the spine in spinal fusions for degenerative spondylolisthesis and spinal trauma. The Panel also determined that the incidence rates of device breakage, deformation, and loosening were similar to those of commercially available device systems and that the rates were clinically acceptable. The types of device-related complications for pedicle screw spinal systems reported to FDA under the MedWatch device reporting program were comparable to those reported in clinical studies and the medical literature for commercially available spinal systems and included broken screws, neurologic injuries, and nonunions (Ref. 66).

The Panel did not find support in the literature or in clinical data for use of the device in the treatment of low back pain. The Panel specifically recommended that low back pain should not be included in the indications for use of the device until clinical data justify its inclusion (Ref. 66).

The Panel believed that the primary risks to health associated with pedicle screw spinal systems are similar to those associated with other class II spinal implant devices. The Panel believed that both clinical and nonclinical parameters need to be controlled to provide reasonable assurance of the safety and effectiveness of the device. The primary nonclinical parameters affecting safety and effectiveness are: (1) Biocompatibility of the materials used in the manufacture of the device; (2) device design; (3) device durability; (4) device strength, and (5) device rigidity. The primary measures of clinical effectiveness of the device are: (1) Fusion, (2) pain relief, (3) functional improvement, and (4) neurologic status. These concerns are the same as those associated with commercially available class II devices, including posteriorly placed interlaminal spinal fixation orthoses (21 CFR 888.3050) and anteriorly placed spinal intervertebral body fixation orthoses (21 CFR 888.3060)

The Panel reviewed the medical literature pertaining to the use of pedicle screw spinal systems in the treatment of severe spondylolisthesis (Refs. 5, 6, 14, 27, 28, 29, 30, 48, 52, 68, 81, 82, 83, 84, 92, 93, 147, 155, 159, 168, 169, 175, and 188) and determined that the risks associated with the device are no different than those associated with the use of the preamendments class II spinal fixation devices or those associated with pedicle screw spinal systems intended for the treatment of other acute or chronic instabilities and deformities. The Panel concluded that the effectiveness of the device is related to its mechanical strength and rigidity, which have been demonstrated to be superior to existing class II devices.

(5) *Risks to health.* The following risks are associated with the pedicle screw spinal system: (a) Mechanical failure. The screw may bend or fracture, loosen or pull-out, the plate or rod may bend or fracture, the connector may slip resulting in loss of fixation and loss of reduction; (b) soft tissue injury. The risks of tissue injury include screw overpenetration of the vertebral body with associated injury to major blood vessels or viscera; pedicle fracture; nerve root injury; spinal cord injury; cauda equina injury; dural tear or cerebrospinal fluid leak; blood vessel injury; and bowel injury; (c) pseudarthrosis. The risk of nonunion, or pseudarthrosis, signifies failure of bony fusion and persistent instability; and (d) need for reoperation. The risk of a possible reoperation includes reoperation for infection or bleeding; revision surgery; removal of device components for device failure, or symptomatic, painful, or prominent hardware; and reoperations for other reasons not related to fusion, such as nerve root decompression. In addition, there are theoretical risks, such as device-related osteoporosis, metal allergy, particulate debris, and metal toxicity, for which no reliable human data exist.

A. Safety and Effectiveness: Nonclinical

1. Biocompatibility of Materials

The biocompatibility of stainless steel and titanium metal alloys used in the fabrication of pedicle screw spinal systems has been investigated extensively with in vitro testing, implantation studies, mechanical testing, toxicological testing, corrosion testing, and clinical trials. These alloys have been demonstrated to be reasonably safe for human usage under a variety of conditions. (Refs. 23, 33, 67, 105, 111, 134, 135, 179, 180, 182, and 197).

Stainless steels, such as 316 L, 316 LVM, and 22Cr-13Ni-5Mn alloys, are susceptible to some degree of crevice, pitting, and stress corrosion. The presence of corrosion products can produce a localized chronic inflammatory response with granuloma formation, macrophage engorgement with particulate matter, and focal areas of necrosis (Refs. 41, 67, 76, 111, 167, 179, and 197). Metallic ion species from leaching or corrosion can produce allergic responses (Refs. 61, 67, 120, and 148). These are recognized and welldescribed tissue reactions to stainless steel implants and metal ions.

Nevertheless, stainless steels have been used extensively with great clinical success for the fabrication of surgical implants, including bone plates, bone screws, and intramedullary rods. The biocompatibility of stainless steels has been regarded as acceptable for implants at various anatomic locations under different pathophysiologic conditions (Refs. 38, 67, 105, 134, 135, 157, 158, 165, 179, and 181).

The corrosion resistance of commercially pure (CP) titanium and Ti-6Al-4V alloy has been welldocumented through in vitro testing, implantation studies, toxicological testing, corrosion testing, and clinical trials. Titanium and its alloys are susceptible to wear as well as corrosion, and thus may cause black discoloration of surrounding tissues and induce aseptic local fibrosis (Refs. 33, 42, 115, 121, 129, 139, 197, and 198). In the soft tissue surrounding titanium alloy orthopedic implants, T-lymphocytes in association with macrophages have been observed, implying an immunological response to the debris (Ref. 103) Macrophage release of bone-resorbing mediators in association with titanium wear debris has also been demonstrated (Ref. 85). The significance of these observations regarding the biologic and toxicologic effects of titanium ions and wear particles in spinal fusion is uncertain since these tissue reactions have been observed only in closed joint systems, such as hip replacements (Refs. 121 and 129). Despite these tissue responses, CP titanium and titanium alloys are still considered relatively safe biomaterials, and may be effectively used with minimal risk when not used as the articulating surface, which leads to the generation of large amounts of wear debris (Refs. 42, 121, 129, 139, 196, 197, and 198). Titanium and its alloys have been used extensively as implant materials since the mid-1960's for the fabrication of implants such as bone plates, bone screws, and hip implants (Refs. 105, 129, 182, 196, 197, and 198).

All available metallic implant materials are imperfect biomaterials. In the trade-off between the theoretical risks arising from metal ion release, corrosion products, and wear debris, and the known benefits of these materials, it appears that both stainless steel and titanium alloys are acceptable for human implantation in the spinal environment.

The Panel believed that the biocompatibility specifications of existing voluntary standards provide reasonable assurance of the safety and effectiveness of devices manufactured of