

Mail Stop 4720

September 15, 2009

Arthur T. Sands, M.D., Ph.D.  
President and Chief Executive Officer  
Lexicon Pharmaceuticals, Inc.  
8800 Technology Forest Place  
The Woodlands, Texas 77381-1160

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

Dear Dr. Sands:

We have limited our review of the above referenced registration statement to only the issue identified herein. Where indicated, we think you should provide additional disclosure in response to this comment. If you disagree, we will consider your explanation as to why our comment is inapplicable or additional disclosure is unnecessary. Please be as detailed as necessary in your explanation.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comment or any other aspect of our review. Feel free to call us at the telephone number listed at the end of this letter.

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 as of 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 the company's disclosure controls and procedures.

\* \* \* \*

As appropriate, please furnish a letter that keys your responses to our comment and provides any requested information. Please understand that we may have additional comments after reviewing your response to our comment.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes all information required under the Securities Act of 1933 and that they have provided all information investors require for an informed investment decision. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and
- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in connection with our review of your filing or in response to our comments on your filing.

We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

Arthur T. Sands, M.D., Ph.D.  
Lexicon Pharmaceuticals, Inc.  
September 15, 2009  
Page 3

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please allow adequate time after the filing of any amendment for further review before submitting a request for acceleration. Please provide this request at least two business days in advance of the requested effective date.

Please contact Laura Crotty at (202) 551-3563 with any questions.

Sincerely,

Jeffrey P. Riedler  
Assistant Director

cc: David P. Oelman  
Vinson & Elkins L.L.P.  
2300 First City Tower  
1001 Fannin  
Houston, Texas 77002-6760