

June 15, 2007

United States Securities and Exchange Commission  
Division of Corporate Finance  
Attn: Jim B. Rosenberg, Senior Assistant Chief Accountant  
100 F Street, NE  
Washington, D.C. 20549

**Re: Isis Pharmaceuticals, Inc.  
Form 10-K for the fiscal year ended December 31, 2006  
File No. 000-19125**

Dear Mr. Rosenberg:

Pursuant to my conversation with Amy Bruckner, Staff Accountant, we respectfully request a one week extension to file our responses to your letter dated June 1, 2007. Accordingly, we will file our responses by June 22, 2007.

Should you have any questions regarding our request, please contact me at (760) 603-2492.

Sincerely,

/s/ Elizabeth L. Hougen

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Elizabeth L. Hougen  
Vice President, Finance and Chief Accounting Officer

cc: B. Lynne Parshall, Esq.  
Grantland E. Bryce, Esq.

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