Fax

DIVISION OF ONCOLOGY DRUG PRODUCTS
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To:	John Worzalla/ LILLY	**From:**	Alvis Dunson, Project Manager
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Pages:	2 (including this page)	**Date:**	December 21, 1999
Re:	IND 40,061/serial nos. 191and 195		

☐ **Urgent** ☑ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

• Comments:

Please refer to your submissions dated November 8 and December 3, 1999, for LY231514 (MTA).

We have reviewed this submission and have the following comments.

At this point in the review, the Medical Officer does not support adding vitamins to your ongoing pivotal, randomized trial in mesothelioma. Thus, the pivotal trial in malignant mesothelioma (H3E-MC-JMCH) should not be altered at this stage. A few reasons follow.

First, no statistical plan has been submitted to guide how the data is to be evaluated and/or compared to the prior accumulated data. Second, at the June 25, 1999, you committed to completing the 280 patient trial even if the results are positive at the interim analysis; adding vitamins to the trial at this time appears to be a deviation from that commitment. Third, the information provided in the Annual Report (serial #191) about the toxicities in the trial (pages 45-46) does not appear to support the addition of vitamins. You may want to design a randomized trial of MTA +/- vitamins in mesothelioma. If you believe that vitamin administration will be an important aspect of the MTA

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label, this may be an important trial that can provide convincing evidence with regard to efficacy and safety of MTA with and without vitamins.

If you have any questions please call me at (301) 594-5767.

Thank you,

Alvis Dunson