Mail Stop 6010

June 8, 2006

Kenneth J. Collins
President and Chief Executive Officer
Replidyne, Inc.
1450 Infinite Drive
Louisville, Colorado 80027

**Re: Replidyne, Inc.**
**Amendment No. 1 to Form S-1 Registration Statement**
**File No. 333-133021**

Dear Mr. Collins:

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.

Comments Applicable to the Entire Document

1. We have noted your response to comment 4. However, a number of the examples included in our comment continue to appear in the registration statement and others were added to the revised disclosure. Technical jargon is not likely to be understood by your readers and should not appear in the forefront of the prospectus. Accordingly, please replace the jargon with an explanation in plain English. If you cannot convey these ideas without jargon, please explain what the jargon means at the first place the terms appear.

Here are some examples, from the summary alone, of jargon that still needs to be addressed:

- Expert treatment guidelines
- Promising platform..having no cross-resistance
- Aminoacyl tRNA synthetases
- Novel class of selective inhibitors of methionyl tRNA synthetase
- Proprietary bacterial DNA replication inhibitor technology
- Reconstituted high-throughput assays targeting the central DNA replication complex
- In-house discovery research platform
- identifying compounds that are inhibitory in the assays
- lead optimization

Please revise the summary and the body of the prospectus as we previously requested.

Prospectus Summary page 1

2. We have not received the supporting information we requested in comment 6. Please provide it with your next amendment.

Risk Factors – page 7

Reimbursement may not be available for our product candidates, which could diminish our sales or affect our ability to sell our products profitably. – page 20

3. We note the revisions you made to this risk factor in the amendment. We do not think that revisions to Medicaid enacted in December of 2003 are "recent." As currently drafted, the disclosure implies that you do not know how these revisions would affect reimbursement for your product. Please revise the disclosure to more specifically describe the proposed or enacted changes that apply to you and your product. If you do not know how they would apply to your product, explain why you don't know.

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. – page 22

4. In the fourth paragraph of this risk factor you refer to a "Section 505(b)(2) filing." Your readers are not likely to know what you are referring to. Please explain. It appears that you may be indicating that your product will be subject to generic competition within four years after FDA approval. If so, this is very material information for investors and

should be clearly and prominently disclosed. We note that at the current time there are 15 pages of risk factors preceding this one and a number of those risk factors do not appear to be as significant as this one. Please revise the document accordingly.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders. – page 28

5. Please revise the last paragraph to clarify that the prohibition does not apply if the transaction is approved by the board.

Use of Proceeds – page 28

6. We have considered your response to comment 13. However, we continue to believe that you need to provide more specific information about how far along the development spectrum that you anticipate the proceeds will enable you to go and what other sources of funding you currently intend to use for these purposes. For example, do you intend to use any of the funds received from Forest Labs for these purposes as well? Disclose whether you currently anticipate that material amounts of additional funding will be necessary to achieve the purposes you have identified. If so, disclose the amounts of other funds that will be necessary and the sources you will obtain them from.

7. We note that you have deleted milestone payments as a use of the proceeds of this offering. Please tell us why.

8. You now say that you will use the "remainder" to fund working capital, capital expenditures and other general corporate purposes. Please be more specific about what items are included in each of these categories. Please provide disclosure about your intended capital expenditures as specified in Item 504 of Regulation S-K.

Principal Stockholders – page 99

9. In comment 18 of our previous letter we requested that you provide the name of the natural person(s) possessing voting and investment authority over the securities listed in the table that are owned by non-natural persons. Your response indicates that the information can now be found on pages 100-101. However, we note that footnotes 1-4 and 7-8 still do not contain this information. Please revise as we previously requested.

Financial Statements, page F-1

Balance Sheets, page F-3

1. Refer to your response to comment 20. Please ensure that you have disclosed the liquidation preference for all periods presented.

Notes to Financial statements page F-10

(5) Related-Party Transaction, page F-23

(a) Clinical Trials Service Agreement with Quintiles, Inc., page F-23

2. In addition to what you have provided in response to comment 22, please quantify the fees you are obligated to pay under the agreement. The expanded discussion should include both the fixed and the variable fees with an explanation of how the variable fees are calculated, and your minimum and/or maximum fee obligations under the agreement, if applicable.

(7) Preferred Stock, page F-26

(e) Redeemable Convertible Preferred Stock Warrants, page F-27

3. It is still not clear in your response to comment 24 how you have considered the conversion feature of the preferred stocks, into which the warrants are exercisable, when determining the warrants to be a liability. Please explain how you have determined that the preferred stocks are mandatorily redeemable, rather than conditionally redeemable, given its conversion feature. Refer to paragraph A9 of SFAS 150.

(9) Stock Options and Employee Benefits, page F-30

4. It does not appear reasonable that the fair value of your common stock was $1.83 per share in April and May 2006 when you filed Form S-1 on April 5, 2006 and the estimated offering range was $3.14 to $3.39. Further, it is not clear what caused any increase in the fair value of your common stock after February 10, 2006 the date you entered into the Forest Laboratories Agreement. Finally, more fully justify the relationship between the fair value of the common stock of $.19 per share at the time of the Series D preferred offering at $1.80 per share. Explain how you valued the liquidation preference given the fact that the money received from the offering is quickly spent on the company's research programs and not available to pay liquidation preferences. Please revise your valuations and the changes in values as necessary or explain fully why no revision is necessary.

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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 supplemental information. Detailed cover letters greatly facilitate our review. We may have additional comments after reviewing your amendment and responses to our comments.

You may contact Keira Ino at 202-551-3659 or Oscar Young at 202-551-3622 if you have questions regarding comments on the financial statements and related matters. Please contact Mary K. Fraser at 202-551-3609 or me at 202-551-3610 with any other questions.

Regards,

Jeffrey P. Riedler
Assistant Director

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