Mail Stop 6010

May 5, 2006

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

Re: Replidyne, Inc.
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 note that your filing contains numerous omissions throughout the prospectus which relate to the offering price range or the number of shares you will sell. These omissions include but are not limited to:

- Summary Financial Data
- The Option Grants Table

- Use Of Proceeds
- Capitalization
- Dilution
- Shares Eligible For Future Sale
- The Principal Stockholders Table
- Description of Capital Stock

Rule 430A requires you to include this information in your filing based upon an estimate of the offering price within a bona fide range you disclose on the cover page and based upon an estimate of the number of shares you will sell. We consider a bona fide range to be $2 if the price is under $20 and 10% if it is above $20. You should include the required information in an amendment prior to circulating a "red herring" prospectus.

2. Provide us with copies of all the graphic, photographic or artistic materials you intend to include in the prospectus prior to its printing and use. Please note that we may have comments. Please also note that all textual information in the graphic material should be brief and comply with the plain English guidelines regarding jargon and technical language.

3. Comments on your application for confidential treatment will be provided in a separate letter when they are ready. Please note that we will not be in a position to accelerate effectiveness until all issues relating to your confidential treatment request have been resolved.

4. In a number of places in your document you have used technical jargon that is not likely to be understood by your readers. Technical jargon 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 of the type of disclosure that need to be replaced:

   - Community antibiotic
   - Penem family
   - Novel class of selective inhibitors of methionyl tRNA synthetase
   - Proprietary bacterial DNA replication inhibitor technology
   - Beta-lactam class of antibiotics
   - *S. aureus*
   - *C. difficile*
   - Statistical non-inferiority
   - Community-acquired pneumonia
   - Prodrug form of the active moiety faropenem

5. Throughout your document you have used a number of acronyms that are not likely to be familiar to your readers. The use of acronyms is a convenience for the writer, but it forces readers to learn a new vocabulary in order to understand the disclosure in your document. Please delete all of the acronyms except those which can be commonly found in general interest publications. Examples of acronyms that should be deleted include:

    - MSRA
    - CMS
    - CRO
    - NDA
    - IDSA
    - CDAD

Prospectus Summary page 1

6. In the second paragraph under "Our Company" on page 1, you present statistical and market share information related to your proposed products. Please provide us with a copy of the document(s) containing the information you are relying on as support for these statements. Mark the copy of the document to show the location of each piece of information you are relying on. Provide similar factual support for all similar claims made throughout the registration statement. We may have additional comments after reviewing the supporting documents.

7. Please revise your Summary to present a balanced summary of your company and financial condition. For example:

    - Disclose that you do not have any FDA approved products and have not recognized revenue from product sales;
    - Disclose your history of losses and quantify your losses for each of the last three years and in interim period;
    - Quantify your accumulated deficit; and
    - Balance the discussion of your strategy with an equally prominent discussion of the risks and obstacles you will encounter in implementing this strategy.

8. Explain how your products are "novel."

Risk Factors – page 6

9. We note that your submitted an NDA in December 2005 for Orapem for acute bacterial sinusitis, community-acquired pneumonia, acute exacerbation of chronic bronchitis and uncomplicated skin structure infections. Were all of the clinical trials supporting this NDA conducted by Bayer? If they were, please clarify this fact throughout the filing. Did you consider whether the fact that you were not involved in these clinical trials creates a risk?

We are dependent on the success of our lead product candidate… - page 6

10. Your risk factor discussion appears to disclose multiple risks, including:

- The risk that you might not obtain FDA approval;
- The risk that you might not obtain FDA approval for both i) acute sinusitis and ii) either community-acquired pneumonia or acute exacerbation of chronic bronchitis; and
- Changing regulatory requirements.

We have limited manufacturing capabilities and will depend on third parties to manufacture Orapem and future products. If these manufacturers fail to meet our or Forest Laboratories' requirements and strict regulatory standards, we may be unable to develop or commercialize our products. – page 10

11. In this risk factor you indicate that Nippon soda is your sole supplier of Orapem and will be your and Forest laboratories' sole supplier of Orapem for the foreseeable future. However, in the first paragraph under the bullets in the risk factor at the top of page 8 you discuss Forest Laboratories manufacturing relationship with its supplier of Orapem tablets, Tropon BmbH. Please reconcile these statements.

Future sales of our common stock in the public market could cause our stock price to fall. – page 24

12. Currently, the language in this risk factor is excessively legalistic. For example, you refer to "affiliates as defined in Rule 144 under the Securities Act" and "volume limitations under Rule 144 under the Securities Act." Your readers are not likely to know what these definitions and limitations are. Please replace these statements with brief explanations of what the referenced laws provide for.

Use of Proceeds – page 28

13. Please refer to Item 504 of Regulation S-K. You need to significantly expand the information you have provided to identify the specific research and potential products that you will use the proceeds for. Disclose the specific amounts that you intend to spend on each of the identified uses and how far along the development spectrum that you anticipate the proceeds will enable you to go. Disclose whether 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. Also, be more specific about the milestone payments, who they will be made to and when you anticipate making them.

Management's Discussion and Analysis of Financial Condition and Results…, page 35

Financial Operations Overview, page 36

Results of Operations, page 41

14. Please provide qualitative and quantitative disclosures that explain the nature of items included in "other research and development" expenses.

15. Where you attribute material fluctuations in your Selling, General and Administrative Expenses to multiple factors, please ensure that you have quantified these factors as required by Financial Reporting Codification Section 501.04.

Business – page 48

16. Please revise the discussion of your license agreement with Daiichi Asubio on page 65 to disclose the amounts you have currently paid under the agreement and the aggregate amount of potential future milestone payments.

17. Please revise to include a discussion of the material terms of your agreement with GSK. At a minimum, your discussion should include aggregate amounts paid to date, aggregate amount of potential future payments, the existence of royalty provisions, term and termination provisions. Additionally, file this agreement as an exhibit.

Principal Stockholders – page 90

18. For each non-natural person listed in the table, please provide the name of the natural person(s) possessing voting and investment authority over the securities.

Financial Statements, page F-1

19. Pro forma loss per share giving effect to conversion of the preferred stock should be presented on the face of the statement of operations and explained in the notes.

Balance Sheets, page F-3

20. Please ensure that you have disclosed the liquidation preference, rather than the liquidation value, for all periods presented here. Refer to paragraph 6 of SFAS 129.

Notes to Financial statements page F-10

(o) Revenue Recognition, page F-14

21. Please tell us why you account for the expense reimbursements under the collaboration and commercialization agreements differently from those received from the government.

(5) Related-Party Transaction, page F-19

(a) Clinical Trials Service Agreement with Quintiles, Inc., page F-19

22. Please disclose the duration and the fee structure of the service agreement.

(6) Commitments, and contingencies, page F-19

23. Where applicable, please revise your disclosures here to provide the following:

- The description of "certain" terminating circumstances that you would be liable to make payments/reimburse engineering costs, and the maximum amount of such liability;
- The amount of the annual minimum purchase commitments;
- The time period within which you would have to fully launch commercially, before having to compensate for delays;

- Where Forest Laboratories are referenced to being responsible for bearing some costs under these agreements, clarify whether they become primarily liable or they are only responsible for reimbursing some of the costs incurred by you;
- Clarify what you mean by "fifty percent of these minimum purchase commitments, if applicable, are creditable against future drug product purchases;"
- The minimum amount of adult oral Orapem tablets to be purchased from Tropon.

In addition, please consider disclosing your minimum obligations from these agreements within the contractual obligations table under the Management's Discussions and Analysis. It would appear that the timing of the minimum purchase obligations or the delay compensations may be reasonably estimated. To the extent that the actual obligation may vary from the estimate should be discussed in a footnote to the table.

(7) Preferred Stock, page F-21

(e) Redeemable Convertible Preferred Stock Warrants, page F-22

24. Please tell us whether you have considered the convertible feature of the preferred stocks, into which the warrants are exercisable, when determining the warrants to be a liability under SFAS 150. Further, please tell us how you have considered EITF 00-19.

(9) Stock Options and Employee Benefits, page F-25

25. Please disclose the "certain conditions" which would release the restrictions on early exercised shares and tell us the accounting impact of such release. In addition, as it appears that some options are eligible for early exercise, please disclose such number of shares for each of the periods presented here.

26. Provide us with any objective evidence which you relied upon as support for your determination of the fair value of the underlying common stock at each grant or issue date through the date of your response. Highlight transactions with unrelated parties, if any, believed by management to be particularly evident of the fair value of common stock. Disclose whether the valuation was contemporaneous or retrospective and if the valuation specialist was a related party. If a contemporaneous valuation was not obtained provide the disclosures required by paragraph 182 of AICPA Practice Aid on Valuation of Privately-Held-Company Equity Securities. Also, progressively bridge your fair market value per share determinations in calendar year 2005 to the current estimated IPO price per share. Explain the timing and effect of significant events such as the successful completion of Phase III trials and the submission on an NDA. Tell us when discussions were initiated with your underwriters. If you do not have an estimated offering price in

your next filing we will defer evaluation of stock-based compensation until your estimated offering price is specified. Continue to provide us with updates to the above analysis for all equity related transactions through the effectiveness date of the registration statement.

Exhibits

27. We note that a number of exhibits, including the opinion of counsel, have not yet been filed. Please include them in your first pre-effective amendment in order to ensure that we have adequate time to review them prior to any request for acceleration of effectiveness of the registration statement.

* * * * *

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.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filings reviewed by the staff to be certain that they have provided all information investors require for an informed 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.

Notwithstanding our comments, in the event the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, acknowledging that

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and
- the company may not assert this action 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 connection with our review of your filing or in response to our comments on your filing.

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please provide this request at least two business days in advance of the requested effective date and allow adequate time after the filing of any amendment for further review before submitting a request for acceleration.

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

Cc: James C.T. Linsfield, Esq.
Cooley Godward LLP
380 Interlocken Crescent – Suite 900
Broomfield, CO 80021