

February 10, 2010

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

Attention: Ms. Nandini Acharya

Re: DEF 14A
Filed March 13, 2009
File No. 000-30111

Dear Ms. Acharya:

On behalf of Lexicon Pharmaceuticals, Inc., we submit the following responses to the comment received on January 25, 2010 from the Securities and Exchange Commission's staff with respect to Lexicon's definitive proxy statement for Lexicon's 2009 annual meeting. Your comment and our response to that comment are set forth below.

DEF 14A

Executive and Director Compensation
Compensation Discussion and Analysis, page 24

1. We note your response to our prior comment 4 and your proposed additional disclosure regarding individual goals. You indicate that individual goals consist principally of the expected individual contributions of each executive officer towards the achievement of the year's corporate goals. To the extent such expected individual contributions are pre-determined and linked to corporate goals, please describe each goal and include an assessment of whether each executive met his or her expected contribution and how such achievement was used to determine the final amount of bonus allocated. If the individual contributions were not pre-determined, identify the achievements the Compensation Committee determined and disclose that the goals were not predetermined.

Response: In our next annual report or proxy statement, we propose to include the following additional disclosure with respect to individual goals:

For executive officers other than Dr. Sands, our president and chief executive officer, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each executive officer towards the achievement of the year's corporate goals, together with Dr. Sands' and the committee's independent assessment of each executive officer's overall performance and contributions to the company during the year, in the course of making subjective judgments about individual performance in connection with compensation determinations. Dr. Sands had no individual goals in [2009] apart from the corporate goals.

The committee's determinations for Dr. Sands were based entirely upon its determination of achievement of the year's corporate goals. For other executive officers, the compensation committee based its determinations principally upon its determination of achievement of the year's corporate goals, but also took into account, to a lesser extent, each executive officer's individual contributions towards the achievement of such corporate goals, together with Dr. Sands' and the committee's independent assessment of each executive officer's overall performance and contributions to the company during the year, in the course of making subjective judgments about individual performance in connection with such determinations.

We believe that disclosure of the individual goals of our executive officers is not material to a reasonable investor's understanding of our executive compensation determination process because such individual goals are not applied in a formulaic manner, but are simply factors (among others, including, as noted, Dr. Sands' and the committee's independent assessment of each executive officer's overall performance and contributions to the company during the year) that are generally taken into account in the course of making subjective determinations in connection with the compensation decision. As noted in our existing proxy statement disclosure, the compensation committee retains broad discretion over the amount and payment of cash bonus awards. The compensation committee is not bound by any pre-determined agreement, formula or other standard with respect to such decisions.

The proposed additional disclosure set forth above modifies the proposed disclosure we submitted in response to your prior comment 4 to clarify that individual goals are factors (among others) that are taken into account in the course of making subjective judgments about individual performance in connection with compensation determinations.

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

Very truly yours,

/s/ Jeffrey L. Wade

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