

September 16, 2009

Securities and Exchange Commission
Division of Corporate Finance
100 F Street, N.E.
Washington, D.C. 20549

Attention: Ms. Laura Crotty

Re: Lexicon Pharmaceuticals, Inc.
Registration Statement on Form S-3
Filed September 2, 2009
File No. 333-161696

Dear Ms. Crotty:

On behalf of Lexicon Pharmaceuticals, Inc., we submit the following responses to the comments received on September 15, 2009 from the Securities and Exchange Commission's staff with respect to Lexicon's registration statement on Form S-3 (File No. 333-161696). Your comments and our responses to those comments are set forth below.

Documents Incorporated by Reference, page 24

1. We note the statement in your Form 10-K for the fiscal year ended December 31, 2008, which is incorporated by reference into the above listed registration statement, that the company's disclosure controls and procedures were "sufficiently effective" to ensure that the information required to be disclosed under the Securities Exchange Act of 1934 was gathered, analyzed and disclosed with adequate timeliness, accuracy and completeness, based on an evaluation of such controls and procedures at the end of the fiscal year. Given the use of the word "sufficiently" it remains unclear whether your chief executive officer and chief financial officer have concluded that your disclosure controls and procedures are effective. Please confirm that in your next Form 10-K you will state, in clear and unqualified language, the conclusions reached by your chief executive officer and chief financial officer on the effectiveness of your disclosure controls and procedures.

Response: We confirm that in our next annual report on Form 10-K we will state, in clear and unqualified language, the conclusions reached by our chief executive officer and chief financial officer on the effectiveness of our disclosure controls and procedures.

Please do not hesitate to contact the undersigned at (281) 863-3321 with any comments or questions concerning this letter or the above-referenced registration statement.

Very truly yours,

/s/ Jeffrey L. Wade

Jeffrey L. Wade
*Executive Vice President and
General Counsel*