

Via Facsimile and U.S. Mail  
Mail Stop 6010

August 2, 2007

Ms. B. Lynne Parshall, J.D.  
Chief Financial Officer  
Isis Pharmaceuticals, Inc.  
1896 Rutherford Road  
Carlsbad, CA 92008

**Re: Isis Pharmaceuticals, Inc.**  
**Form 10-K for the Fiscal Year Ended December 31, 2006**  
**Filed March 16, 2007**  
**File No. 000-19125**

Dear Ms. Parshall:

We have completed our review of your Form 10-K and have no further comments at this time.

Sincerely,

Joel N. Parker  
Accounting Branch Chief