

Via Facsimile and U.S. Mail
Mail Stop 4720

December 29, 2009

Michael G. McGuinness
Chief Operating and Financial Officer
Manhattan Pharmaceuticals, Inc.
48 Wall Street
New York, NY 10005

Re: Manhattan Pharmaceuticals, Inc.
Form 10-K for the Fiscal Year Ended December 31, 2008
Filed March 31, 2009
File Number: 001-32639

Dear Mr. McGuinness:

We have reviewed your filing and have the following comments. We have limited our review to your financial statements and related disclosures and do not intend to expand our review to other portions of your document. 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.

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 comments or on any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

Item 9A(T). Controls and Procedures, page 52

1. Your CEO and CFO concluded that the “disclosure controls and procedures were effective as of that date in alerting them on a timely basis” to information that is required to be disclosed. Your interim Forms 10-Q contain similar language. This conclusion does not appear to satisfy Item 307 of Regulation S-K and Rule 13a-15(e) under the Exchange Act. Rule 13a-15(e) states that disclosure controls and procedures should ensure that information required to be disclosed “is

- recorded, processed, summarized and reported, within the time periods specified in the Commission's rules and forms." Please confirm that the disclosure controls and procedures ensure that information required to be disclosed is recorded, processed, summarized and reported within the time periods specified in the Commission's rules and procedures. If you are unable to confirm this statement,
- Please provide further explanation including a description of any weaknesses that prevented the CEO and CFO from concluding that the disclosure controls and procedures were effective; and
 - Amend the Form 10-K to describe the weaknesses.
2. It is not clear what the intent is of your disclosure in the second paragraph: "There can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions." Please revise to clarify that the disclosure controls and procedures are designed to provide reasonable assurance of achieving their objectives. In addition, please revise to state, if true, that the controls and procedures are, in fact, effective at the "reasonable assurance" level. Please refer to Section II.F.4 of Management's Reports on Internal Control Over Financial Reporting and Certification of Disclosure in Exchange Act Periodic Reports, SEC Release No. 33-8238, available on our website at <http://www.sec.gov/rules/final/33-8238.htm>.

Exhibits 31.1 and 31.2

3. Please tell us why your executive certifications do not include the entire introductory language of paragraph 4 of Item 601(b)(31) of Regulation S-K to also address your officers' responsibility for establishing and maintaining internal control over financial reporting. This comment also applies to the certifications filed for the quarterly periods ended March 31, 2009, June 30, 2009 and September 30, 2009.

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

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 Exchange Act of 1934 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.

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In connection with responding to our comments, please provide, in your letter, a statement from the company acknowledging that:

- the company is responsible for the adequacy and accuracy of the disclosure in the filing;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing; and
- the company may not assert staff comments 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 our review of your filing or in response to our comments on your filing.

You may contact Vanessa Robertson, Staff Accountant, at (202) 551-3649 or Joel Parker, Accounting Branch Chief, at (202) 551-3651 if you have any questions regarding the comments. In this regard, do not hesitate to contact me, at (202) 551-3679.

Sincerely,

Jim B. Rosenberg
Senior Assistant Chief
Accountant