

Via Facsimile and U.S. Mail
Mail Stop 4720

February 16, 2010

Ronald A. Lowy
Chief Executive Officer
Helicos BioSciences Corporation
One Kendall Square, Building 700
Cambridge, MA 02139

**Re: Helicos BioSciences Corporation
Form 10-K for Fiscal Year Ended December 31, 2008
Schedule 14A Filed April 24, 2009
File No. 001-33484**

Dear Mr. Lowy:

We have reviewed your January 20, 2010 response to our December 17, 2009 comment letter and have the following additional 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 filings, 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 filings.

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 filings. 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.

Form 10-K for the fiscal year ended December 31, 2008

Item 1. Business, page 3

Research and Development, page 14

1. We note your response to our prior comment 1. Please confirm that you will include the substance of your response regarding the Expression Analysis, Inc.

return, including the information contained in your Form 8-K filed January 30, 2009, in your next Form 10-K.

Intellectual Property, page 18

2. We note your response to our prior comment 4 and your proposed disclosure regarding the Roche License Agreement and the AZTE License Agreement, both of which state that the company agrees to pay a “double digit percentage” of sublicense income amounts received based on sublicenses granted to third parties. Please revise your disclosure to provide a more narrow range for the percentage you will pay and provide general information regarding the tier structure, as applicable, i.e., how the rate will increase as the tiers progress.

* * *

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

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filings to be certain that the filings include 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.

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 filings;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filings; 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 filings or in response to our comments on your filings.

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Please contact Laura Crotty, Staff Attorney, at (202) 551-3563 or myself at (202) 551-3715 if you have questions regarding the processing of your response as well as any questions regarding comments and related matters.

Sincerely,

Jeffrey P. Riedler
Assistant Director