

Mail Stop 4561

October 8, 2009

Isy Goldwasser
Chief Executive Officer
Symyx Technologies, Inc.
1263 East Arques Avenue
Sunnyvale, CA 94085

**Re: Symyx Technologies, Inc.
Form 10-K for the Fiscal Year Ended December 31, 2008
Form 10-Q for the Fiscal Quarter Ended March 31, 2009
Form 10-Q for the Fiscal Quarter Ended June 30, 2009
Form 8-K Filed July 29, 2009
File No. 000-27765**

Dear Mr. Goldwasser:

We have reviewed your response letter dated September 4, 2009 in connection with the above-referenced filings and have the following comments. If 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 raise additional comments. Unless otherwise noted, where prior comments are referred to they refer to our letter dated August 11, 2009.

Form 10-K for the Fiscal Year Ended December 31, 2008

Item 11. Executive Compensation (incorporated from Definitive Proxy Statement on Schedule 14A, filed on April 29, 2009)

Compensation Discussion and Analysis

Setting Executive Compensation, page 19

1. We note your response to prior comment number 11 indicating that you do not believe that you are required to identify all of the companies that make up the compensation peer group against whom you benchmark certain elements of executive compensation, due to the relatively large number of companies and the process by which the group is identified. However, where a company

- benchmarks total compensation or any material element of compensation, all of the component companies of the peer group should be named so that investors can ascertain the similarity and differences between the registrant and the companies it considers peers for compensation purposes. See Item 402(b)(2)(xiv) of Regulation S-K. Accordingly, please provide in your response letter a list of all of the component companies in what you refer to as your “historical” compensation peer group, and confirm that you will provide conforming disclosure in future filings, to the extent relevant at the time of filing. To address the concern that a long list of companies would interrupt the flow of the compensation discussion and analysis, you may wish to provide the full list of peer group companies in an appendix to the filing that you cross-reference in the body of the filing.
2. In addition, we note that you intend to revise future filings to provide additional information regarding your benchmarking methods and the processes for identifying the compensation peer group (to the extent relevant at the time of filing), which we presume will include the metrics by which the company selected the peer group companies, as referenced in your response. In this regard, please clarify in your response letter and in future filings how the company measures “size” (e.g., total revenues, number of employees, etc.) when selecting “publicly traded companies of similar size” to Symyx for benchmarking purposes.
 3. We refer to your response to prior comment number 12, in which you have provided the information requested by our prior comment with respect to all of the companies that participated in Radford’s survey for 2008, as opposed to the compensation peer group (a subset of the Radford survey) that you apparently used for purposes of benchmarking compensation for your named executive officers. Please explain to us more clearly why you are unable to disclose where actual base salary and cash incentive compensation paid to your named executive officers fell relative to the targeted 75th percentile against the actual compensation peer group that Symyx used for benchmarking. In particular, it is unclear to us how you could have determined quantitative targets for these elements of compensation but be unable to determine how actual payouts compared to the targeted percentile. In future filings relating to years in which the company engages in benchmarking compensation, please disclose where actual payments fall relative to the targeted percentile against the peer group companies for each applicable element of compensation for each named executive officer. To the extent that you do not engage in benchmarking in a particular year, please make this clear in your disclosure.

Discretionary Cash Bonuses, page 22

4. We note your response to prior comment number 14 relating to the discretionary cash bonuses awarded to certain of your named executive officers for fiscal 2008.

You still do not appear to have identified with specificity each of the individual contributions or the “documented goals” (in both cases to the extent material to your executive compensation policies and decisions) that you indicate you considered in determining to award discretionary cash bonuses, nor have you sufficiently described the reasons you believe the amounts awarded to the applicable named executive officers as discretionary cash bonuses are appropriate in light of the various items considered in making these awards. In this regard, please address the following:

- Elaborate on the elements of “individual performance” that you indicate were considered for each named executive officer awarded a discretionary bonus for 2008, and explain how management and your compensation committee measured “the financial performance of the business unit or function in which such executive serves” for purposes of awarding these discretionary bonuses.
 - For Mr. Cronin, your Senior Vice President, Sales, please describe the “target plans” against which you indicate bookings levels were compared in determining the amount of his discretionary bonus for 2008.
 - Further, we note from your response that the discretionary bonuses were awarded at specified percentages of the target bonus amounts payable under your 2007 Executive Annual Cash Incentive Plan. Please expand this discussion to explain more clearly why discretionary bonus awards were tied to target bonus amounts under the annual bonus plan, and how the actual percentages and resulting discretionary bonus amounts paid to the named executive officers were determined.
5. Your response to prior comment number 14 states that Mr. Heritage was awarded a discretionary bonus of \$141,728 for 2008. However, this award to Mr. Heritage is not reflected in the “Bonus” column of the summary compensation table, nor is it discussed under the heading “Discretionary Cash Bonuses” in your proxy statement. Please advise.

Form 8-K Filed July 29, 2009

Exhibit 99.1

6. We note that the measure you refer to as EBITDA excludes items that are not specified in the definition of EBITDA as described in SEC Release No. 33-8176. If this measure will be presented in future filings, please revise the title of the measure you present. Please also note that a measure characterized as “EBITDA” should be reconciled to net income as presented in the statement of operations under GAAP. Refer to Questions 14 and 15 of Frequently Asked Questions Regarding the Use of Non-GAAP Financial Measures.

Isy Goldwasser
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Please respond to these comments within 10 business days or tell us when you will provide us with a response. Please submit all correspondence and supplemental materials on EDGAR as required by Rule 101 of Regulation S-T. If you amend your filings, you may wish to provide us with marked copies of any amendment to expedite our review. Please furnish a cover letter that keys your response 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 any amendment and your response to our comments.

You may contact Jennifer Fugario, Staff Accountant, at (202) 551-3482 if you have any questions regarding comments on the financial statements and related matters. Please address questions regarding all other comments to Katherine Wray, Staff Attorney, at (202) 551-3483 or Mark P. Shuman, Branch Chief – Legal, at (202) 551-3462. If you need further assistance, you may contact me at (202) 551-3406.

Sincerely,

Patrick Gilmore
Accounting Branch Chief