

Mail Stop 4561

November 20, 2006

John P. McAlister, III  
President and Chief Executive Officer  
Tripos, Inc.  
1699 S. Hanley Rd  
St. Louis, MO 63144

**Re: Tripos, Inc.**  
**Form 10-K for the fiscal year ended December 31, 2005**  
**Form 10-Q for the quarterly period ended September 30, 2006**  
**File No. 000-23666**

Dear Mr. McAlister:

We have reviewed the above referenced filing and have the following comments. Please note that we have limited our review to only your financial statements and related disclosures and do not intend to expand our review to other portions of your document. We may ask you to provide us with supplemental information so we may better understand your disclosure. Please be as detailed as necessary in your explanation. 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.

Form 10-K for the fiscal year ended December 31, 2005

Consolidated Statements of Operations

1. You disclose that you allocate revenues from perpetual software arrangements involving multiple elements to each element based on the relative fair values as determined by the vendor specific objective evidence ("VSOE") for each element. We note that revenue related to these multiple element arrangements is presented within a single line item within the Consolidated Statements of Operations. Tell us how this presentation complies with Rule 5-03(b) of Regulation S-X. In this regard, tell us what consideration you gave to presenting product and service

revenue, and related cost of revenue, on separate line items for your perpetual software arrangements pursuant to Rule 5-03(b) of Regulation S-X.

2. You disclose within your revenue recognition footnote that you do not have VSOE to determine fair value of the maintenance and support in term arrangements and therefore recognize revenues from these bundled time-based licenses ratably over the license term. We note that revenue related to these bundled arrangements is included within the same line item as multiple element arrangements where VSOE of fair value has been established for maintenance and support services and training. Where there is a lack of VSOE of fair value among the arrangement elements, SOP 97-2 prohibits separation of the total arrangement fee for recognition purposes. Absent a compelling argument under GAAP and Rule 5-03(b)(1) of Regulation S-X *that supports* allocating the arrangement fee in the income statement, you should amend your presentation to include separate revenue, and related cost of revenue, line items for bundled arrangements that are not separable because of the absence of VSOE for the undelivered PCS element. You should also include a footnote description to inform investors of the nature of the additional line item. Please also describe to us other possible allocation methodologies for income statement presentation purposes that you considered but rejected.
3. We note your presentation within the Consolidated Statements of Operations includes revenue and related cost of services line items that entitled “products & support” as well as “products & services”. Note the Rule 5-03(b) of Regulation S-X requires separate presentation of products and services. Tell us how your presentation complies with this requirement.

Form 10-Q for the Quarterly Period Ended September 30, 2006

Notes to Unaudited Consolidated Financial Statements

(9) Goodwill and Intangible Assets, page 17

4. Based on your disclosure, it does not appear you have tested for impairment since your last annual test. If this is correct, tell us how you considered the significant decline in your market capitalization in fiscal year 2006 and why you believe this decline is not a triggering event for an impairment test. We refer you to paragraph 28 of SFAS 142. In addition, please describe how you determine fair value for your reporting units and how your fair value measurements comply with paragraphs 23 through 25 of SFAS 142. As part of your response, tell us how the total fair value measurement of your reporting units compares to your market capitalization.

(14) Segments, page 21

5. We note there has been a significant decrease to the revenue generated from your Discovery Research operating segment. We further note that you have recognized an operating loss from your discovery research operating segment of approximately \$2 million for the nine-months ended September 30, 2006. Tell us how you evaluated these factors when determining whether it was necessary to test your Discovery Research segment's long-lived assets for recovery as of September 30, 2006. We refer you to paragraph 8.e of SFAS 144. In addition, clarify how you determined the fair of your Discovery Research segment's long-lived assets exceeds the carrying amount as of September 30, 2006.

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. You may wish to provide us with marked copies of any amendments to expedite our review. Please furnish a cover letter with any amendments 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 any amendment and your 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 Exchange Act of 1934 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.

In connection with responding to our comments, please provide, in writing, a statement from the company acknowledging that:

- the company is responsible for the adequacy and accuracy of the disclosure in the filing;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing; and
- the company may not assert staff comments 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 our review of your filing or in response to our comments on your filing.

John P. McAlister, III  
Tripos, Inc.  
November 20, 2006  
Page 4

You may contact Jason Niethamer at 202-551-3855, Chris White at 202-551-3461 or me at 202-551-3730 if you have questions regarding the above comments.

Sincerely,

Stephen Krikorian  
Accounting Branch Chief