

Mail Stop 6010

May 18, 2007

Mr. Stanley N. Lapidus
President and Chief Executive Officer
Helicos BioSciences Corporation
One Kendall Square
Building 700
Cambridge, Massachusetts 02139

**Re: Helicos BioSciences Corporation
Amendment No. 4 to Registration Statement on Form S-1
Filed May 7, 2007
File No. 333-140973**

Dear Mr. Lapidus:

We have reviewed your filing and have the following comments. Where indicated, we think you should revise your document in response to these comments. If you disagree, we will consider your explanation as to why our comment is inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with supplemental information so we may better understand your disclosure. After reviewing this information, we may or may not raise additional comments.

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.

Management's Discussion and Analysis of Financial Condition and Results of Operations

Critical Accounting Policies and Significant Judgments and Estimates

Stock-based compensation, page 46

1. Please refer to your response to prior comment three. Please explain to us why using companies that completed their initial public offering within the past 10 years is appropriate. Explain to us how you considered the historical volatility of the similar companies listed in your response to estimate your volatility. Also, tell

- us why these companies are considered similar. It appears that the companies listed in your response are not similar in size, financial leverage or stage of life cycle. For example, companies listed are not in the development stage and all have product sales. Please tell us any additional factors you considered to explain why these companies are similar.
2. Your revised disclosures refer to an “independent valuation specialist” and an “independent valuation firm.” The use of an independent valuation specialist or firm equates to the use of a valuation expert. Please name this expert and provide their consent in your registration statement.

Consolidated Financial Statements

Notes to Consolidated Financial Statements

Note 8. Commitments and Contingencies, page F-17

3. Please refer to prior comment 11. You appear to have omitted discussion of the termination provisions for the Caltech license agreement. Please provide this disclosure or explain your basis for excluding it from the filing.

Note 10. Redeemable Convertible Preferred Stock, page F-19

4. Please refer to prior comment 12. You describe the accounting for the beneficial conversion feature as an “immediate charge to the consolidated statement of operations.” Please revise this disclosure to clarify your accounting for the deemed dividend implicit in the beneficial conversion feature.

* * * * *

As appropriate, please amend your filing in response to these comments. You may wish to provide us with marked copies of the amendment to expedite our review. Please furnish a cover letter with your amendment that keys your responses to our comments and provides any requested supplemental information. Detailed cover letters greatly facilitate our review. Please file your cover letter on EDGAR under the form type label CORRESP. Please understand that we may have additional comments after reviewing your amendment and responses to our comments.

Mr. Stanley N. Lapidus
Helicos BioSciences Corporation
May 18, 2007
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.

You may contact Frank Wyman at (202) 551-3660 or Don Abbott at (202) 551-3608 if you have questions regarding comments on the financial statements and related matters. Please contact Sonia Barros at (202) 551-3655 or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey P. Riedler
Assistant Director

cc: Lawrence S. Wittenberg, Esq.
Edward A. King, Esq.
Goodwin Procter LLP
Exchange Place
53 State Street
Boston, Massachusetts 02109