September 6, 2007

Mail Stop 6010

William P. Moffitt III
President and Chief Executive Officer
Nanosphere, Inc.
4088 Commercial Avenue
Northbrook, Illinois 60062

Re: Nanosphere, Inc.
Registration Statement on Form S-1
Filed August 13, 2007
File No. 333-145356

Dear Mr. Moffitt:

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 information so we may better understand your disclosure. After reviewing this information, we may 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 any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

Prospectus

1. Please confirm that any preliminary prospectus you circulate will include all non-Rule 430A information. This includes the price range and related information based on a bona fide estimate of the public offering price within that range, and other information that was left blank throughout the document. Also, note that we may have additional comments after you file this information.

Artwork

2. We note that you have disclosed a picture of your Verigene System. Please expand your disclosure to state that the products depicted have not yet received all necessary domestic or international regulatory approvals for sale.

Summary, page 1

Our Company, page 1

3. We note that you make numerous claims regarding the expected efficacy of the Verigene System and its diagnostic tests, including that it "achieves ultra-sensitive protein detection at limits beyond current diagnostic technologies." It is our understanding that until the FDA has reached conclusions on the efficacy of your product candidates, FDA regulations prohibit such promotional statements. Please remove from your prospectus statements that are inconsistent with the FDA regulations.

4. Clarify that you have had minimal product sales to date, particularly given your disclosure in the next paragraph regarding the multi-billion dollar market.

5. Clarify the state of development and the status of domestic regulatory approval for all diagnostic tests referenced in your summary, including tests for cystic fibrosis, cancer and cardiovascular diseases. Also explain whether you intend to market your products internationally and the status of any applicable international regulatory approvals.

Our Market Opportunity, page 1

6. Please provide us with the industry reports cited throughout the prospectus, clearly marked to support references made in your prospectus. For example, you cite to the Boston Biomedical Consultants on page 1. Also, please tell us whether the studies you cite were financed by you or prepared for you or at your direction or for the registration statement and whether the studies are publicly available. Also provide us with support for other market data appearing throughout your prospectus.

Risk Factors

We and our customers are subject to various governmental regulations . . ., page 9

7. It appears that the disclosure accompanying this risk factor addresses two different risks to your business, one from ongoing federal regulation and another from failing to receive FDA approval of your products. In light of your disclosure on page 28 that your ability to generate future revenues depends on your ability to obtain FDA approval for your Verigene System and initial menu of diagnostic tests, please discuss separately the risks to your business from delays in obtaining or failing to obtain FDA clearance of such products.

Use of Proceeds, page 23

8. Please clarify what developments you intend to make to your product manufacturing infrastructure with the proceeds of this offering. For example, briefly describe whether these developments involve purchasing or upgrading equipment or hiring additional personnel.

Capitalization, page 24

9. Please revise to remove the caption relating to cash and cash equivalents from your presentation of capitalization.

Dilution, page 25

10. Please expand the disclosure following your first table to describe and quantify how dilution per share to new stockholders, book value per share after this offering, and increase in book value per share attributable to new investors would change assuming the underwriters exercise their over-allotment option in full.

11. With a view toward clarified disclosure in the prospectus, please disclose how the numbers, amounts and percentages in the second table on page 25 would change, assuming all outstanding options are exercised.

Management's Discussion and Analysis . . ., page 27

Fiscal 2006 Compared to 2005, page 30

12. Please explain why cost of product sales decreased from fiscal year 2005 to fiscal year 2006.

13. We note that your discussion of the significant changes in research and development expenses and sales, general and administrative expenses is limited and does not quantify the specific reasons for material changes in line items in the financial statements. Please revise to present and quantify each significant factor that contributed to the changes, including offsetting factors. Please also apply this comment to your discussion of the three months ended March 31, 2007.

Liquidity and Capital Resources, page 31

14. We note that you are in the development stage and have had minimal revenues over the past three years. Please expand your disclosure to provide a more detailed discussion of the Company's strategic plan of operations which will include the specific time frame and funding needs for each phase of the

development of operating activities. We note, for example, that certain certifications and applications for regulatory clearance have been submitted.

Contractual Obligations, page 34

15. We note the caption "purchase obligations" in your table of contractual obligations. Please revise to include the amounts or otherwise omit the caption.

Business, page 37

Overview

16. Discuss your product sales to date, including the countries where sales took place.

Strategy, page 40

17. Please provide us with support for your disclosure here and on pages 27 and 37 that "there is a large and growing demand for molecular diagnostic testing" in hospital laboratories.

18. We note your disclosure on pages 4 and 41 that use of FDA-cleared products "do not subject the laboratory to extensive additional regulatory requirements and risks." Please tell us how this disclosure is consistent with your risk factor disclosure on page 9, which describes governmental regulations to which you and your customers are subject. Additionally, please clarify your disclosure on pages 4 and 41 that "there is a strong demand for FDA cleared tests because they are less complex to use . . ." It is not apparent why such tests are necessarily less complicated than tests not cleared by the FDA.

Our Products, page 41

19. Given your disclosure on page 9 that the Verigene System does not process a sufficiently broad menu of tests for some hospitals and laboratories to adopt it, please describe in more detail the degree to which design has progressed on the protein and genomic assays in development. We note, for example, that your diagnostic test for cardiac troponin is undergoing clinical studies. Describe whether your other diagnostic tests are also undergoing similar studies and, if not, when you anticipate commencing such studies.

Our Technology, page 45

20. Please explain clearly the significance of "sharp melt transition curves" and how such curves demonstrate the superior specificity and accuracy of your technology.

Also explain whether you or a third-party conducted the tests that yielded the results depicted in the graph on page 46.

Manufacturing, page 48

21. We note your disclosure on page F-7 that you have requested FDA certification of your manufacturing facilities and processes. Please reconcile this statement with your disclosure here that you have built and validated a quality system that complies with FDA regulations.

Marketing, page 49

22. We note your disclosure that you have commenced the process of obtaining required regulatory approvals in selected international markets. Please identify the products that are the subject of these requests and the international markets in which you have requested regulatory approval.

Competition, page 49

23. Please expand your disclosure to identify your current competitive position in the industry and the primary methods of competition. For example, describe whether competition is based primarily on product cost, quality and acceptance by healthcare providers and third-party payors. Also describe any known negative factors that pertain to your competitive position and compare your competitors' financial resources and experience in marketing and manufacturing products to your own.

Government Regulation, page 49

24. Given that you intend to sell or lease your products to hospital-based laboratories, please expand your disclosure to discuss governmental regulation of third-party payors, including Medicare and Medicaid, as well as private payors, which may follow the policies of these public programs. Although you may not receive payment directly from such payors, it appears that your business may be indirectly impacted by hospitals' ability to obtain coverage and reimbursement for tests performed using your products. Also briefly discuss applicable foreign regulation of healthcare reimbursement programs.

25. Expand your disclosure to describe applicable healthcare fraud and abuse and health information privacy laws and how your business may be affected by such laws, if material.

Management, page 56

26. We note your disclosure on page 80 that describes additional positions that your directors currently hold but are not disclosed here. For example, in note one you disclose that Mr. Slezak is currently the trustee for AOQ Trust and managing member of Eagle Capital, which is the managing member of Alfa-Tech, LLC. Please expand your directors' business backgrounds to include all current occupations. Refer to Item 401(e)(1) of Regulation S-K.

27. As a related matter, we note your disclosures here and on pages 79 and 80 that Mssrs. Slezak, Crisan and Nahirney are currently employed with entities that have previously purchased securities from your company. Given that these entities and persons beneficially own a significant portion of your outstanding securities and in light of the arrangement identified in the following comment, please explain to us why you have excluded from these directors' business backgrounds an identification of such entities as affiliates of your company. Please refer to Item 401(e)(1).

28. We note your disclosure on page 56 that five of your seven directors were elected pursuant to an arrangement among you, your investors and your management stockholders or under the terms of your certificate of incorporation. Please describe these arrangements in more detail, including the specific terms for nominating and voting for the election of directors. Identify specifically which two directors were elected by holders of your Series C-2 and your Series D Convertible Preferred Stock and the other three directors elected pursuant to the "arrangement." Also, name the management stockholders who are a party to this arrangement, as required by Item 401(a).

Board Committes, page 57

29. We note your disclosure on page 82 regarding related-party transactions involving Bain Capital, Lurie Investments and their respective affiliates. Given that Mssrs. Nahirney and Slezak are members of your compensation committee and appear to be affiliated with these entities, please expand your disclosure here to provide the information required by Item 407(e)(4)(1)(C).

Executive Compensation, page 60

Overview of Compensation Program, page 60

30. Please explain under what circumstances your compensation committee recommends for approval of the board of directors the annual compensation of your executives. Also reconcile this disclosure with your disclosure on page 61

that your compensation committee "has the final authority regarding the overall compensation structure for" your executive officers.

Role of Our Compensation Committee, page 60

31. We note your disclosure on page 61 that your compensation committee considers recommendations from Mr. Moffitt regarding performance evaluations and setting compensation levels for your executives. Expand to state whether the compensation committee and ultimately the board of directors, if applicable, approved the recommendations made by Mr. Moffitt. If the compensation levels established by your board of directors were different from those recommended by your compensation committee, explain how they differed. Also disclose whether the recommendations of Mr. Moffitt were adopted without change by your compensation committee, or explain how they differed.

Annual Cash Compensation, page 61

32. We note your disclosure here and on page 60 that you determine the amount of compensation paid to your executives and adjustments to your executives' base salaries based on, among other factors, market increases and the amount of compensation paid by "similarly situated companies to their executives with similar roles and responsibilities." Given your disclosure that you do not use a formal peer group or formal benchmarking, please expand to identify these other companies and define what you mean by "similarly situated" and "similar roles and responsibilities." Also specify how the amount of and adjustments to compensation paid to your executives relates to the data you have analyzed from the peer companies.

33. Please expand your disclosure to describe the specific basis for increasing each named executive officers' base salary for 2006, including the elements of individual performance taken into account. We note your disclosure that such adjustments were to align their salaries with their performance, increased experience, and changes in roles and responsibilities, which does not appear to sufficiently explain the reasons for each adjustment. See Item 402(b)(2)(vii) and (ix). Also expand to compare and discuss the differences in compensation among all of your executive officers, including amounts paid pursuant to other components of your compensation program.

Annual Cash Incentive Compensation, page 62

34. We note your disclosure that the "compensation committee works with management to establish performance targets for the individual executive officers, and to review and approve individual performance criteria within the performance

targets for the executive officers." We also note that Section 3.2 of Exhibit 10.8 suggests that Mr. Moffitt must agree on his applicable performance goals. Please clarify the specific role of members of management in making compensation decisions, including the extent to which they have input regarding their own compensation. For example, do members of management establish their own performance goals or bonus targets and must these goals be agreed upon before being formally implemented? Please see Item 402(b)(2)(xv) of Regulation S-K. Also identify which performance goals and bonus targets referenced in your disclosure were agreed upon and which were set solely by the compensation committee.

35. We note your disclosure on page 63 that four of your named executives received a cash bonus based on partial achievement of their applicable performance targets. Please expand to describe the specific targets achieved and the targets that were not achieved with respect to each executive.

36. It is not apparent whether the management incentive bonus plan referenced in your disclosure is incorporated into the employment agreements of your executives or whether it is an independent agreement between you and your executives. Please explain.

Equity Incentive Compensation, page 63

Stock Option Awards, page 64

37. Please disclose with specificity the basis for Mr. McGarrity's stock option award, including any goals and achievements upon which it was based. See Item 402(b)(2)(v)-(vii). Also describe with specificity the performance-based milestones the achievement of which will accelerate vesting of these options.

Post-2006 Actions, page 67

38. Please disclose Mr. Moody's base salary and that he received a $15,000 sign-on bonus pursuant to the terms of his employment agreement. Also disclose the corporate performance milestones that will result in immediate vesting of the stock options granted to the executive officers named in this section.

Arrangements with Named Executive Officers, page 75

39. We note that according to Section 3.1 of Exhibit 10.8, Mr. Moffitt's base salary may not be reduced below $350,000. We also note that according to Section 3.2 of Exhibit 10.8, Mr. Moffitt's target bonus under the senior management bonus plan may not be reduced below $150,000. Please expand your disclosure to include this information.

40. We note your disclosure on pages 63 and F-20 that you and Mr. Moffitt entered into an "Amended Bonus Agreement" on March 16, 2006, pursuant to which he was recently paid a $2.3 million bonus. Please file a copy of this agreement as an exhibit to this registration statement.

Non-Employee Director Compensation Table, page 78

41. We note you have disclosed the consulting fees paid to Dr. Mirkin in the third column of your table. Since these fees were not paid for his services as a director, please revise this table to include such fees under the column captioned "All Other Compensation." Please refer to Item 402(k)(2)(ii) and (vii).

Certain Relationships and Related Party Transactions, page 81

42. Please expand your disclosure here to provide the information required by Item 404(a), including the name of the related person and dollar amount of their interest, for each transaction involving your preferred stock since the beginning of fiscal year 2004. We note specifically your disclosure on page F-15 that you sold Series C-2 and Series D preferred stock to new and existing investors since the beginning of fiscal year 2004. We also note your disclosure on pages F-15, II-2 and II-3 that in September 2004 you exchanged outstanding Series A, B, and C preferred stock for Series C-2 preferred stock and also converted warrants to acquire Series B and C preferred stock into warrants to acquire shares of Series C-2 preferred stock. Please note that disclosure is required if a transaction resulted in the person becoming a 5% shareholder or continues after that date, such as through the ongoing receipt of payments. See Telephone Interpretation Manual, Section I, No. 41. Item 404(a) also requires disclosure of transactions since the beginning of fiscal year 2004 between you and any person who was an executive officer, director, or immediate family member at any time during that period. See Instruction 1.a. to Item 404(a).

43. We note your disclosure on pages 30 and 32 that "certain existing investors" extended you $1.3 million in bridge loans prior to the closing of your Series D financing, which amount was converted in shares of your Series D Convertible Preferred Stock. Please revise to identify these investors and to provide the information required by Item 404(a)(5). Provide similar disclosure with respect to short-term notes you issued to existing stockholders in 2005 and 2006, which transaction is identified on page F-11. Also, please file copies of the agreements that pertain to the bridge loans and 2006 note transaction as exhibits to this registration statement.

44. Please expand your disclosure in an appropriate section of the prospectus to identify and describe the indemnification agreements you intend to enter into with your officers and directors.

Second Amended and Restated Stockholders' Agreement, page 82

45. Please expand your disclosure here to include the information required by Item 404(a)(1), (4), and (6).

Policies and Procedures for Related Party Transactions, page 83

46. Please expand your disclosure here to describe in more detail your policies and procedures for the review, approval, or ratification of related party transactions. For example, define what you consider to be a "related party transaction" and describe the information that must be presented to your audit committee and such committee's standard of review. Also describe any procedures in the event that a member of your audit committee has an interest in the proposed transaction.

Underwriting, page 94

47. We note that your underwriters expect to sell your common stock to accounts over which they exercise discretionary authority. Please confirm to us that you will include in your prospectus the identity of these underwriters prior to circulating any version of this registration statement. Please see Item 508(j) of Regulation S-K.

48. According to a press release dated May 16, 2006 on your Web site and the signature page to Exhibit 10.4, Allen & Company invested in your Series D preferred stock financing. Given that Allen & Company will be underwriting this public offering, please tell us the amount of securities purchased and whether they still hold such securities. Also tell us whether Allen & Company is a party to the investors' rights agreements referenced in your disclosure and describe any rights they have pursuant to such agreements, including rights that pertain to the nomination and election of directors.

Financial Statements, page F-1

49. Please update the financial statements as required by Rule 3-12 of Regulation S-X and include an updated accountant's consent in any amended filings.

Balance Sheets, page F-3

50. We note that conversion of all the outstanding Series B, C, C-2 and D convertible preferred stock into common stock will be effective prior to the closing of the offering. Tell us your consideration of providing pro forma information that shows the effect of the conversion.

Statement of Cash Flows, page F-6

51. We note that you sold Series D convertible preferred stock for a total consideration of $53,310,465. Please reconcile this to the amount of proceeds from the issuance of Series D convertible preferred stock of $46,793,897 shown in your statements of cash flows.

Statement of Stockholders' Deficit, page F-5

52. Revise to disclose the date and number of shares of stock issued for cash or other consideration for each transaction since inception. Refer to paragraph 11(d) to SFAS 7. Alternatively, please tell us how your current disclosure meets the requirements of paragraph 11 or why such disclosure is not required.

Note 4, Related Party Transactions, page F-10

53. We note in 2006, the Company issued to existing stockholders short term notes for total proceeds of $1,320,148 along with $5,019,062 of similar notes issued in 2005. Related party notes payable should be separately disclosed on the face of the balance sheet. Refer to Article 4-08(k) of Regulation S-X. Please revise accordingly.

Note 5. Equity Incentive Plan, page F-11

54. Provide us with an itemized chronological schedule detailing each issuance of your common shares, preferred shares, stock options and warrants since August 2006 through the date of your response. Include the following information for each issuance or grant date:

- Number of shares issued or issuable in the grant
- Purchase price or exercise price per share
- Any restriction or vesting terms
- Management's fair value per share estimate
- How management determined the fair value estimate

- Identity of the recipient and relationship to the company
- Nature and terms of any concurrent transactions with the recipient
- Amount of any recorded compensation element and accounting literature relied upon to support the accounting.

In the analysis requested above, highlight any transactions with unrelated parties believed by management to be particularly evident of an objective fair value per share determination. Please provide us with a chronological bridge of management's fair value per share determinations to the current estimated IPO price per share. Also, indicate when discussions were initiated with your underwriter(s) about possible offering price ranges. We will delay our assessment of your response pending inclusion of the estimated IPO price in the filing.

Note 7. License Agreements, page F-14

55. To assist a reader in understanding the license agreement with Northwestern University, please disclose all the major terms of this agreement. For example, please discuss the royalty terms and rates or tell us why you believe additional disclosure is not required.

56. We also note that you recorded $5.2 million in initial license fees and patents which were recorded as intangible assets as of March 31, 2007. Please tell us more about these intangible assets. Specifically how they were valued and where you are in the process of obtaining FDA approval. Refer to SFAS 142 in your response.

Part II

Item 16. Exhibits and Financial Statement Schedules, page II-3

57. Please file as exhibits to this registration statement the stock purchase agreements for your Series C-2 and Series D Convertible Preferred Stock financings.

58. We understand that you will be requesting confidential treatment for portions of exhibits to your registration statement. We will review and provide any comments on your request separately. Please resolve all comments regarding your request prior to requesting effectiveness of this registration statement. Please also mark each exhibit in your exhibit list that is subject to your confidential treatment request.

Item 17. Undertakings, page II-4

59. Please include the full undertakings referenced in (3) and (4). Please refer to Item 512(a)(5)(ii) and (a)(6).

* * * * * * *

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 responses to our comments.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes all information required under the Securities Act of 1933 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.

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 staff comments and the declaration of effectiveness 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 will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

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 at Dennis Hult at (202) 551-3618 or Angela Crane, Accounting Branch Chief, at (202) 551-3554 if you have questions regarding comments on the financial statements and related matters. Please contact Geoffrey Kruczek at (202) 551-3641 or me at (202) 551-3800 with any other questions.

Sincerely,

Peggy Fisher
Assistant Director

cc (via fax): Esteban A. Ferrer, Esq.—Paul, Hastings, Janofsky & Walker LLP
Ann Lawrence, Esq.—Paul, Hastings, Janofsky & Walker LLP