

September 21, 2011

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 Year Ended December 31, 2010
Form 10-Q for the Quarterly Period Ended March 31, 2011
Schedule 14A
File No. 000-19125

Dear Mr. Rosenberg:

On behalf of Isis Pharmaceuticals, Inc. (the "Company," "Isis" or "we"), enclosed for electronic filing via EDGAR pursuant to the Securities Act of 1933, please find a status update to your follow-up comments in reference to the Company's Form 10-Q for the quarterly period ended March 31, 2011, File No. 000-19125.

Based on our conversation with Ms. Nakada on September 19, 2011, we will respond to the Staff's follow-up comments contained in its September 9, 2011 letter by October 7, 2011.

Should you have any questions regarding our responses or require any additional information, please contact me at (760) 603-2492 or B. Lynne Parshall, Chief Operating Officer and Chief Financial Officer at (760) 603-2460.

Sincerely,

/s/ Elizabeth Hougen

Elizabeth Hougen
Vice President Finance and Chief Accounting Officer,
Isis Pharmaceuticals, Inc.
