INTEGRA
LIMIT UNCERTAINTY

To the attention of Quality Assurance Dpt or Regulatory Affairs Dpt or Management

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LIMIT UNCERTAINTY

Saint Priest, March 21, 2014

Subject: **URGENT - FIELD SAFETY NOTICE**
Medical devices:
SynPlug® Cement Restrictor */ 804030, 804015, 804016, 804017, 804018, 804019, 804020, 804021, 804022, 804024, 804026*
OptiPlug® Cement Restrictor */ 804036, 804038, 804040, 804042, 804044, 804046*
Legal manufacturer: ISOTIS Orthobiologics, Inc. – 2 Goodyear – Suite A – Irvine – California – 92618 USA
Concerned batches: *All batches*

Dear Valued Customer,

This Field Safety Notice (FSN) is to notify healthcare professionals about reports in literature of patients experiencing osteolysis (bone loss) following the use of OptiPlug® Biodegradable Cement Restrictors in cemented total hip arthroplasty procedures. This unanticipated adverse event was reported in three medical publications, one of which reported a periprosthetic fracture associated with osteolysis.

OptiPlug® Biodegradable Cement Restrictors are intramedullary cement restrictors intended to be used to occlude the intramedullary canal prior to the cementation of hip or shoulder arthroplasty. SynPlug® Biodegradable Cement Restrictors are identical to OptiPlug® Biodegradable Cement Restrictors except with respect to their mass and the sizes of cement restrictors offered. Due to the similarity between the two products, the information in this letter applies to both OptiPlug® and SynPlug® Biodegradable Cement Restrictors.

IsoTis OrthoBiologics has become aware of recent publications in medical literature that report instances of osteolysis and associated periprosthetic fracture near the site of OptiPlug® Cement Restrictors after total hip arthroplasty procedures. These adverse events were observed between 1 and 5 years post-implantation in post-operative follow-up x-rays. A total of 132 patients were affected by osteolysis, including one patient with a periprosthetic fracture, in the three publications.

Through a literature review, one earlier publication was identified that provided information on SynPlug® Cement Restrictor use and long term follow-up. This 11-year study was not specifically designed to look at the outcome of SynPlug® Cement Restrictor use, but osteolysis was one of several parameters examined. The study authors did not find osteolysis or periprosthetic fractures in the vicinity of the SynPlug® Cement Restrictors.

In the last 24 months, IsoTis OrthoBiologics has received 14 complaints of osteolysis in patients who received OptiPlug® or SynPlug® Cement Restrictors, including 2 patients who experienced associated periprosthetic fractures. All but 1 osteolysis complaint were received by IsoTis OrthoBiologics 4 to 8 years following implantation. No complaints for osteolysis or associated periprosthetic fracture were received between early 2001 and November 2011. All of the patients cited in the publications and complaint reports received by IsoTis OrthoBiologics were asymptomatic, with osteolysis detected through x-rays performed as part of follow-up exams post-implantation. IsoTis Orthobiologics has not made a determination as to the root cause of these reported incidents.