



DIVISION OF
CORPORATION FINANCE

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

June 2, 2011

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

**Re: Lexicon Pharmaceuticals, Inc.
Post-Effective Amendment No. 1 to Form S-3 on Form S-1
Filed May 26, 2011
File No. 333-171953**

Dear Dr. Sands:

We have limited our review of your registration statement to those issues we have addressed in our comments.

Please respond to this letter by amending your registration statement and providing the requested information. Where you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

1. The legal opinion filed as Exhibit 5.1 to your registration statement improperly assumes that at the time of any offering or sale of common stock, the Company will have a sufficient number of authorized shares. Please amend your registration statement to include a revised legal opinion that avoids assumption of material facts underlying the opinion.
2. Please confirm that the amount or volume of securities to be sold in the offering and specific information relating to the underwriters and plan of distribution will be disclosed prior to effectiveness of the registration statement.

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 the information the Securities Act of 1933 and all applicable Securities Act rules require. 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.

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Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company 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.

Please refer to Rules 460 and 461 regarding requests for acceleration. 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. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

You may contact Bryan Pitko at (202) 551-3203 or Daniel Greenspan at (202) 551-3623 if you have any questions. In this regard, please feel free to contact me at (202) 551-3715.

Sincerely,

Jeffrey Riedler
Assistant Director

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