

2905



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UTILITY PATENT APPLICATION TRANSMITTAL <small>(Only) for new nonprovisional applications under 37 CFR 1.53(b)</small>	Attorney Docket No. X14173A
	First Named Inventor or Application Identifier NIYIKIZA Clet
	Express Mail Label No. EL832896550 US

Application Elements
See MPEP chapter 600 concerning utility patent application contents.

1. Fee Transmittal Form (Submit an original, and a duplicate for fee processing)

2. Specification [Total Pages **21**]
 - Descriptive title of the Invention
 - Cross References to Related Applications
 - Statement Regarding Fed sponsored R & D
 - Reference to Microfiche Appendix
 - Background of the Invention
 - Brief Summary of the Invention
 - Brief Description of the Drawings (if filed)
 - Detailed Description
 - Claims
 - Abstract of the Disclosure

3. Drawing(s) (35 USC 113) [Total Sheets]

4. Oath or Declaration [Total Pages **3**]
 a. Newly executed (original or copy)
 b. Copy from a prior application (37 CFR 1.63(d)) (for continuation/divisional with Box 17 completed) [Note Box 5 below]
 i. DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).

5. Incorporation By Reference (useable if Box 4b is checked) The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

ADDRESS TO: Commissioner for Patents
 Mail Stop Patent Application
 P.O. Box 1450
 Alexandria, VA 22313-1450

6. Microfiche Computer Program (Appendix)

7. Nucleotide and/or Amino Acid Sequence Submission applicable, all necessary
 a. Computer Readable Copy
 b. Paper Copy (identical to computer copy)
 c. Statement verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

8. Assignment Papers (cover sheet & document(s))

9. 37 CFR 3.73(b) Statement (when there is an assignee) Power of Attorney

10. English Translation Document (if applicable)

11. Information Disclosure Statement (IDS)/PTO-1449 2 Copies of IDS Citations

12. Preliminary Amendment

13. Return Receipt Postcard (MPEP 503) (Should be specifically itemized)

14. Small Entity Statement filed in prior application, Status still proper and desired

15. Certified Copy of Priority Document(s) (if foreign priority is claimed)

16. Other:
Amendment and Petition to Correct Inventorship

17. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information:
 Continuation Divisional Continuation-in-part (CIP) of prior application No. **10/297,821**

18. CORRESPONDENCE ADDRESS

Customer Number or Bar Code Label: **25885** or Correspondence address below

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Eli Lilly and Company

ADDRESS: Patent Division, P.O. Box 6288

25885
 PATENT TRADEMARK OFFICE

CITY	Indianapolis	STATE	Indiana	ZIP CODE	46206-6288
COUNTRY	U.S.A.	TELEPHONE	317-277-7443	FAX	317-276-3861

SUBMITTED BY

Typed or Printed Name: Elizabeth A. McGraw
 Signature: *[Signature]*
 Complete (if applicable): Reg. Number 44,646
 Date: 29 Nov 2005

"Express Mail" mailing label number: **EL 832896550 US**
 Date of Deposit: **29 Nov. 2005**

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[Signature] *[Signature]*
 Printed Name: **QUEEN THOMAS** Signature

13261 U.S. PTO 11/288807



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FEE TRANSMITTAL

Effective December 8, 2004

638 U.S. PTO

Complete if Known	
Serial No.	
Application Date	
US Nat'l Entry Date (if applicable)	
First Named Inventor	NIYIKIZA Clet
Group Art Unit	
Examiner Name	
Conf. No.	
Attorney Docket Number	X14173A

TOTAL AMOUNT OF PAYMENT	(\$)1360.00
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METHOD OF PAYMENT (check one)

FEE CALCULATION (continued)

1. The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number: 05-0840

Deposit Account Name: Eli Lilly and Company

Charge Any Additional Fee Required

Charge the Issue Fee Set in 37 CFR 1.18 at the time of allowance

Large Entity Fee Code	Large Entity Fee (\$)	Fee Description	Fee Paid
1051	130	Surcharge-late filing fee or oath	
1052	50	Surcharge-late provisional filing fee or cover sheet.	
1053	130	Non-English specification	
1251	120	Extension for reply within first month	
1252	450	Extension for reply within second month	
1253	1,020	Extension for reply within third month	
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1255	2,160	Extension for reply within fifth month	
1401	500	Notice of Appeal	
1402	500	Filing a brief in support of an appeal	
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1453	1,500	Petition to revive-unintentional	
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1801	790	Request for Continued Examination (RCE)	

FEE CALCULATION

1. In connection with the filing, search and exam fees

Code	Description	Fee	Fee Paid
1011	Basic filing fee (Utility)	\$300.00	300.00
1111	Utility search fee	\$500.00	500.00
1311	Utility examination fee	\$200.00	200.00
SUBTOTAL (1)		(\$)1,000	

Code	Total claims	Extra	Fee Paid (\$)
1202	10 - 20 =	X 50 =	\$

Other fee (specify)

Independent claims

1201	2 - 3 =	X 200 =	\$
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Other fee (specify)

Multiple Dependent Claim

Yes or No (if yes)

360 = \$360

Other fee (specify)

Claims and Excess Length Fees

1081 Total length (spec + drawings)

21 - 100 = excess pages

\$

No extra charge for first 100 pages. Must pay \$250 for each adtl 50 pages (or fraction thereof).

Other fee (specify)

SUBTOTAL (2) (\$) 360.-

SUBTOTAL (3) (\$)

SUBMITTED BY		Complete (if applicable)	
Typed or Printed Name	Elizabeth A. McGraw	Reg. Number	44,646
Signature		Date	29-Nov-2005

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Other fee (specify)

Other fee (specify)

Other fee (specify)

Other fee (specify)

SUBTOTAL (3) (\$)

SUBMITTED BY Complete (if applicable)

Typed or Printed Name: Elizabeth A. McGraw Reg. Number: 44,646

Signature: *E.A. McGraw* Date: 29-Nov-2005

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NOVEL ANTIFOLATE COMBINATION THERAPIES

5 Potentially, life-threatening toxicity remains a major limitation to the optimal
administration of antifolates. (see, generally, Antifolate Drugs in Cancer Therapy, edited
by Jackman, Ann L., Humana Press, Totowa, NJ, 1999.) In some cases, a supportive
intervention is routinely used to permit safe, maximal dosing. For example, steroids, such
as dexamethone, can be used to prevent the formation of skin rashes caused by the
10 antifolate. (Antifolate, pg 197.)

Antifolates represent one of the most thoroughly studied classes of antineoplastic
agents, with aminopterin initially demonstrating clinical activity approximately 50 years
ago. Methotrexate was developed shortly thereafter, and today is a standard component
of effective chemotherapeutic regimens for malignancies such as lymphoma, breast cancer,
15 and head and neck cancer. (Bonnadonna G, Zambetti M, Valagussa P. Sequential or
alternating doxorubicin and CMF regimens in breast cancer with more than three positive
nodes: Ten year results. *JAMA* 1995;273(7):542-547; Bonnadonna G, Valagussa P,
Moliterni A, Zambetti M, Brambilla C. Adjuvant cyclophosphamide, methotrexate, and
fluorouracil in node-positive breast cancer: The results of 20 years of follow-up. *N Engl J*
20 *Med* 1995;332(14):901-906; and Hong WK, Schaefer S, Issell B, et al. A prospective
randomized trial of methotrexate versus cisplatin in the treatment of recurrent squamous
cell carcinoma of the head and neck. *Cancer* 1983;52:206-210.) Antifolates inhibit one or
several key folate-requiring enzymes of the thymidine and purine biosynthetic pathways, in
particular, thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycylamide
25 ribonucleotide formyltransferase (GARFT), by competing with reduced folates for binding
sites of these enzymes. (Shih C, Habeck LL, Mendelsohn LG, Chen VJ, Schultz RM.
Multiple folate enzyme inhibition: Mechanism of a novel pyrrolopyrimidine-based
antifolate LY231514 (MTA). *Advan Enzyme Regul*, 1998; 38:135-152 and Shih C, Chen
VJ, Gossett LS, et al. LY231514, a pyrrolo[2,3-d]pyrimidine-based antifolate that inhibits
30 multiple folate-requiring enzymes. *Cancer Res* 1997;57:1116-1123.) Several antifolate
drugs are currently in development. Examples of antifolates that have thymidylate

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