Lilly

Eli Lilly and Company

US Regulatory Affairs
1700 Rockville Pike, Suite 450
Rockville, Maryland 20852
301.770.0788
Fax: 301.881.6317

February 16, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncology Drug Products, HFD-150
Attn: Mr. Alvis Dunson, Project Manager
1451 Rockville Pike
Rockville, Maryland 20852-1448

Briefing Document

LY231514 (MTA, MultiTargeted Antifolate); IND # 40,061 Serial No.: 207
Briefing Document for March 1 Meeting to Discuss Vitamin Supplementation in the Ongoing Mesothelioma Registration Trial

Reference is made to Eli Lilly and Company's submission to the LY231514 IND (#40,061) on January 25, 2000 (serial no. 203).

We thank the FDA for granting the meeting on March 1, 2000 from 10:30 A.M. until noon to discuss the implications of adding vitamins to the ongoing mesothelioma registration trial (H3E-MC-JMCH). The briefing document is enclosed. The major points for discussion at this meeting are as follows:

- The rationale for the intervention of adding folic acid for patient safety
- The implications of adding folic acid to the ongoing mesothelioma registration trial (H3E-MC-JMBQ)
- Lilly's proposal for changes in the second-line NSCLC registration trial (H3E-MC-JMBQ).

As related to the third point above, Lilly proposed changes to the current NSCLC registration trial (H3E-MC-JMBQ) on October 14, 1999 (serial no. 186). On December 1, 1999 the Medical Reviewer, Dr. White, sent to Lilly several questions regarding the October 14 Lilly proposal. Lilly has not previously provided answers to Dr. White's questions due to the fact that we were focusing on the folic acid supplementation issue and also we were awaiting the results of the Oncology Drug Advisory Committee meeting in December where docetaxel for second-line NSCLC was discussed.

Lilly now is again proposing changes to this NSCLC registration trial in today's briefing document, and to aid the FDA in preparing to answer our questions regarding this trial, we have provided answers to Dr. White's December 1 questions (see Attachment 2 to the Briefing Document for these answers).

We again thank the Division of Oncology Drug Products for its assistance in the development of LY231514. Please call Mr. John Worzalla at (317) 276-5052 or me at (317) 277-3799 if there are any questions. Thank you for your continued cooperation and assistance.

Sincerely,

ELI LILLY AND COMPANY

Gregory T. Brophy, Ph.D.
Director
U.S. Regulatory Affairs

Enclosure
Briefing Document

dmm

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

INVESTIGATIONAL NEW DRUG APPLICATION (IND)

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

Form Approved: OMB No. 0910-0014. Expiration Date: September 30, 2002. See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR
ELI LILLY AND COMPANY

2. DATE OF SUBMISSION
February 16, 2000

3. ADDRESS *(Number, Street, City, State and Zip Code)*
Lilly Corporate Center
Indianapolis, IN 46285

4. TELEPHONE NUMBER *(Include Area Code)*
(317) 276-2000

5. NAME(S) OF DRUG *(Include all available names: Trade, Generic, Chemical, Code)*
Compound LY231514 Disodium (MTA)

6. IND NUMBER *(If previously assigned)*
IND 40,061

7. INDICATION(S) *(Covered by this submission)*
NA

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED: ☐ PHASE 1 ☐ PHASE 2 ☐ PHASE 3 ☐ OTHER NA *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES *(21 CFR Part 314.420)*, AND PRODUCT LICENSE APPLICATIONS *(21 CFR Part 601)* REFERRED TO IN THIS APPLICATION.
NA

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submission should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER
207

11. THIS SUBMISSION CONTAINS THE FOLLOWING: *(Check all that apply)*

☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND) ☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):	INFORMATION AMENDMENT(S):	IND SAFETY REPORT(S):
☐ NEW PROTOCOL	☐ CHEMISTRY/MICROBIOLOGY	☐ INITIAL WRITTEN REPORT
☐ CHANGE IN PROTOCOL	☐ PHARMACOLOGY/TOXICOLOGY	☐ FOLLOW-UP TO A WRITTEN REPORT
☐ NEW INVESTIGATOR	☐ CLINICAL	

☐ RESPONSE TO FDA REQUEST FOR INFORMATION ☐ ANNUAL REPORT ■ GENERAL CORRESPONDENCE
☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED ☐ OTHER _____ *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

☐ TREATMENT IND 21 CFR 312.35(b) ☐ TREATMENT PROTOCOL 21 CFR 312.35(a) ☐ CHARGE REQUEST/NOTIFICATION 21 CFR 312.7(d)

FOR FDA USE ONLY

CDR/DBIND/DGD RECEIPT STAMP	DDR RECEIPT STAMP	IND NUMBER ASSIGNED:
		DIVISION ASSIGNMENT:

FORM FDA 1571 (1/97) PREVIOUS EDITION IS OBSOLETE. PAGE 1 OF 2

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ELAP00013760

12. CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

- ☐ 1. Form FDA 1571 [21 CFR 312.23(a)(1)]
- ☐ 2. Table of Contents [21 CFR 312.23(a)(2)]
- ☐ 3. Introductory statement [21 CFR 312.23(a)(3)]
- ☐ 4. General investigational plan [21 CFR 312.23(a)(3)]
- ☐ 5. Investigator's brochure [21 CFR 312.23(a)(5)]
- ☐ 6. Protocol(s) [21 CFR 312.23(a)(6)]
  - ☐ a. Study protocol(s) [21 CFR 312.23(a)(6)]
  - ☐ b. Investigator data [21CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
  - ☐ c. Facilities data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
  - ☐ d. Institutional Review Board data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
- ☐ 7. Chemistry, manufacturing, and control data [21 CFR 312.23(a)(7)]
- ☐ ☐ Environmental assessment or claim for exclusion [21 CFR 312.23(a)(7)(iv)(e)]
- ☐ 8. Pharmacology and toxicology data [21 CFR 312.23(a)(8)]
- ☐ 9. Previous human experience [21 CFR 312.23(a)(9)]
- ☐ 10. Additional information [21 CFR 312.23(a)(10)]

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? ☐ YES ☐ NO

NA

IF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? ☐ YES ☐ NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

James Rusthoven, M.D.

15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

Same as #14 Above

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set fourth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	
Gregory T. Brophy, Ph.D., Director U.S. Regulatory Affairs		
18. ADDRESS *(Number, Street, City, State and Zip Code)*	19. TELEPHONE NUMBER *(Include Area Code)*	20. DATE
Eli Lilly and Company Lilly Corporate Center Indianapolis, IN 46285	(317) 277-3799	02/16/00

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

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Washington, DC 20201

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