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May 22, 2009

United States Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E., Mail Stop 3030
Washington, DC 20549

Attn: Russell Mancuso

Re: Oculus Innovative Sciences, Inc.
Registration Statement on Form S-1
File No. 333-158539

Dear Mr. Mancuso:

I am securities counsel for Oculus Innovative Sciences, Inc. (the "Company"). I enclose for filing under the Securities Act of 1933, as amended, Amendment No. 2 to the Form S-1, File No. 333-158539, together with certain exhibits thereto (the "Registration Statement").

The Registration Statement contains revisions that have been made in response to comments received from the staff of the Securities and Exchange Commission (the "Staff") in their letter dated April 27, 2009. Set forth below are the Company's responses to the Staff's comments. The numbering of the responses corresponds to the numbering of the comments in the letter from the Staff.

Fee Table

Comment 1. It appears from your prospectus that you intend to offer and sell "Units" comprised of common stock and warrants. Therefore, please include in your fee table the number of "Units" you intend to offer and sell and calculate the registration fee based on the fixed offering price of those "Units." Then include the appropriate fee calculation for your offering of the warrants and shares underlying the units and the shares underlying the warrants.

Response 1. The Company has complied with the Staff's comment.

Prospectus Cover

Comment 2. Your disclosure on pages 18-19 indicates that the selling stockholders will act independent of you with respect to the securities they are offering for resale. The second paragraph of your prospectus cover implies that the securities to be offered and sold by them are part of your offering. Please reconcile.

Response 2. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.

- Comment 3. If the selling stockholders are selling independent of your fixed-price offering, please highlight that price difference in your disclosure regarding the offering price on the prospectus cover. Briefly explain the price difference in your prospectus summary, and add appropriate risk factors.
- Response 3. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 4. Please identify the placement agent for your offering here. See Regulation S-K Item 501(b)(8).
- Response 4. The Company has complied with the Staff's comment.
- Comment 5. Please ensure your cover page fully complies with Regulation S-K Item 501(b)(4). For example, we note it appears that you have not identified whether a market exists for the warrants included in the Units.
- Response 5. The Company has complied with the Staff's comment.

Selling Security Holders, page 16

- Comment 6. Your disclosure on pages 2 and 50 regarding the February 24, 2009 purchase agreement indicates that the investors in that offering have not yet paid the full purchase price for the securities. Generally, it is inconsistent with section 5 of the Securities Act to register shares for resale before the related private transaction is complete. Please provide us with your analysis of how the private transaction was complete at the time you filed this registration statement. Cite all authority on which you rely.
- Response 6. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 7. It appears from your notes to the selling security holders' table that you are registering the resale of common stock underlying Series C warrants. Given your disclosure in those notes and on page 2 that the Series C warrants have not yet been issued to you, it is premature to register the underlying common stock for resale. Please revise or advise.
- Response 7. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 8. Given the nature and size of the transaction you have registered for the selling stockholders, including the shares in the related registration statement file number 333-157776, advise the staff of the Company's basis for determining that the transaction is appropriately characterized as a transaction that is eligible to be made on a shelf basis under Rule 415(a)(1)(i). We note, for example, that:
- you have registered for resale by one of your directors and parties related to him a significant number of shares relative to the amount of shares outstanding and held by non-affiliates;
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- many of those shares cannot yet be acquired by your director and related parties; and
- the plans for a second tranche, the exercise period of the warrants and your plans to issue replacements for exercised warrants appear to result in a situation where you will be engaged in ongoing capital raising from these investors while they may be obtaining funds from the public in this offering.

- Response 8. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 9. With a view toward disclosure, please tell use the market price on the date of the purchase agreements with the selling security holders compared to the per share price of the securities you sold.
- Response 9. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 10. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of the dollar amount of each payment (including the value of any payments to be made in common stock) in connection with the sale of the securities that you have made or may be required to make to any selling stockholder, any affiliate of a selling stockholder, or any person with whom any selling stockholder has a contractual relationship regarding the transaction (including any interest payments, liquidated damages, payments made to “finders” or “placement agents,” and any other payments or potential payments). Please provide footnote disclosure of the terms of each such payment.
- Further, please provide use, with a view toward disclosure in the prospectus, with disclosure of the net proceeds to the issuer from the sale of the securities and the total possible payments to all selling stockholders and any of their affiliates in the first year following the sale of securities.
- Response 10. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 11. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of the total possible profit the selling stockholders could realize as a result of any exercise of the warrants, presented in a table with the following information disclosed separately:
- the market price per share of the securities underlying the warrants on the dates of the purchase agreement;
 - the exercise price per share of the underlying securities on the dates of the purchase agreement, calculated as follows:
 - if the exercise price per share is set at a fixed price, use the price per share established in the warrant; and
 - if the exercise price per share is not set at a fixed price and, instead, is set at a floating rate in relationship to the market price of the underlying security, determine the exercise price as of the date of the purchase agreement;
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- the total possible shares underlying the warrants;
- the combined market price of the total number of shares underlying the warrants, calculated by using the market price per share on the dates of the purchase agreement and the total possible shares underlying the warrants;
- the total possible shares the selling shareholders may receive and the combined exercise price of the total number of shares underlying the warrants calculated by using the exercise price on the dates of the purchase agreement and the total possible number of shares the selling stockholders may receive; and
- the total possible discount to the market price as of the dates of the purchase agreement, calculated by subtracting the total exercise price on the dates of the purchase agreement from the combined market price of the total number of shares underlying the warrants on that date.

If there are provisions in the warrants that could result in a change in the price per share upon the occurrence of certain events, please provide additional tabular disclosure as appropriate. For example, if the exercise price per share is fixed unless and until the market price falls below a stated price, at which point the exercise price per share drops to a lower price, please provide additional disclosure.

Response 11. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.

Comment 12. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of the total possible profit to be realized as a result of any conversion/exercise discounts for securities underlying any other warrants, options, notes, or other securities of the issuer that are held by the selling stockholders or any affiliates of the selling stockholders, presented in a table with the following information disclosed separately:

- market price per share of the underlying securities on the date of the sale of that other security;
 - the conversion/exercise price per share as of the date of the sale of that other security, calculated as follows:
 - if the conversion/exercise price per share is set at a fixed price, use the price per share on the date of the sale of that other security; and
 - if the conversion/exercise price per share is not set at a fixed price and, instead, is set at a floating rate in relationship to the market price of the underlying security, use the conversion/exercise discount rate and the market rate per share on the date of the sale of that other security and determine the conversion price per share as of that date;
 - the total possible shares to be received under the particular securities (assuming complete conversion/exercise);
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- the combined market price of the total number of underlying shares, calculated by using the market price per share on the date of the sale of that other security and the total possible shares to be received;
- the total possible shares to be received and the combined conversion/exercise price of the total number of shares underlying that other security calculated by using the conversion/exercise price on the date of the sale of that other security and the total possible number of underlying shares; and
- the total possible discount to the market price as of the date of the sale of that other security, calculated by subtracting the total conversion/exercise price on the date of the sale of that other security from the combined market price of the total number of underlying shares on that date.

Response 12. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.

Comment 13. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of all prior securities transactions between the issuer (or any of its predecessors) and the selling stockholders, any affiliates of the selling stockholders, or any person with whom the selling stockholders has a contractual relationship regarding the transaction (or any predecessors of those persons), with the table including the following information disclosed separately for each transaction:

- the date of the transaction;
 - the number of shares of the class of securities subject to the units transactions that were outstanding prior to the transactions;
 - the number of shares of the class of securities subject to the transactions that were outstanding prior to the transactions and held by persons other than the selling stockholders, affiliates of the company, or affiliates of the selling stockholders;
 - the number of shares of the class of securities subject to the transactions that were issued or issuable in connection with the transactions;
 - the percentage of total issued and outstanding securities that were issued or issuable in the transactions (assuming full issuance), with the percentage calculated by taking the number of shares issued or issuable in connection with the applicable transactions, and dividing that number by the number of shares issued and outstanding prior to the applicable transactions and held by persons other than the selling stockholders, affiliates of the company, or affiliates of the selling stockholders.
 - the market price per share of the class of securities subject to the transactions immediately prior to the transactions (reverse split adjusted, if necessary); and
 - the current market price per share of the class of securities subject to the transaction (reverse split adjusted, if necessary).
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Response 13. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.

Comment 14. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure comparing:

- the number of shares outstanding prior to the date of the purchase agreements that are held by persons other than the selling stockholders, affiliates of the company, and affiliates of the selling stockholders;
- the number of shares registered for resale by the selling stockholders or affiliates of the selling stockholders in prior registration statements;
- the number of shares registered for resale by the selling stockholders or affiliates of the selling stockholder that continue to be held by the selling stockholders or affiliates of the selling stockholders;
- the number of shares that have been sold in registered resale transactions by the selling stockholders or affiliates of the selling stockholders; and
- the number of shares registered for resale on behalf of the selling shareholders or affiliates of the selling stockholders in the current transaction.

In this analysis, the calculation of the number of outstanding shares should not include any securities underlying any outstanding convertible securities, options, or warrants.

Response 14. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.

Comment 15. Please tell us, with a view toward disclosure in the prospectus, whether — based on information obtained from the selling stockholders — the selling stockholders have an existing short position in the company's common stock and, if the selling stockholders have an existing short position in the company's stock, the following additional information:

- the date on which the selling stockholders entered into that short position; and
- the relationship of the date on which the selling stockholders entered into that short position to the date of the announcement of the purchase agreements and the filing of the registration statement (*e.g.*, before or after the announcement of the purchase agreements, before the filing or after the filing of the registration statement, *etc.*).

Response 15. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.

Comment 16. Please provide us, with a view toward disclosure in the prospectus, with:

- a materially complete description of the relationships and arrangements that have existed in the past three years or are to be performed in the future between the issuer (or any of its predecessors) and the selling stockholders, any affiliates of the selling stockholders, or any person with whom any selling stockholders have a contractual relationship regarding the transaction (or any predecessors of those persons) — the information provided should include, in reasonable detail, a complete description of the rights and obligations of the parties in connection with the purchase agreements; and
- copies of all agreements between the issuer (or any of its predecessors) and the selling stockholders, any affiliates of the selling stockholders, or any person with whom any of the selling stockholders has a contractual relationship regarding the transaction (or any predecessors of those persons) in connections with the purchase agreements.

If it is your view that such a description of the relationships and arrangements between and among those parties already is presented in the prospectus and that all agreements between and/or among those parties are included as exhibits to the registration statement, please provide us with confirmation of your view in this regard.

- Response 16. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 17. Please disclose the identity of the natural persons who exercises the sole or shared voting and/or dispositive powers with respect to the shares to be offered by Cranshire Capital. It appears from note 4 to your table that you have only identified the natural person who has voting control over Downsview. Also disclose the identity of the natural persons who exercise sole or shared voting and/or dispositive powers with respect to the shares offered by Merriman Curhan Ford & Co and Rockmore.
- Response 17. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 18. Please tell us whether any of the selling stockholders is a broker-dealer or affiliate of a broker-dealer.
- Response 18. The Company has determined to no longer register the resale of the securities held by the selling security holders. As such, the Company has removed the disclosure related to the secondary offering from the Registration Statement.
- Comment 19. Please tell us how you determined the number of shares to register for the selling stockholders in your previous registration statement, how you determined the number to register in the current registration statement, and why the prior registration statement did not include the shares included in the current registration statement.
- Response 19. The Company is aware of the Staff's position regarding Rule 415, as articulated by the Staff in comment 8 in its letter dated April 27, 2009 to the Company. The Company determined to register less than 33% of its outstanding securities in the prior registration statement because the Company believed it would result in the prior registration statement being declared effective by the Staff more quickly than if the Company had registered in excess of 33% of its outstanding securities. The selling shareholders in the prior registration statement had certain registration rights and the Company would have had to pay liquidated damages if the prior registration statement was not declared effective by a certain deadline.

The Company later determined to work with a Placement Agent on a registered offering and filed the current Registration Statement. The Company included additional shares for the selling shareholders that were not included in the prior registration statement in the current Registration Statement. However, the Company has now decided, given that sufficient time has elapsed so that many selling shareholders will soon be able to sell their shares pursuant an exemption from registration, that it would be more efficient and cost-effective to remove the selling shareholders from the Registration Statement and pursue only the primary offering at this time.

Comment 20. Please update your disclosures required by Item 402 of Regulation S-K to include compensation information for your last completed fiscal year — the fiscal year ended March 31, 2009.

Response 20. The Company has complied with the Staff's comment.

Undertakings, page II-8

Comment 21. Please include the undertakings required by Regulation S-K Item 512(a)(5)(ii) and (a)(6). Also, please do not change the language of Regulation S-K Item 512(a)(5)(i).

Response 21. The Company has complied with the Staff's comment.

If you have further questions or comments, please feel free to contact us. We are happy to cooperate in any way we can.

Regards,

/s/ Amy M. Trombly