

Mail Stop 6010

February 23, 2009

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

**Re: Helicos BioSciences Corporation
Amendment No. 1 to
Registration Statement on Form S-3
Filed February 13, 2009
File No. 333-156885**

Dear Mr. Lowy:

We have limited our review of your filing to the issues we have addressed in our 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.

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

General

1. We note your response to our prior comment 1 relating to the treatment of your transaction as a primary offering. We are unable to concur with your analysis as to why the transaction should be treated as a secondary offering. Given that the Atlas entities, the Flagship entities, the Highland entities and the Versant entities have representatives in the Board of Directors, that Vision has the right to designate one observer to attend all meetings of the Board of Directors, that the selling stockholders have held the shares for a short period of time, and that the selling stockholders are offering a large amount of shares as compared to the total number of shares outstanding held by non-affiliates, the transaction appears to be

a primary offering. Since you are not eligible to conduct an offering on a delayed and continuous basis under Rule 415(a)(1)(x), you must register the transaction on a form you are eligible to use to register the transaction as a primary offering, identify the selling shareholders as underwriters and include a price at which the underwriters will sell the securities.

Selling Stockholders, page 20

2. We note your response to our prior comment 2 and the related changes to the selling stockholders table. It appears that Stephens is offering shares that it does not own prior to the offering since the maximum number of shares being offered is greater than the number of shares owned prior to the offering. Please revise your disclosure to clarify.

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As appropriate, please amend your registration statement 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 information. Detailed cover letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your amendment and response to our comments.

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.

Please contact Sebastian Gomez Abero at (202) 551-3578 or me at (202) 551-3715 with any questions.

Sincerely,

Jeffrey P. Riedler
Assistant Director

cc: Stuart M. Cable, Esq.
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