

- Pediatric uses of pedicle screw spinal systems that cover an immature population were cleared through the 510(k) process prior to the issuance of the 2001 technical amendment
- Current class II clearances for pediatric use include:
  - Scoliosis, fracture/dislocation, trauma, and spondylolisthesis

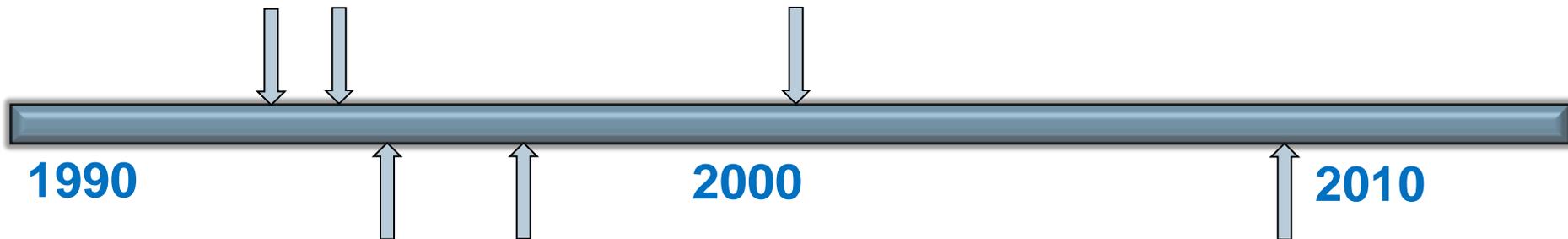
**The panel will be asked to comment on whether the use of “skeletal mature” terminology is necessary in the indications for use.**

# Regulatory History

## *Pedicle Screw Systems*

**Classification Panel Meetings for Thoracolumbosacral Pedicle Screw Systems (1993, 1994)**

**Technical Amendment Publication (2001)**



**1990**

**2000**

**2010**

**Classification Proposed and Final Rules for Thoracolumbosacral Pedicle Screw Systems (1995, 1998)**

**515(i) Call for Information (2009)**

# Responses to the 515(i) Order

- FDA received responses from 20 pedicle screw spinal system manufacturers
- Responses unanimously recommended reclassification into Class II
- Several manufacturers made recommendations outside of the scope of the 515(i) Order
  - Classification of cervical and pediatric pedicle screw uses
  - Revision of the definition of DDD to remove “discogenic origin”

# **CLINICAL BACKGROUND AND LITERATURE REVIEW**

## **Class III Indications - Pedicle Screw Spinal Systems**

- **“Other” Spondylolisthesis**
- **Degenerative Disc Disease**

### **Vincent J. Devlin, M.D.**

Orthopaedic Spine Surgeon, Medical Officer

Posterior Spine Devices Branch

Division of Orthopedic Devices

Office of Device Evaluation

# Pedicle Screw Constructs vs. Alternatives

## *(Hooks, Wires, Cables)*

### Advantages

- Increased construct stability
- Allow fixation when the posterior spinal elements are absent or fractured
- Improved fusion rates
- Implants do not enter spinal canal
- Rigid orthosis is not required post-op

### Disadvantages

- Complexity



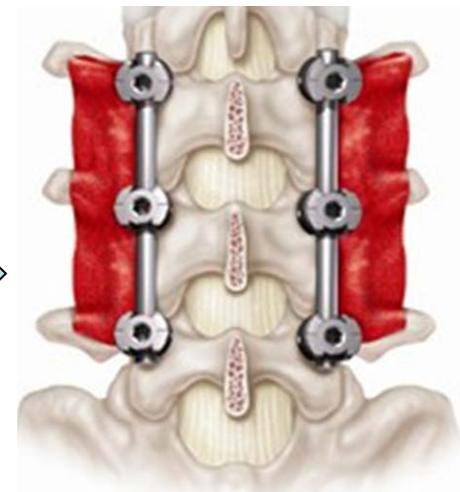
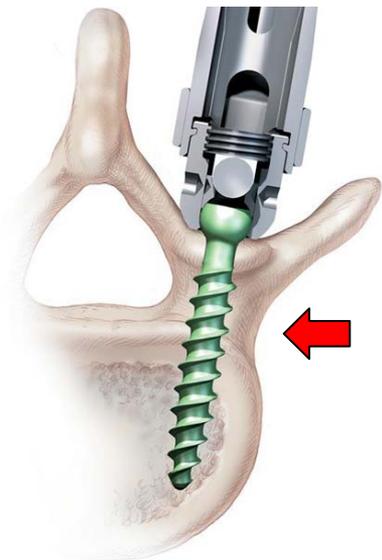
# Pedicle Screw Spinal Systems

*Screws Used in Combination with Longitudinal Members*

**Spinal Anchor**

**Longitudinal Members**

**Pedicle Screw System**



**Pedicle**

**Plate**

**Rod**

**Construct**

## Pedicle Screw Systems as Adjunct to Fusion For Treatment of Acute and Chronic Instabilities or Deformities

### Class II

Severe Spondylolisthesis, L5-S1, Grades 3 and 4

Degenerative Spondylolisthesis with Neurologic Symptoms

Fracture / Dislocation

Scoliosis / Kyphosis

Spinal Tumor

Failed Fusion (Pseudarthrosis)

### Class III

“Other” Spondylolisthesis

Degenerative Disc Disease

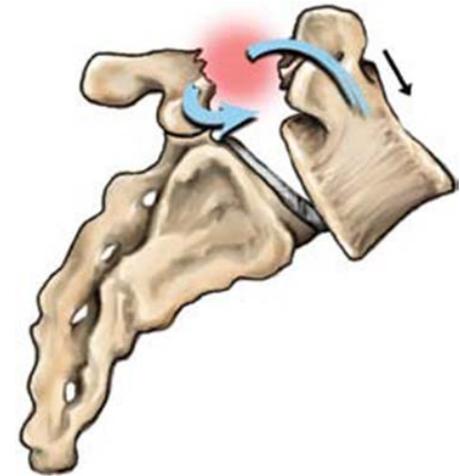


# Background

## Spondylolisthesis

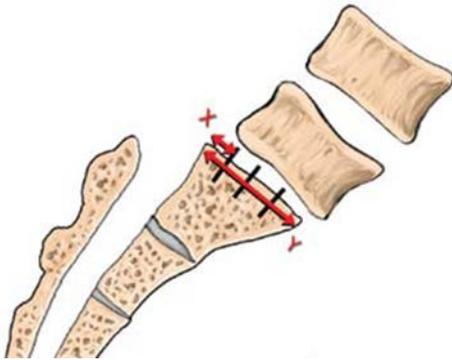
# Spondylolisthesis

- Origin of term:
  - “Spondylo” = vertebra;
  - “Lysis” = break or defect
- Defined as anterior displacement of one vertebra in relation to the subjacent vertebra
- Displacement is the end result of different disease processes

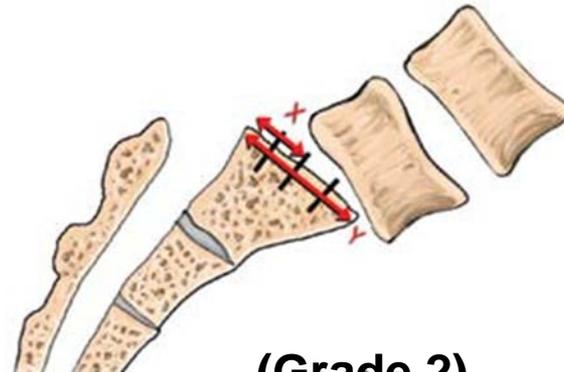


# Severity – Grade

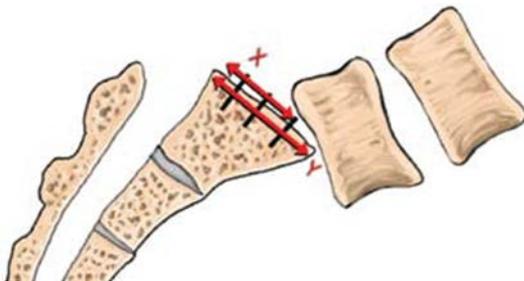
Defines translation of superior vertebra relative to subjacent vertebra



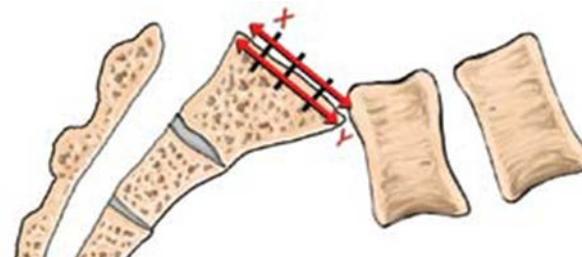
**(Grade 1)**  
**(1-25%)**



**(Grade 2)**  
**(26-50%)**



**(Grade 3)**  
**(51-75%)**



**(Grade 4)**  
**(76-100%)**

# Spondylolisthesis Types Wiltse Classification (1976)



<b>Type 1</b>	<b>Dysplastic (Congenital)</b>
<b>Type 2</b>	<b>Isthmic (Lesion involving pars interarticularis)</b> <ul style="list-style-type: none"> <li>▪ <b>Subtype 2A: Stress fracture</b></li> <li>▪ <b>Subtype 2B: Elongated or attenuated pars</b></li> <li>▪ <b>Subtype 2C: Acute pars fracture</b></li> </ul>
<b>Type 3</b>	<b>Degenerative</b>
<b>Type 4</b>	<b>Post-Traumatic (fracture not involving pars region)</b>
<b>Type 5</b>	<b>Pathologic</b>
<b>Type 6</b>	<b>Post-Surgical or Iatrogenic</b>

# Spondylolisthesis Types

## Marchetti and Bartolozzi (1982, 1997)

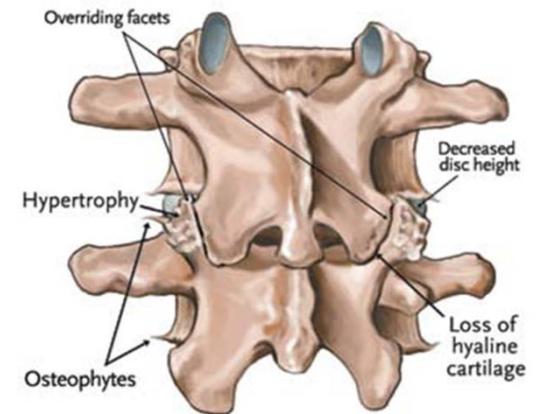
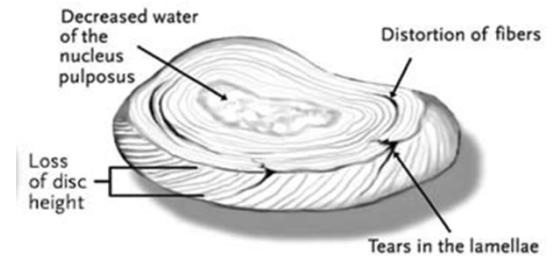


- Suggested classification based on the presence/absence of dysplasia (abnormal tissue development) at the slip level
- Presence/absence of a pars defect is an anatomic feature which fails to separate spondylolisthesis types

Developmental	Acquired
High Dysplasia	Degenerative
Low Dysplasia	Post-Surgical
	Traumatic
	Pathologic

# Spondylolisthesis Types

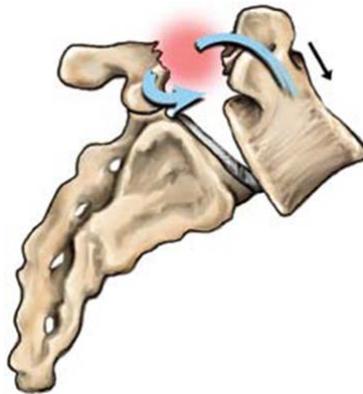
## Degenerative



- Most common type in adults
- Slippage limited to grade 1 or grade 2 by intact posterior bony elements
- **Pedicle screw use is Class II**

# Spondylolisthesis Types

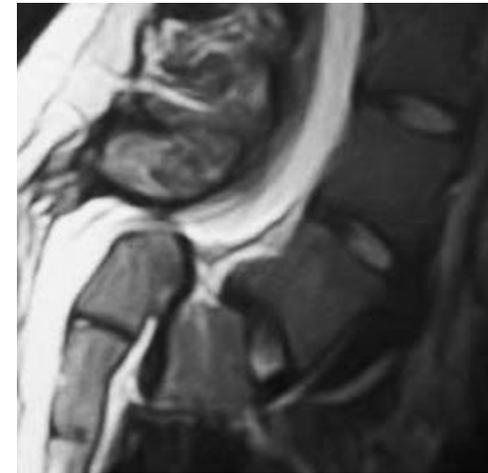
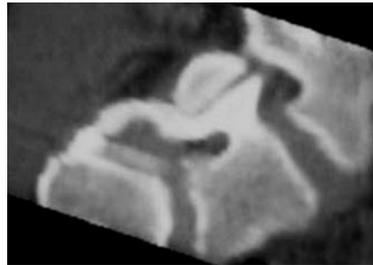
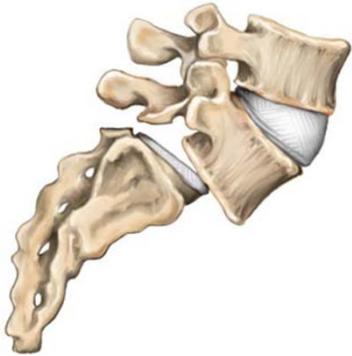
## Isthmic



- Grade 1 and 2 slippage
- Low grade slippage
- Pedicle screw use is **Class III**

- Grade 3 and 4 slippage
- “Severe” or High Grade
- Pedicle screw use is **Class II**

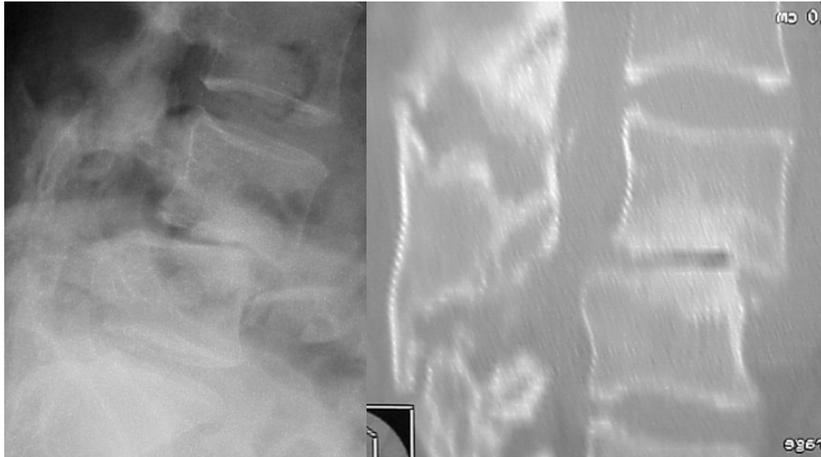
# Developmental / Dysplastic



- Grade 1 and 2 slippage
- Low grade slippage
- Pedicle screw use is **Class III**

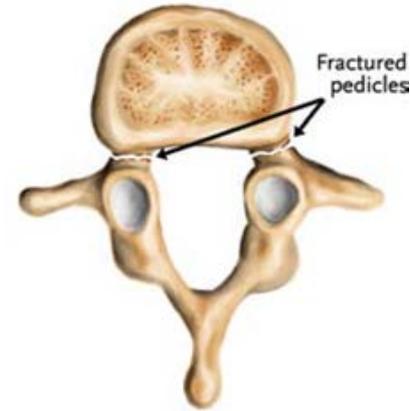
- Grade 3 and 4 slippage
- “Severe” or high grade
- Pedicle screw use is **Class II**

## Post-Surgical

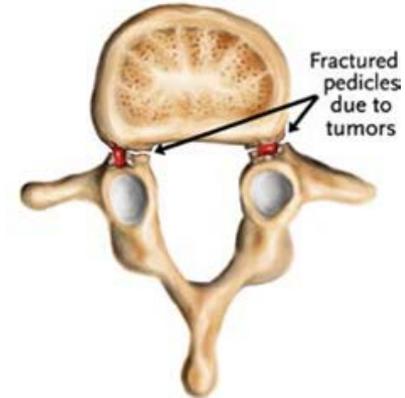


- Pedicle screw use is **Class II** if fusion failure is present
- Pedicle screw use is **Class III** for other types

## Traumatic

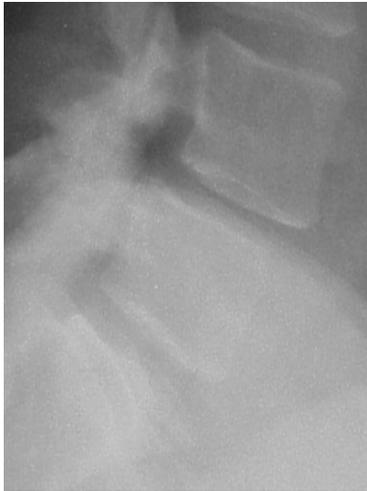


## Pathologic



Pedicle screw use is **Class II** for Trauma and Tumor indications

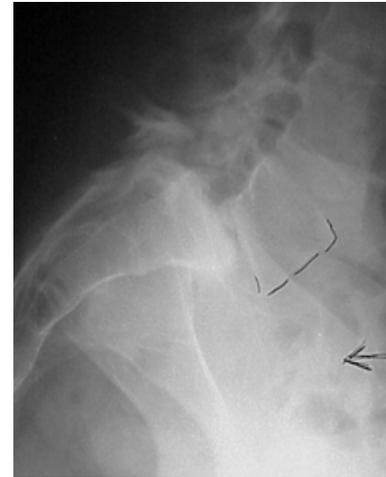
# Spondylolisthesis Types Currently Considered as Class II Indications



**Grade 1  
Degenerative  
Spondylolisthesis**



**Grade 2  
Degenerative  
Spondylolisthesis**



**Grade 3  
“Severe”  
Spondylolisthesis**



**Grade 4  
“Severe”  
Spondylolisthesis**



**FDA Class II Indications Include All Grades of Spondylolisthesis**

# Spondylolisthesis Grades and Types

## *Relation to Current FDA Regulatory Status*

Spondylo	Grade 1	Grade 2	Grade 3	Grade 4
Degenerative	Class II	Class II	<i>n/a</i>	<i>n/a</i>
Severe	<i>n/a</i>	<i>n/a</i>	Class II	Class II
“Other”	<i>Class III – To be considered by Panel</i>	<i>Class III – To be considered by Panel</i>	<i>n/a</i>	<i>n/a</i>

- **Non-Degenerative Spondylolisthesis (Grade 1 and 2)** is the major type of spondylo excluded from current Class II indications
- **Low-grade “isthmic” spondylolisthesis (Grade 1 and 2)** is the largest category contained in this Class III group



# Background

## Degenerative Disc Disease (DDD)

# Degenerative Disc Disease (DDD)

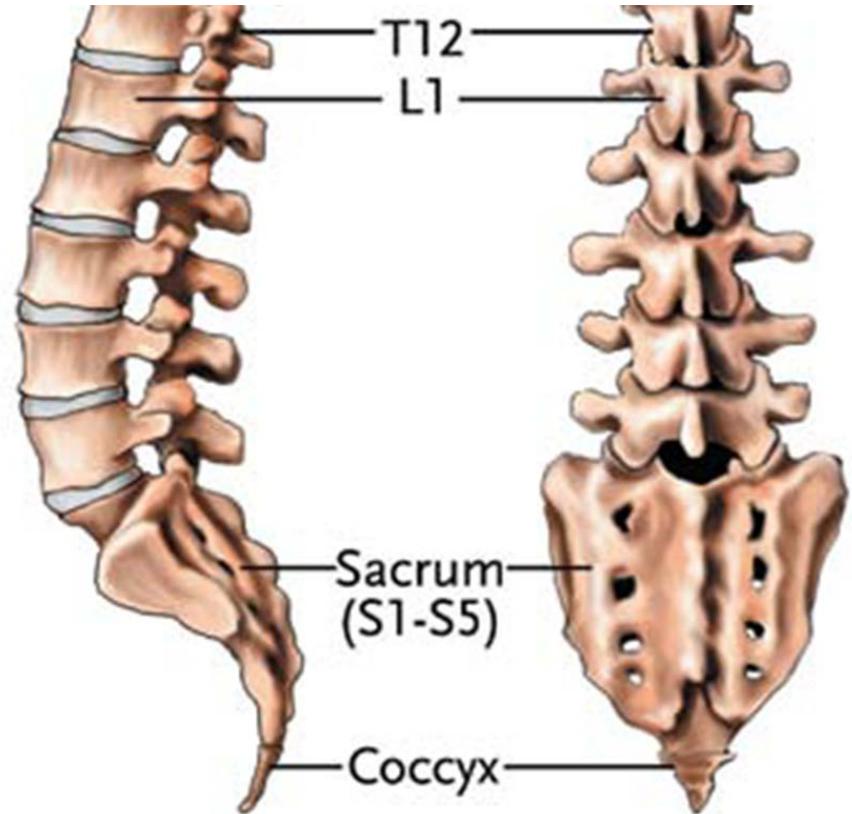
- Lack of consensus exists regarding definition and classification of DDD
- Degenerative changes may or may not be associated with clinical symptoms
- Degenerative process may begin in early life and influenced by genetic, physiologic, and environmental factors as well as normal aging
- Socioeconomic and psychosocial factors also play a role regarding treatment outcomes

**The panel will be asked to address appropriate terminology for use in the description of degenerative spinal conditions and discuss limitations associated with use of the term “DDD”.**

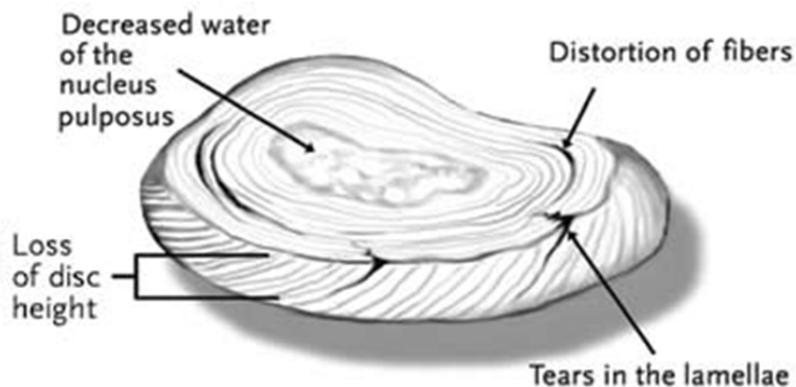
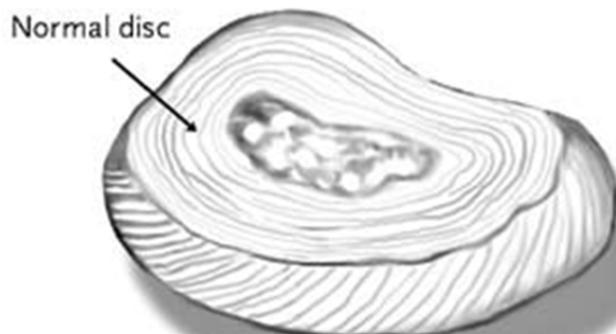
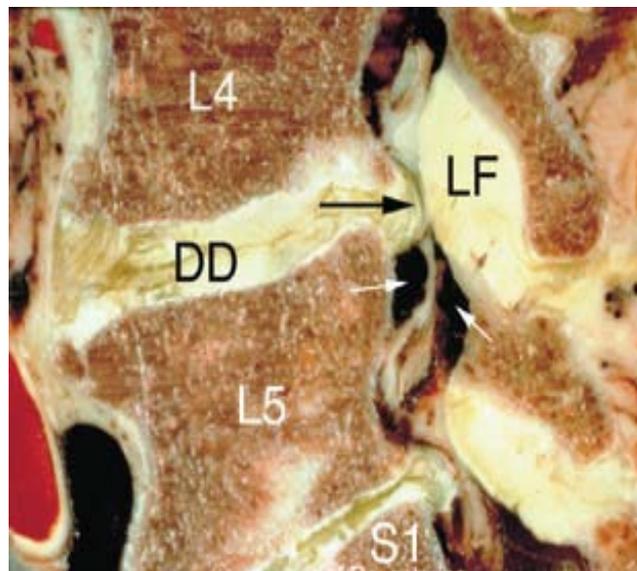
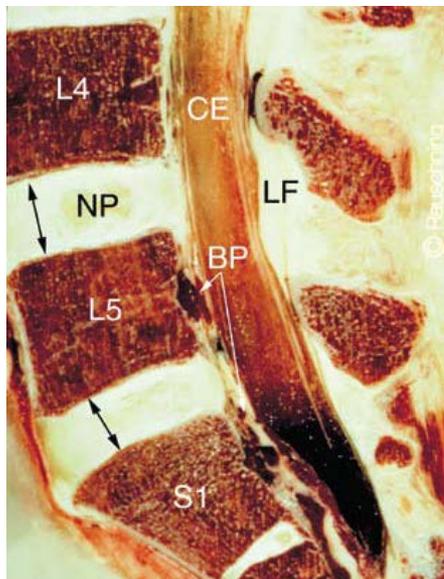
# Spinal Motion Segment

## Functional Spinal Unit

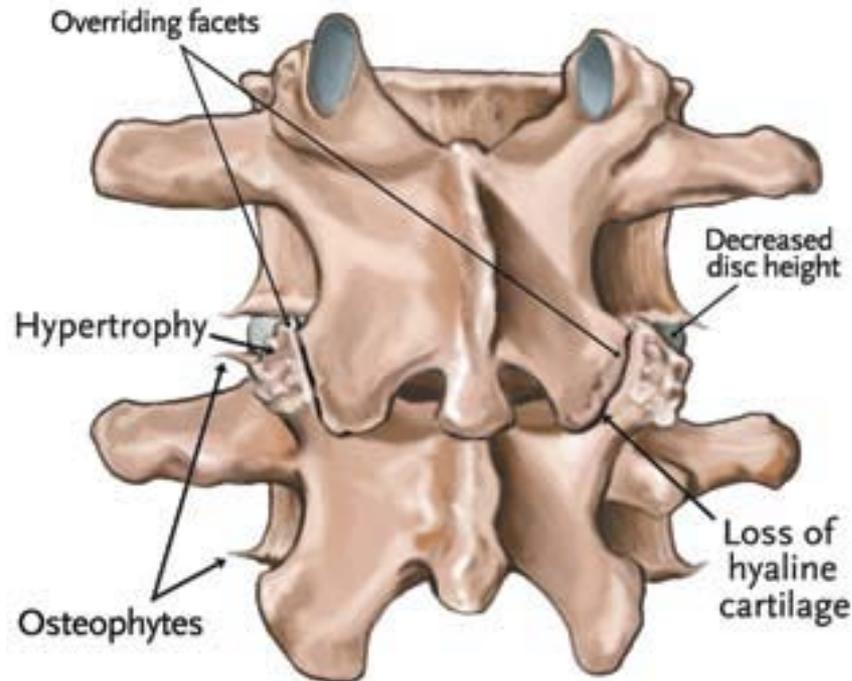
- Adjacent Vertebra
- Disc
- Facet Joints
- Spinal ligaments
- Adjacent Neural Structures



# Degenerative Disc Changes



# Facet Joint Degeneration



- **Decreased disc height may result in overriding of the facets**
- **Loss of joint cartilage and joint hypertrophy may develop**
- **Encroachment upon adjacent neural structures (i.e. spinal stenosis) may occur**

# Progression of Degenerative Disc Disease

**Spine  
Skeletal  
maturity**

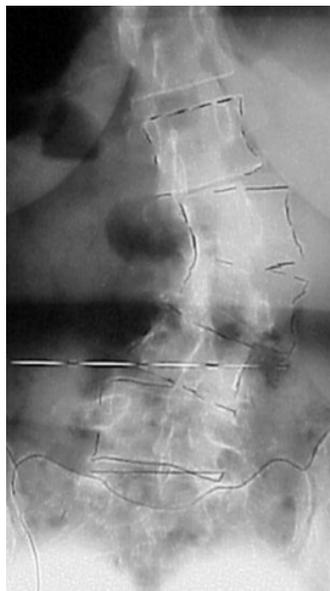
- 3<sup>rd</sup> - 4<sup>th</sup> Decade**
- Disc degenerates
  - MRI changes

- 5<sup>th</sup> - 6<sup>th</sup> Decade**
- Facet DJD
  - Disc collapse

**Stable spine  
ankylosis**

**Unfavorable Degeneration**

**Stenosis Spondylo Deformity**



## Regulatory Definitions for DDD *Variable*

- Clinical symptoms
  - (Back and/or radicular pain)
- Physical examination
- Imaging modalities
  - MRI, CT, X-ray, Discogram
- May include grade 1 degenerative spondylo
- May include subjects with prior spinal procedures
  - Discectomy
  - Laminotomy/Laminectomy
  - Nucleolysis
- Degeneration may involve multiple structures:
  - Disc
  - Vertebral endplates
  - Ligamentum flavum
  - Facet joints
  - Facet joint capsules

## FDA Definition of DDD as per *Guidance Document for the Preparation of IDEs for Spinal Systems (2000)*

“ ...DDD should be defined as back and/or radicular pain with degeneration of the disc as confirmed by patient history, physical examination, and radiographic studies with 1 or more of the following factors (as measured radiographically, either by CT, MRI, plain film, myelography, discography, etc.):

- instability as defined by 3mm translation or 5° angulation;
- osteophyte formation of *facet joints* or vertebral endplates;
- decreased disc height, on average by >2mm, but dependent upon the spinal level;
- *scarring/thickening of ligamentum flavum, annulus fibrosis, or facet joint capsule*;
- herniated nucleus pulposus;
- *facet joint degeneration/changes*; and/or
- vacuum phenomenon ...”

## **FDA Definition of DDD per *Guidance for Industry and FDA Staff: Spinal System 510(k)s***

“... DDD is defined as back pain of *discogenic origin* with degeneration of the disc confirmed by history and radiographic studies...”

## **FDA Summary of Safety and Effectiveness Data (P050010)**

“... DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have *no more than Grade 1 spondylolisthesis* at the involved level...”

# Panel Focus in Relation to DDD

- Discuss whether or not to reclassify the Class III indications of pedicle screw spinal systems including DDD
- Panel meeting is not intended to discuss comparative effectiveness of alternative treatments
- FDA recognizes that primary treatment for majority of patients with DDD is nonoperative, and that patients treated with surgery are selected from the population that has failed nonoperative treatment
- Many factors which influence outcomes regarding treatment of DDD fall outside FDA's authority and lie within the scope of practice of medicine



# Targeted Literature Review

# Literature Review

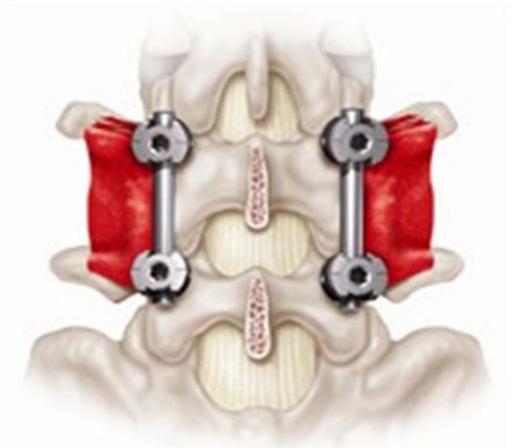
- Review of clinical literature 1994-2013 related to “Other Spondylolisthesis” and DDD (Class III)
- Safety and effectiveness data was tabulated
- Compared to the Cohort Study (Yuan, 1994)
- Adequate number of cases reviewed ( $n=1829$ )
- Confirmed the comprehensive literature review submitted by OSMA in 2009 and extended this search through the present day



# **FDA Review**

## *Spondylolisthesis - Class III Indications*

# Lumbar Fusion Procedures Utilizing Pedicle Screws



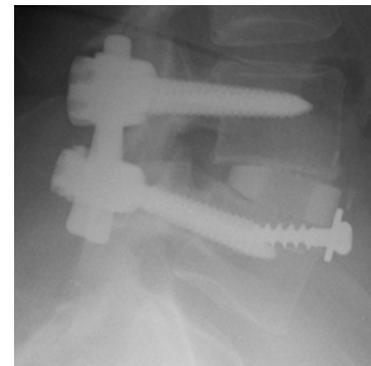
**Posterolateral Fusion**



**TLIF**



**PLIF**



**ALIF**



# Effectiveness

## “Other Spondylolisthesis” (Class III)

- ***Posterolateral Fusion ± Pedicle Fixation***
  - Conflicting reports regarding improvement in patient outcomes and fusion rates with pedicle screw use
- ***Interbody Procedures*** (ALIF, TLIF, PLIF) with Pedicle Screws vs. ***Posterolateral Fusion ± Screws***
  - Higher Fusion Rates with addition of interbody fusion
  - Higher rate of successful clinical outcomes with interbody
- Similar fusion rates and clinical outcomes reported for conventional open TLIF and minimally invasive TLIF

# Low-Grade Isthmic Spondylolisthesis (Kwon, 2005)

- Systematic review
- Pooled treatment outcomes from 34 studies containing in excess of 1000 subjects
- Surgical fusion techniques analyzed included pedicle screw spinal systems as well as interbody fusion techniques

# Effectiveness

## “Other Spondylolisthesis” (Class III)

### Fusion Rates (Kwon, 2005)

- Higher fusion rates with posterolateral fusion and instrumentation (90.2%) vs. noninstrumented fusion (77.4%)
- Higher fusion rates with combination of interbody fusion and pedicle fixation (98.2%) vs. posterolateral fusion ± pedicle screws (83.3%)
- Fusion rates with pedicle fixation for Class III spondylo are similar to or exceed the 89% fusion rate in the Cohort Study (1994)

# Effectiveness

## “Other Spondylolisthesis” (Class III)

### Patient Outcomes (Kwon, 2005)

- Higher rate of successful clinical outcomes with posterolateral fusion and instrumentation (84.9%) vs. noninstrumented fusion (64.4%)
- Higher rate of successful clinical outcomes with combination of interbody fusion and pedicle fixation (86.4%) vs. posterolateral fusion  $\pm$  pedicle screws (74.8%)
- Clinical outcomes for Class III spondylo treated with pedicle systems similar to Cohort Study

# Safety

## “Other Spondylolisthesis” (Class III)

### Sansur (2010)

- Adult spondylolisthesis ( $n = 10,242$ )
- High grade spondylolisthesis (grades 3,4,5) were associated with a higher rate of complications than low grade (grade 1,2) spondylolisthesis (22.9% vs. 8.3%)
- Degenerative spondylolisthesis was associated with a higher rate of complications than isthmic spondylolisthesis (8.5% vs. 6.6%)

# Safety

## Spondylolisthesis (Class III) - FDA Analysis

Adverse Event	Spondylo (Class III)	Cohort Study (Class II)
Neurologic Injury	0.9%	0.8%
Infection	0.9%	2.6%
Screw malposition	2.1%	1.3%
Reoperation/Revision	3.6%	17.6%
Removal	1.3%	12.5%

## **FDA Conclusions From Clinical Studies Regarding Pedicle Screw Spinal Systems for Class III Fusion Indications for “Other Spondylolisthesis”**

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...Clinical evidence appears to support a reasonable assurance of safety and effectiveness for pedicle screw spinal systems used in isolation, or in combination with interbody fusion, for treatment of spondylolisthesis “other than” either severe spondylolisthesis (grades 3 and 4) at L5-S1 or degenerative spondylolisthesis with objective evidence of neurologic impairment (i.e Class III indications)....

**The panel will be asked to address the safety, effectiveness, and re-classification of pedicle screw spinal systems for Class III fusion indications for “other spondylolisthesis”.**

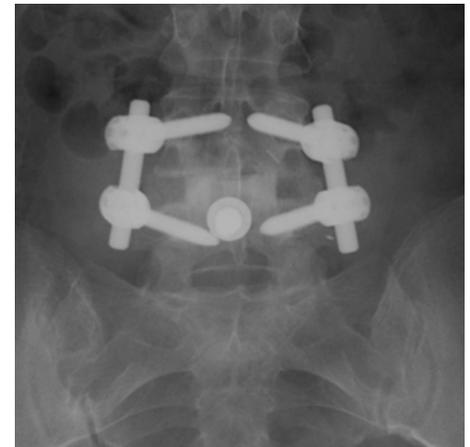


# **FDA Review**

## *Degenerative Disc Disease (DDD)*

# Degenerative Disc Disease (DDD)

Rationale for use of pedicle screw spinal systems in the treatment of DDD relates to the ability of rigid spinal instrumentation to limit strain during the process of fusion healing, thereby enhancing fusion success



# Effectiveness

## Degenerative Disc Disease (DDD)

### Fusion Rates

- Data exists to support higher posterolateral fusion rates with use of pedicle screw systems compared to fusion without pedicle screw use
- Higher fusion rates achieved when interbody fusion (ALIF or PLIF) was performed in combination with pedicle systems compared to either posterolateral fusion with screws or non-instrumented posterolateral fusion
- Fusion rates with pedicle fixation for DDD equal or exceed the 89% fusion rate in the Cohort Study (1994)

# Fusion Rates Using Pedicle Fixation Degenerative Disc Disease (DDD)

Study	Procedure / Implant	Fusion Rate
Brantigan/2000*	PLIF + screws ( <i>n</i> =178)	91%
Fritzell/2002	PLIF or ALIF + screws ( <i>n</i> =75) PSF + screws ( <i>n</i> =74)	91% 87%
Christensen/2002	ASF + PSF + Screws ( <i>n</i> =73) PSF + screws ( <i>n</i> =73)	92% 80%
Zigler/2007*	ALIF + screws ( <i>n</i> =75)	97%
Yuan/1994 Cohort Study	PSF + screws ( <i>n</i> =1794)	89%

\* FDA Approved Clinical Trials

# Patient Outcomes Using Pedicle Fixation Degenerative Disc Disease (DDD)

## Patient Outcomes

- ***Posterolateral Fusion ± Pedicle Fixation***
  - Conflicting reports regarding improvement in patient outcomes or fusion rates with screws
- ***Combined Procedures (ALIF, TLIF, PLIF) with Pedicle Fixation vs. Posterior Fusion***
  - Suggest improved clinical outcomes with combined procedures
- Lower rate of successful clinical outcomes with posterior procedures vs. procedures which include interbody fusion attributed to persistent motion and nociception by inflammatory mediators at the non-fused disc space

# Patient Outcomes Using Pedicle Fixation Degenerative Disc Disease (DDD)

Investigator	Study Results
Videbaek/2006	<p><u>Circumferential fusion (ALIF/pedicle screws) vs. Posterolateral fusion/pedicle screws</u> (n=148)</p> <ul style="list-style-type: none"> <li>▪ Improved outcomes with circumferential fusion (ODI, SF-36, LBPR, DPQ, fusion rate, reoperation rate)</li> </ul>
Brantigan/2000	<p><u>PLIF and pedicle fixation system</u> (n=178)</p> <ul style="list-style-type: none"> <li>▪ 86% success per FDA criteria (↓ pain, maintenance and/or improvement in neurologic status)</li> </ul>
Zigler/2007	<p><u>Circumferential fusion (ALIF/pedicle screws)</u> (n=75)</p> <ul style="list-style-type: none"> <li>▪ Success: Neurologic (81%), SF-36 (70%), ODI (64%),</li> </ul>
Hackenberg/2005	<p><u>TLIF with Pedicle Screw Fixation</u> (n=30)</p> <ul style="list-style-type: none"> <li>▪ Significant reduction in pain (VAS) and disability (ODI)</li> </ul>

# Safety

## Degenerative Disc Disease (DDD)

- The identified risks to health associated with use of pedicle screw spinal systems for fusion indications were similar for treatment of DDD (Class III) compared to existing Class II indications
- Complication rates were similar for treatment of DDD (Class III) compared to existing Class II indications
- Complication rates were 1% or less for a majority of events in studies reporting treatment of DDD (Class III) with pedicle screw spinal systems

# Safety

## Degenerative Disc Disease (DDD) - FDA Analysis

Adverse Event	DDD (Class III)	Cohort Study (Class II)
Plate/Rod/Screw Breakage	1.3%	0.2%
Pseudarthrosis	5.9%	3.7%
Infection (Overall)	3.9%	2.6%
Superficial	2.6%	--
Deep	0.9%	--
Reoperation/Revision	10.9%	17.6%
Removal	5.5%	12.5%

# Limitations

## Literature Review - DDD

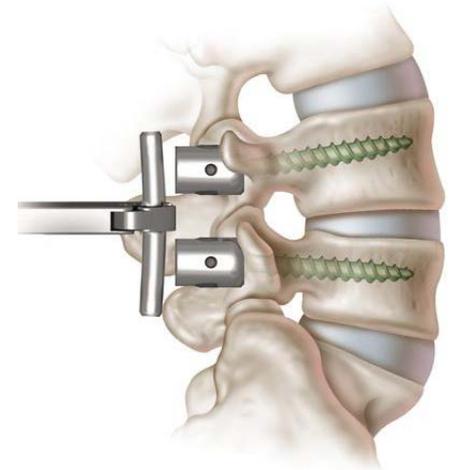
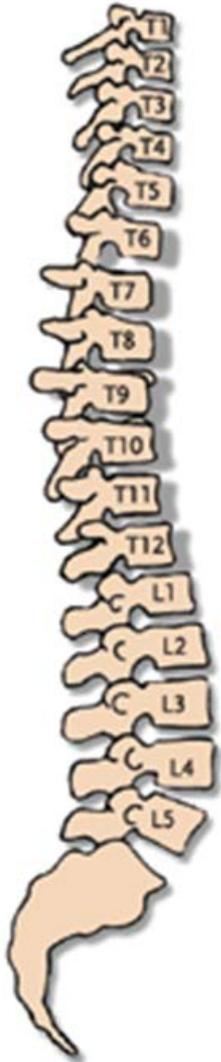
- Lack of consensus regarding definition of the DDD population
- Inconsistent methods utilized for reporting patient outcomes
- Variable criteria used to define fusion success
- Inconsistent reporting of adverse events
- Multiple surgical approaches utilized
- Variations regarding type of graft materials utilized
- Variable definitions for reoperations (i.e. elective removals, adjacent level procedures)
- Interpretation of effectiveness data is limited by lack of diagnostic specificity for DDD as variable response to fusion according to diagnostic subgroups has been reported (Glassman, 2009)

# **FDA Conclusions From Clinical Studies Regarding Pedicle Screw Spinal Systems for Class III Fusion Indications for “Degenerative Disc Disease (DDD)”**

...Clinical evidence appears to support a reasonable assurance of safety and effectiveness for pedicle screw spinal systems used in isolation, or in combination with interbody fusion, for treatment of degenerative disc disease....

**The panel will be asked to address the safety, effectiveness, and re-classification of pedicle screw spinal systems for Class III fusion indications for DDD.**

# Thank You





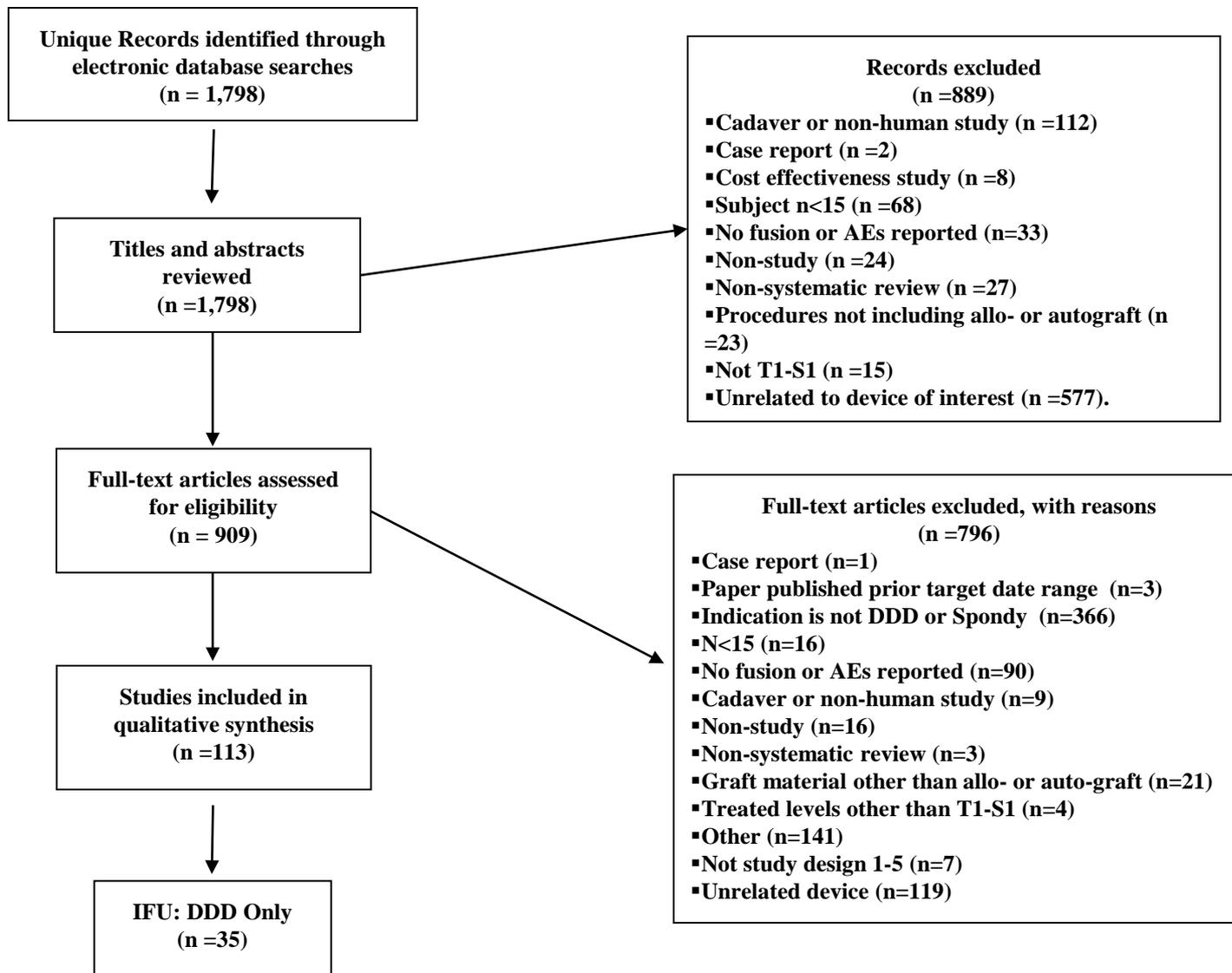
# **SYSTEMATIC LITERATURE REVIEW FOR DEGENERATIVE DISC DISEASE**

**Anna Ghambaryan, MD., MS., Ph.D.**

Division of Epidemiology

Office of Surveillance and Biometrics

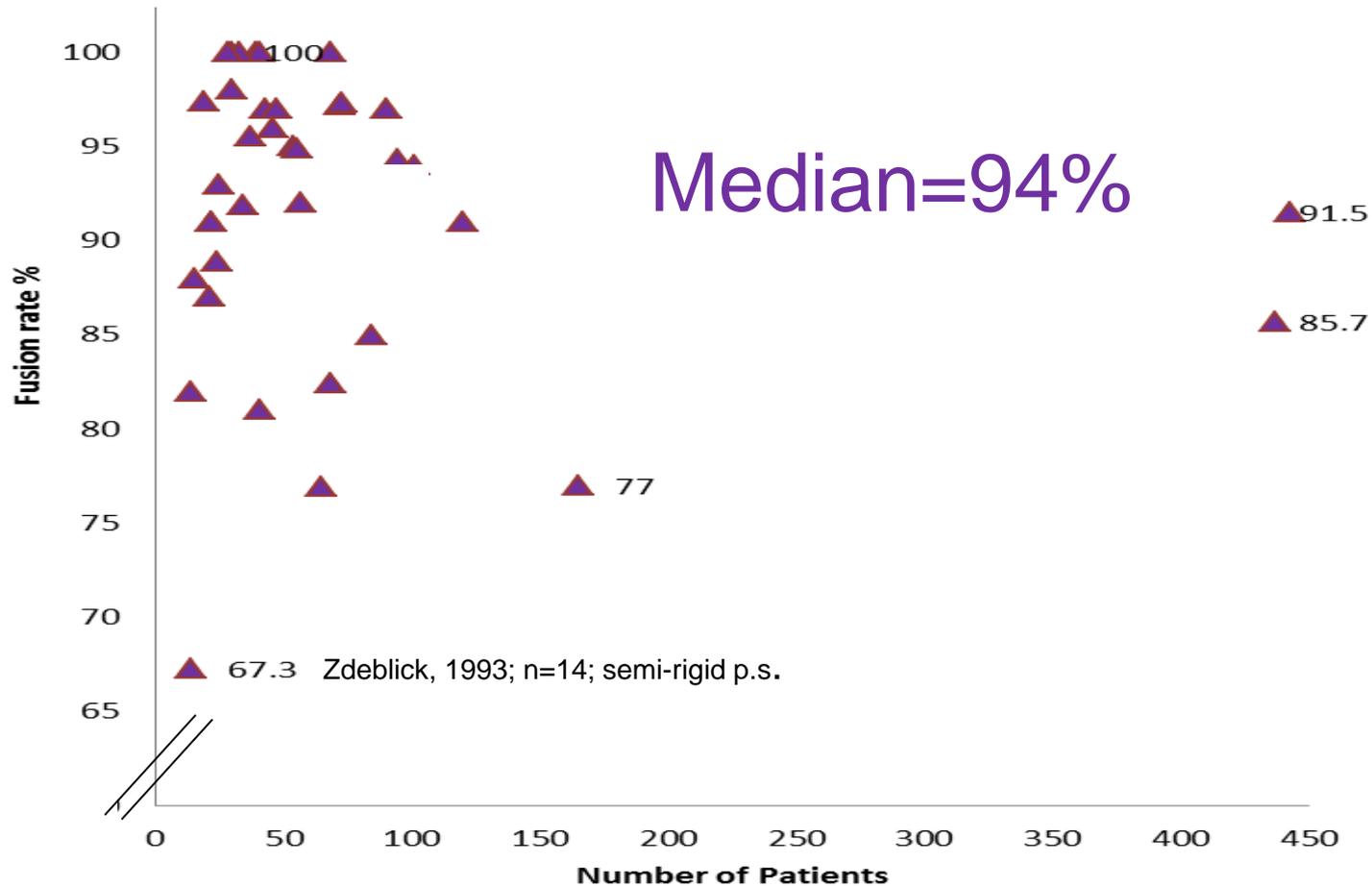
Center for Devices and Radiological Health



# Literature Review Summary

- 31 Primary studies
  - Randomized Controlled Trials (n=9)
  - Observational Studies (n=22)
- 4 Secondary studies
  - Systematic Literature Reviews (n=3)
  - Meta-Analysis (n=1)
- Follow up = 6-96 months
- Age Range = 15-85 years
  - Mean = 36-74 years

# Effectiveness: Fusion Rate



# Safety at 6-18 months: Adverse Events

- Revision and Reoperation
  - 17 studies
  - Range = 0-37.5%; median revision = 9.4%
  - Main Reasons - Pain and pseudoarthrosis
- Infection
  - 14 studies
  - Range = 0-7.4%
- Neurological Complication
  - 13 studies
  - Range = 0-14.8%; Audat (2012) = 14.8%, 0-5.8%

# Summary

- Key Findings

- Fusion rates = 67.3-100%, median = 94.15%
- Adverse Events
  - Revisions and reoperations, infections, and neurological complications

- Limitations

- Definitions (varies)
  - DDD; fusion; revision; re-operation
- Heterogeneity
  - Age
  - Illness / severity
  - Treatment: different constructs; level of fusion; number of levels; surgical approach / techniques



# **DYNAMIC STABILIZATION**

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**Biomedical Engineer**  
**Anterior Spine Devices Branch**  
**Division of Orthopedic Devices**  
**Office of Device Evaluation**

# Device Description

## Traditional Rigid System

- Contains rigid, uniform, metallic rods
- Clinical data typically not required to support fusion indications
- Designs and clinical effectiveness generally understood

## Dynamic Stabilization System (DSS)

- Contains semi-rigid, non-uniform, or non-metallic rods (e.g., polymer cords, moveable screw heads, and springs)
- Clearances were not supported with clinical data

**The panel will be requested to provide feedback on what is considered 'Dynamic Stabilization' and which features fall under the scope of DSS.**

# Regulatory History - DSS

- Majority of 510(k) clearances based on bench and cadaver data
- After clearances, bench testing was found not predictive of clinical outcomes
- 1 recall due to device failures that were not predicted by bench testing

# Public Health Question

- Are DSS performing equivalently to traditional rigid pedicle screw systems in terms of:
  - Fusion rates
  - Device breakage
  - Need for secondary surgeries
  - Explant analyses and failure modes

## Section 522 of FD&C Act

Authority to order postmarket surveillance of any class II and class III medical device that meets any of the following criteria:

- failure of the device would be reasonably likely to have a serious adverse health consequence
- expected to have significant use in pediatric populations
- intended to be implanted in the body for more than one year
- intended to be a life-supporting device used outside of a user facility

# Current Status of 522 Studies

- 16 DSS systems under 522
- Study status:
  - 1 plan pending
  - 5 progress inadequate
  - 10 on hold (“other”)
    - Sponsor is not marketing product

# DSS Literature Search

- Literature search conducted to support 522s, extended to current day
- Majority of literature is for non-fusion intended use
- Predominant devices discussed are Dynesys and Graf (not marketed in the US), and hybrid constructs
- Retrospective case series of PEEK rods for fusion (Ormond, 2012; Delure, 2012)
- Maximum follow up 18 months, additional follow up suggested by authors

# Summary of Evidence- DSS

- There is limited clinical evidence available to support the reasonable assurance of safety and effectiveness for dynamic stabilization systems when used as an adjunct to fusion for Class III and Class II indications
  - 522s
  - Literature search
- May present an unreasonable risk of illness or injury

**The panel will be asked to discuss whether any unique risks to health are associated with DSS as an adjunct to fusion, and whether special controls are sufficient to mitigate these risks.**



# **Clinical Evidence: Adverse Event Analysis (MAUDE Search)**

# MAUDE Search- Adverse Events

- MDR reporting: the mechanism for the FDA to receive significant medical device adverse events from manufacturers, importers and user facilities.
- January 1, 2003 to December 31, 2012
- 6595 unique MDRs



# MAUDE Search: Results

Adverse event (as reported in device or patient problem code)	Pedicle Screws Class III NKB	Pedicle Screws Class II MNH/MNI	Dynamic Stabilization NQP
<b>Total MDRs reported</b>	<b>N=1733</b>	<b>N=1138</b>	<b>N=463</b>
Malpositioned device/Surgeon error	165 (9.5%)	123 (10.8%)	7 (1.5%)
Device disassembly	697 (40.2%)	518 (45.5%)	45 (9.7%)
Device breakage	538 (31%)	397 (34.9%)	277 (59.8%)
Device malfunction	92 (5.3%)	58 (5.1%)	12 (2.6%)
Surrounding bone issues	64 (3.7%)	19 (1.7%)	0 (0.0%)
Infection	30 (1.7%)	20 (1.8%)	9 (1.9%)
Pain	219 (12.6%)	167 (14.7%)	126 (27.2%)
Fall	20 (1.2%)	19 (1.7%)	9 (1.9%)
Additional procedures necessary	<b>38.6%</b>	388 (34.1%)	217 (46.9%)
Device removal	<b>43.6%</b>	368 (32.2%)	56 (12.1%)
Not specified (device codes)	167 (9.6%)	50 (4.4%)	43 (9.3%)
Not specified (patient codes)	1126 (65%)	571 (50.2%)	164 (35.4%)

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Fall	20 (1.2%)	19 (1.7%)	9 (1.9%)
<b>Additional procedures necessary</b>	<b>72 (4.2%)</b>	<b>388 (34.1%)</b>	<b>217 (46.9%)</b>
Device removal	97 (5.6%)	368 (32.2%)	56 (12.1%)
Not specified (device codes)	167 (9.6%)	50 (4.4%)	43 (9.3%)
Not specified (patient codes)	1126 (65%)	571 (50.2%)	164 (35.4%)

# MAUDE Search: Limitations

- Product code may not correspond to the indication that was treated.
- Single MDR may be associated with more than one problem code.
- Lack of problem code does not signify a specific adverse event type did not occur.
- Problem codes were used instead of text searches to eliminate bias.
- Problem codes may have been used incorrectly or inconsistently.

# Summary: Dynamic Stabilization

- FDA believes that the safety and effectiveness profile for DSSs are not currently well understood, so reasonable assurance of safety and effectiveness cannot be established.
- This subset of devices may present an unreasonable risk of illness or injury.

# Summary:

## Rigid Pedicle Screw Spinal Systems

- FDA believes that there is a reasonable assurance of safety and effectiveness for traditional, rigid pedicle screw spinal systems when used for DDD and types of spondylolisthesis other than severe spondylolisthesis (grades 3 or 4) or degenerative spondylolisthesis with objective evidence of neurologic impairment)
- Risks to health can be mitigated with general and special controls



# **RISKS TO HEALTH & SPECIAL CONTROLS**

# Risks to Health

- Malposition
- Implant loosening
- Device breakage
- Disassembly
- Malfunction-Device
- Bone fracture
- Graft settling/displacement
- Loss of correction
- Bleeding/Vascular injury
- Neurologic injury
- Pseudarthrosis
- Back/leg pain
- Dural Injury/CSF leak
- Wound Problems
- Infection/Sepsis
- Skin irritation
- Cardiac
- Respiratory
- Gastrointestinal
- Revision surgery
- Death

**The panel will be asked to address the completeness of the risks to health for traditional rigid systems and dynamic stabilization systems.**

# Proposed Special Controls

- Proposed special controls
  - Labeling
  - Biocompatibility
  - Sterility
  - Mechanical testing
  
- FDA correlates the ability of each special control identified to mitigate an identified risk to health
- Reliance on standards published through ASTM International and International Organization for Standardization (ISO)

# Labeling

- Must bear all information required for the safe and effective use of the device
  - Indications for use including levels of fixation
  - Clear description of device technological features including identification of device materials
  - Device specific warnings, precautions, and contraindications
  - Identification of MR compatibility status
  - Sterilization and cleaning instructions
  - Detailed instructions of each surgical step accompanied by magnified illustrations

# Labeling

- Specific recommendations proposed by 515(i) respondents
  - Removal of warning:

“Warning: The safety and effectiveness of pedicle screw spinal systems have been established only for spinal conditions with significant mechanical instability or deformity requiring fusion with instrumentation. These conditions are significant mechanical instability or deformity of the thoracic, lumbar, and sacral spine secondary to severe spondylolisthesis (grades 3 and 4) of the L5-S1 vertebra, degenerative spondylolisthesis with objective evidence of neurologic impairment, fracture, dislocation, scoliosis, kyphosis, spinal tumor, and failed previous fusion (pseudoarthrosis). The safety and effectiveness of these devices for any other conditions are unknown.”

**The panel will be asked to comment on whether inclusion or removal of the aforementioned warning is appropriate.**

# Biocompatibility

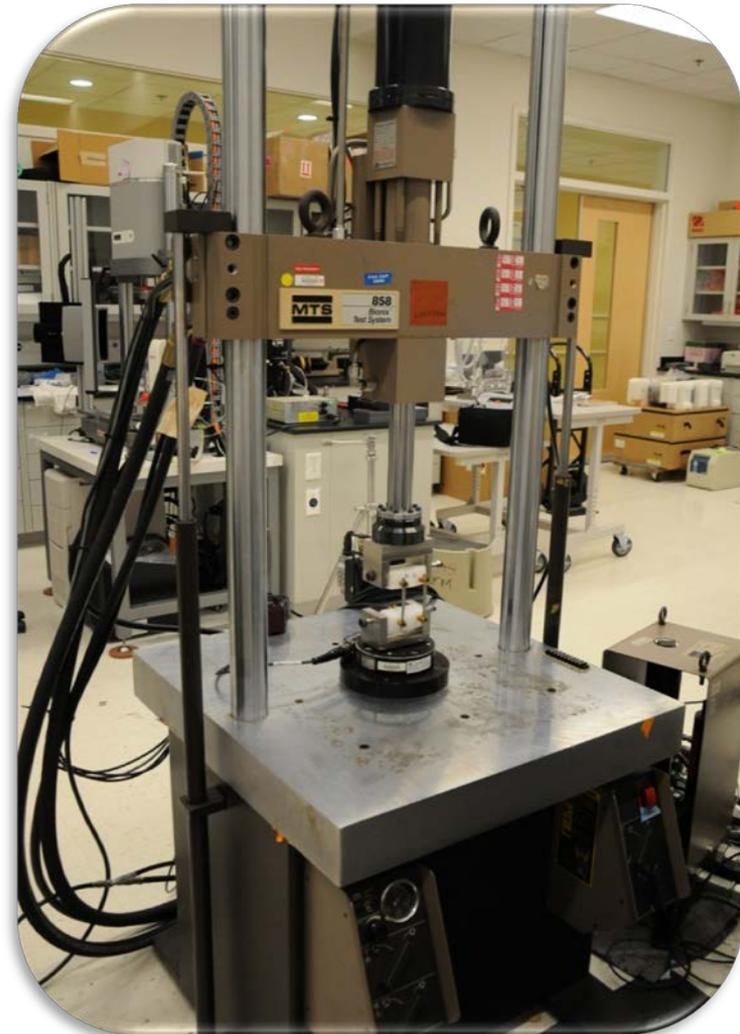
- Material characterization, including conformance to material standards, must demonstrate biocompatibility of the device materials and any potential byproducts (e.g., wear debris, leachates, etc)
  - Identification of relevant patient contact type and duration (e.g., ISO 10993: *Biological Evaluation of Medical Devices*)
  - Identification of relevant Material Standards (e.g., ASTM F136, ASTM F67, ASTM F1537)

# Sterility

- Sterilization validation must demonstrate the sterility of, or the ability to sterilize, the device components.
  - Device components and instruments
  - Sterility Assurance Level (SAL) of  $10^{-6}$

# Mechanical Testing

- Non-clinical performance testing must demonstrate the mechanical function and durability of the device components. Mechanical testing should include:
  - Static Testing of construct and/or subassembly
  - Fatigue Testing of construct and/or subassembly



# Construct Testing (e.g., ASTM F1717)

*Standard Test Methods for Spinal Implant Constructs in a Vertebrectomy Model*

- Used to compare device performance in a worst-case vertebrectomy model
- Mechanical Tests
  - Static Compression Bending
  - Dynamic Compression Bending
  - Static Torsion

# Subassembly Testing (e.g., ASTM F1798)

*Standard Guide for Evaluating Static and Fatigue Properties of Interconnection Mechanisms and Subassemblies Used in Spinal Arthrodesis Implants*

- Used to compare the interconnection mechanism between components (e.g., screws, hooks, and rods)
- Mechanical Tests
  - Axial gripping
  - Torsional gripping
  - Flexion/extension
  - Fatigue



# **Mitigation of Risks to Health**

# Risks to Health

<i>Identified Risk</i>	<i>Recommended Mitigation Measures</i>			
	<i>Labeling</i>	<i>Biocompatibility</i>	<i>Sterility</i>	<i>Mechanical Testing</i>
Malposition	Yes			Yes
Implant Loosening	Yes	Yes		<del>Yes</del>
Device Breakage	Yes			Yes
Disassembly	Yes			
Bone Fracture	Yes			
Graft Settling/ Displacement	Yes			Yes
Loss of Correction	Yes			Yes
Pseudarthrosis	Yes	Yes		
Bleeding/Vascular Injury	Yes			
Neurologic Injury	Yes			

# Risks to Health

<b>Identified Risk</b>	<b>Recommended Mitigation Measures</b>			
	<b>Labeling</b>	<b>Biocompatibility</b>	<b>Sterility</b>	<b>Mechanical Testing</b>
Dural Injury/CSF Leak	Yes			
Wound	Yes			
Infection/Sepsis	Yes		Yes	
Skin Irritation	Yes	Yes		
Cardiac	Yes			
Back/leg pain	Yes			
Gastrointestinal	Yes			
Respiratory	Yes			
Revision Surgery	Yes	Yes	Yes	Yes
Death	Yes	Yes	Yes	Yes

# Summary: Proposed Special Controls

- **Labeling** – *Labeling must bear all information required for the safe and effective use of the device*
- **Biocompatibility** - *Material characterization, including conformance to material standards, must demonstrate biocompatibility of the device materials and any potential byproducts (e.g., wear debris, leachates, etc).*
- **Sterility** - *Validation must demonstrate the sterility of, or the ability to sterilize, the device components.*
- **Mechanical testing** - *Non-clinical performance testing must demonstrate the mechanical function and durability of the device components.*
- **Other(s)?**

The panel will be asked to comment on the adequacy of the proposed special controls to mitigate the risks to health for traditional, rigid pedicle screw spinal systems and dynamic stabilization systems.



# **FDA Conclusions: Safety and Effectiveness**

# FDA Conclusions

## *Dynamic Stabilization Systems*

- Small amount of published literature suggests that the safety and effectiveness profile for dynamic stabilization systems as an adjunct to fusion is not well established for this device subgroup.
- Considering all clinical evidence:
  - Risks to health not well characterized
  - Special controls utilized for traditional rigid systems may not appropriate to mitigate the risks to health for dynamic stabilization systems.
  - May present an unreasonable risk of illness or injury. 95

# FDA Conclusions

## *Traditional Rigid Systems*

- Considering all clinical evidence:
  - The available scientific evidence supports a reasonable assurance of safety and effectiveness for the use of traditional rigid pedicle screw spinal systems in the treatment of DDD and spondylolisthesis other than either severe spondylolisthesis (grades 3 and 4) at L5-S1 or degenerative spondylolisthesis with objective evidence of neurologic impairment
  - The proposed special controls are sufficient
  - There is not an unreasonable risk of illness or injury for the traditional, rigid pedicle screw spinal systems when general and special controls are applied



**Thank You**

**Questions?**