Introduction
Late stage osteoarthritic (OA) disease and rheumatoid arthritis (RA) cause severe, chronic joint pain that can be treated with radiosynovectomy (RSV). A limitation of RSV has been the suboptimal characteristics of the radiocolloids including leakage from the joint resulting in irradiation of tissues beyond the synovium. To overcome these limitations we developed a novel Sn-117m homogeneous colloid that has been tested in two animal inflammatory arthritis models for its effects. Sn-117m (t½=14 d) decays by isomeric transition, producing both gamma rays at 159 keV, 86% abundance as well as monoenergetic conversion electrons (~140 keV; >110%) with a discreet range of about 290 µm, providing the therapeutic advantage of depositing energy in the synovial wall with minimal or no effect to surrounding tissue. Colloids used in RSV should be large enough to avoid leakage and small enough for macrophage engulfment (2-20 µm). We tested our Sn-117m colloid on two animal models.

Objective
In previous studies using a non-GLP OA rat model (n=79), three doses of Sn-117m colloid demonstrated average knee joint retention of 99.8%, safety, and efficacy. Our new objectives were to (1) validate the gCMP production, sterilization, and stability testing at room temperature.

Rheumatoid arthritis and osteoarthritis rat models
Collagen induced RA rat models and surgically created meniscal tear OA rat models were established in Lewis rats as previously described [1,2]. The rats were randomized into the groups shown in Figure 1 where injections occurred in the right knee except for Group 4 which received injections in both knees. Rats were evaluated for biodistribution, blood chemistry, CBC, autoradiography, radiation field, radiation excretion, and histopathology at various time-points.

Materials & Methods
Sn-117m colloid
A method was developed for manufacturing a particle suspension consisting of Sn-117m particles prepared using a patent pending homogeneous precipitate process which produces particles in a tight size distribution of ~10 µm. The Sn-117m colloid underwent gCMP production, sterilization, and stability testing at room temperature.

Results
Sn-117m colloid
The Sn-117m colloid was reliably and reproducibly manufactured at ~10 µm, was free of endotoxin, and stable at room temperature through at least 2 half-lives (Figure 2). Particle size distribution (data not shown) remained unchanged at five weeks.

Conclusion
Sn-117m homogeneous colloid could be reliably and reproducibly created under gCMP conditions using our proprietary methodology. The colloid is stable for at least two half-lives.

GMP OA rat model
These results demonstrated that this unique Sn-117m colloid, when accurately delivered intra-articularly, had exceptionally high retention in the joint space in an OA rat model. In general, isotope excretion in the urine and feces was at background within 24 hours. The radiation field in rats when extrapolated to anticipated doses used in dogs or humans is projected to be well below NRC release criteria. Full results of these OA and RA rat trials, which are incomplete at this time, will be reported at a later date.

These positive results have led to the initiation of a trial using Sn-117m colloid in five normal dogs (completed) to demonstrate safety, as well as a trial using Sn-117m colloid in 48 client-owned dogs with naturally occurring elbow OA.

References