

Via Facsimile and U.S. Mail
Mail Stop 6010

January 25, 2008

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

**Re: Lexicon Pharmaceuticals, Inc.
Form 10-K for the Fiscal Year Ended December 31, 2006
Form 10-Q for the Quarterly Period Ended September 30, 2007
File No. 0-30111**

Dear Dr. Sands:

We have reviewed your December 21, 2007 response to our November 16, 2007 letter and have the following comments. In our comments, we ask you to provide us with information to better understand your disclosure. Where a comment requests you to revise disclosure, the information you provide should show us what the revised disclosure will look like and identify the annual or quarterly filing, as applicable, in which you intend to first include it. If you do not believe that revised disclosure is necessary, explain the reason in your response. After reviewing the information provided, we may raise additional comments and/or request that you amend your filing.

Form 10-K for the Fiscal Year Ended December 31, 2006

Notes to Consolidated Financial Statements

Note 2: Summary of Significant Accounting Policies

Revenue Recognition, page F-8

1. In your response to our previous comment one you indicate that you do not consider your collaborator's option to extend the initial research period in determining the service period over which you amortize your upfront fees because you have historical evidence that indicates that some collaborators have exercised their option while others have not. However, your response and revenue recognition disclosure is unclear on how you treat the unamortized portion of your deferred upfront fees when it becomes probable that your collaborator will exercise its option to extend the research period. Please revise the proposed disclosure to clarify how you account for the upfront fee when it becomes probable that your collaborator will extend the research period. In this regard, if

you do not amortize the remaining deferred upfront fees over the remaining service period including the period of extension, please explain to us how your accounting complies with GAAP by referencing the authoritative literature you rely upon to support your accounting.

Form 10-Q for the Quarterly Period Ended September 30, 2007

Notes to Consolidated Financial Statements

Note 7: Arrangements with Symphony Icon, Inc., page 9

2. We acknowledge your response to our previous comment 3a. You indicate that you believe your option to purchase Symphony Icon from Holdings is a variable interest in Symphony Icon as defined under paragraph 2c of FIN 46R. Please elaborate for us how this option qualifies as a variable interest under paragraph 2c of FIN 46R. In this regard, please demonstrate for us how this option represents an investment in Symphony Icon and how it is at risk as addressed in paragraphs 5 and B7 of FIN 46R. In addition, please revise your proposed disclosure to identify your variable interest, how it is at risk and, consistent with your response, that you intend to exercise your option if the development of Symphony Icon is successful.
3. We acknowledge your response to our previous comment 3d. Please elaborate on why you analogize to the guidance in paragraph 8a of EITF 00-6 to record the value of your option to purchase Symphony Icon as a charge to minority interests on the balance sheet. In this regard, paragraph 8a appears to apply solely to forward purchase contracts and appears to be superceded by paragraph 20 since the effectiveness of SFAS 150; requiring the contract to be valued at fair value and precluding minority interest accounting going forward. In your response, please explain to us why it is not appropriate to carry your option to purchase Symphony Icon as an asset. To further understand your accounting and given that Symphony Icon has funding in excess of the minority interest carried on your balance sheet as a result of charging the \$8.6 million value of your option to acquire Symphony Icon and your \$2.2 million share of transaction costs to minority interests, please explain to us how you intend to account for:
 - any losses of Symphony Icon in excess of the minority interest carried on your balance sheet that have already been funded by Holdings; and
 - any dissolution of Symphony Icon in which funds are returned to Holdings in an amount greater than the minority interests carried on your balance sheet.

Note 8: Agreements with Invus, L.P., page 10

4. In your response to our previous comment 4a you indicate that you intend to revise your disclosure in future filings to clarify the mechanics of the terminations

of the warrants associated with your Invus agreement. As previously requested, please provide us the disclosure you intend to include in your future filings.

5. We acknowledge your response to our previous comment 4b. You indicate in your response that you may not have sufficient shares of common stock authorized to settle your potential obligations under the rights offerings if your common stock price were to drop below \$2.37 per share. You also appear to conclude that there would be no net settlement in either cash or shares if your stock price declines below \$2.37 per share because there would be no gain or loss associated with a transaction at the then fair value. Paragraph 19 of EITF 00-19 clearly indicates that if an instrument could cause a company to seek an increase in authorized shares, share settlement is not within the control of the company and asset or liability classification is required. As it does not appear that there is an explicit or implicit limit on the number of shares that could be issued under the rights offerings, please revise your accounting and disclosure to record the fair value of your obligation to conduct rights offerings as a liability and mark the liability to fair value at each reporting date with the changes in value being reflected in your statements of operations. In addition, consistent with the guidance in paragraphs 10 and 11 of EITF 00-19 please explain to us whether the existence of these rights offerings and the potential issuance of shares in excess of those authorized taints any other outstanding options, warrants or similar instruments. Otherwise, please explain to us the mechanics of how future share issuances at a then fair value of less than \$2.37 per share will be capped to avoid exceeding your currently authorized share limit.

Please respond to these comments within 10 business days or tell us when you will provide us with a response. Please submit a letter that keys your responses to our comments and provides the requested information. Detailed letters greatly facilitate our review. Please furnish your letter to us via EDGAR under the form type label CORRESP.

If you have any questions, please contact Mark Brunhofer, Senior Staff Accountant, at (202) 551-3638. In this regard, do not hesitate to contact me, at (202) 551-3679.

Sincerely,

Jim B. Rosenberg
Senior Assistant Chief
Accountant