Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

ORIGINAL

Central Research

September 25, 1997

Department of Clinical Research

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologic
Drug Products (HFD 590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
Serial No. 51
NDA-20-760- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
Serial No. 52 *(Cover letter only)

RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to a teleconference on September 15, 1997 between Dr. Mamodikoe Makhene, Medical Reviewer and Dr. Raymond B. Johnson, Mr. Michael Zelasky, and Ms. Ann Dohmann of Pfizer.

During the September 15 teleconference we discussed two papers which addressed the low percentage of endocervical cultures with *Neisseria gonorrhoeae* or *Chlamydia trachomatis* in patients with pelvic inflammatory disease. Dr. Makhene requested a copy of these papers (Query #293).

On September 16 these papers were forwarded to Dr. Makhene's attention via Federal Express. They are now being formally submitted to complete our records.

A desk copy of this cover letter is being provided to Ms. Pauline Fogarty, Project Manager.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

APPEARS THIS WAY ON ORIGINAL

Sincerely yours,

Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

lab
Enclosures
Desk Copy: Ms. P. Fogarty (Cover letter only)

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

Pfizer

Central Research

September 25, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH
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Department of Clinical Research

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologic
Drug Products (HFD 590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
Serial No. 51
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
Serial No. 52 *(Cover letter only)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to a teleconference on September 15, 1997 between Dr. Mamodikoe Makhene, Medical Reviewer and Dr. Raymond B. Johnson, Mr. Michael Zelasky, and Ms. Ann Dohmann of Pfizer.

During the September 15 teleconference we discussed two papers which addressed the low percentage of endocervical cultures with *Neisseria gonorrhoeae* or *Chlamydia trachomatis* in patients with pelvic inflammatory disease. Dr. Makhene requested a copy of these papers (Query #293).

On September 16 these papers were forwarded to Dr. Makhene's attention via Federal Express. They are now being formally submitted to complete our records.

A desk copy of this cover letter is being provided to Ms. Pauline Fogarty, Project Manager.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

lab
Enclosures
Desk Copy: Ms. P. Fogarty (Cover letter only)

B1
ORIG AMENDMENT
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Central Research Division
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Eastern Point Road
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Tel 860 441 4100

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EVALUATION AND RESEARCH

Central Research

Department of Clinical Research

September 22, 1997

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologic
Drug Products (HFD 590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
Serial No. 49
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
Serial No. 50 *(Cover letter only)

RESPONSE TO FDA REQUEST FOR INFORMATION- MICROBIOLOGY

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to our August 28, 1997 submission to our pending New Drug Applications. Reference is also made to teleconferences and Email, on August 5 and 19, 1997, between Dr. Sousan Altaie, Microbiology Reviewer and Ms. Ann Dohmann of Pfizer.

On August 5, Dr. Altaie requested the following: APPEARS THIS WAY ON ORIGINAL

- Scattergrams for clinical microbiology data for TROVAN (Query #244, **Enclosure #1**).
- Redo the clinical microbiology tables in Section 7, taking into account only those patients from whom the following four parameters were determined: MIC, zone, clinical response and bacteriological response (Query #243, **Enclosure #2**).
- Prepare scattergrams of all in vitro microbiology data (in house and published) (Query #245)

On August 19, Dr. Altaie requested that Pfizer provide further breakdowns of scattergram plots to show U.S. and Non-U.S. clinical isolates (Query #266, also provided in **Enclosure #1**).

A draft response to queries 243, 244 and 266 was forwarded to Dr. Altaie's attention via Federal Express on August 29, 1997. This response is now being formally submitted to complete our records. Please note that a more detailed explanation of the content of this submission is included in the enclosed memo.

The response to query #245 was already formally submitted on August 28, 1997.

A desk copy of this cover letter is being provided to Ms. Pauline Fogarty, Project Manager. If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

Linda Bulkowitch for:
Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

APPEARS THIS WAY ON ORIGINAL

lab
Enclosures
Desk Copy: Ms. P. Fogarty (Cover letter only)

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

NEW CORRESP

ORIGINAL

Central Research

September 18, 1997

Department of Clinical Research

CENTER FOR DRUG EVALUATION AND RESEARCH
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SEP 19 1997
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CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologi
Drug Products (HFD 590)
Office of Drug Evaluation IV
ATT. DOCUMENT CONTROL ROOM #12B-3
5600 Fishers Lane
Rockville, MD 20857

/s/ [redacted]

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
Serial No. 47
NDA-20-760- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
Serial No. 48 *(Cover letter only)
GENERAL CORREPONDENCE

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to our August 11, 1997 meeting with the Division (b)(4) [redacted]

We are, herewith, submitting the slides that were presented by Michael DeBari, Pfizer Clinical Systems, and Linda Bulkovitch, Pfizer Regulatory Affairs (**Enclosure #1**).

As requested, a revised table listing encrypted Email user names, titles and Email addresses (RRT List) was forwarded to Dr. Leissa's attention via encrypted Email on August 18, 1997. It is currently being submitted to complete our records (**Enclosure #2**). Also requested was the enclosed updated query tracking chart (**Enclosure #3**).

A desk copy of this submission is being provided to Ms. Pauline Fogarty, Project Manager.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

APPEARS THIS WAY ON ORIGINAL [redacted]

Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

lab
Enclosures
Desk Copy: Ms. P. Fogarty (Complete)

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

NC

NEW CORRESP

ORIGINAL

Central Research

/s/ [redacted] 10/1/97 NAT

September 18, 1997

Department of Clinical Research

CENTER FOR DRUG EVALUATION AND RESEARCH
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SEP 19 1997
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CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologic
Drug Products (HFD 590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-3
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
[redacted] (b)(4)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
[redacted] (b)(4)

GENERAL CORREPONDENCE

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to our August 11, 1997 meeting with the Division [redacted] (b)(4)

We are, herewith, submitting the slides that were presented by Michael DeBari, Pfizer Clinical Systems, and Linda Bulkovitch, Pfizer Regulatory Affairs (**Enclosure #1**).

As requested, a revised table listing encrypted Email user names, titles and Email addresses (RRT List) was forwarded to Dr. Leissa's attention via encrypted Email on August 18, 1997. It is currently being submitted to complete our records (**Enclosure #2**). Also requested was the enclosed updated query tracking chart (**Enclosure #3**).

A desk copy of this submission is being provided to Ms. Pauline Fogarty, Project Manager.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

[redacted] APPEARS THIS WAY ON ORIGINAL

Ronald I. Trust

Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

lab
Enclosures
Desk Copy: Ms. P. Fogarty (Complete)

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

ORIGINAL

Central Research

BM

ORIG AMENDME

September 18, 1997

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologic
Drug Products (HFD 590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Department of Clinical Research

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
(b)(4)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)

(b)(4)

(b)(4)

[redacted]

A desk copy of this cover letter is being provided to Ms. Pauline Fogarty, Project Manager and to Dr. Alivisatos.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

Linda Bulkowitz for

Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

(b)(4)

[redacted]

lab
Enclosures
Desk Copy (Cover Letter): Ms. P. Fogarty
Dr. R. Alivisatos

APPEARS THIS WAY ON ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

ORIGINAL

Central Research

BM
ORIG AMENDMENT

Department of Clinical Research

August 26, 1997

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immunologic
Drug Products (HFD-590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

/s/ [redacted]
9/4/97

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
INFORMATION AMENDMENT - CLINICAL
ELECTRONIC SUBMISSION UPDATE

Reference is made to our pending New Drug Applications submitted on December 30, 1996. Reference is also made to our August 8, 1997 teleconference with Dr. Brad Leissa, Medical Team Leader and Ms. Pauline Fogarty, Project Manager, and to our August 15, 1997 submission that outlined corrections in clinical tables that need to be made to our pending New Drug Applications and Four Month Safety Update.

Provided herewith are hard copy corrected pages of the tables affected in our New Drug Applications and our Four Month Safety Update. These pages are being submitted to update the archival copy of the NDAs. The following are enclosed:

- A listing of the affected tables (**Enclosure #1**), depicting the page(s) within each table that was affected, followed by the corrected pages in yellow for ease of differentiation (**Enclosure #2**). Please note that the affected Appendix V study report listings are only being provided in the Esub, as per our original submission.
- A listing of additional corrections to complete or replace other sections of the NDAs in which either a table had been omitted or the incorrect table was placed in the NDAs (**Enclosure #3**), followed by the correct pages in yellow for ease of differentiation (**Enclosure #4**).
- A listing of case report forms that should have been included in the PDF versions of the update to the New Drug Applications (**Enclosure #5**). Please note that none of these additional CRFs (3) were for patients who prematurely discontinued from the trial for an adverse event.

Please note that each of these listings were previously provided in our August 15, 1997 submission.

Reference is also made to the FDA Form 483 which was prepared at the conclusion of FDA's inspection and cited certain discrepancies between source documents and information captured in the Case Report Forms for meningitis study **#154-149**. The relevant corrections in data, referred to as "Errata," were provided to the Office of Compliance as part of our response to the 483 which addresses these observations. This was also provided in our August 15, 1997 submission.

In regards to the Esub amendment, arrangements to deliver the (b)(4) [redacted] will be made in the near future. The Esub Update will contain electronic files of all enclosures, the Errata and the additional PDF Case Report Forms.

Please note that none of the files from the original (b)(4) [redacted] will be overwritten by this (b)(4) [redacted] update. The corrected tables will be listed first (with the corrected pages noted), followed by the table in error. Please also note that where many errors occurred in one section of the application (e.g., Appendix V of the study reports), a separate list will be used to outline the pages in a table that were changed. A separate table listing the corrected pages will therefore be used for studies **#154-134**, **#154-101**, **#154-128**, **#154-132**, **#154-139**, **#154-140**, **#154-119**, and **#154-125**.

As agreed with Ms. Fogarty, the hard copy archive will be corrected on Thursday, September 4, 1997.

As stated previously, none of the errors noted have any impact on the safety and efficacy conclusions presented in our NDAs.

A desk copy of this cover letter is being provided to Ms. Fogarty.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

Linda Bulkowitch for:

Ronald I. Trust. Ph.D., MBA
Associate Director II
Regulatory Affairs Department

APPEARS THIS WAY ON ORIGINAL

lab
Enclosures
Desk Copy: Ms. P. Fogarty (Cover letter only)
Serial No. 43 NDA-20,759
44 NDA-20,760 *(Cover letter only)

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BM

ORIG AMENDMENT

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

Central Research

Department of Clinical Research

August 15, 1997

Mark Goldberger, M.D., Director
Division of Special Pathogens and Immu
Drug Products (HFD-590)
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Dear Doctor Goldberger:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
INFORMATION AMENDMENT - CLINICAL
ELECTRONIC SUBMISSION UPDATE

Reference is made to our pending New Drug Applications submitted on December 30, 1996. Reference is also made to our August 8, 1997 teleconference with Dr. Brad Leissa, Medical Team Leader and Ms. Pauline Fogarty, Project Manager.

As you are aware, the Office of Compliance has recently completed GMP, clinical investigator and, most recently, a sponsor/monitor inspection at our facility (b)(4) [redacted]

The recently completed clinical inspection (b)(4) [redacted] facility also included a clinical investigator (b)(4) [redacted]

The FDA Form 483 which was prepared at the conclusion of this inspection cites certain discrepancies between source documents and information captured in the Case Report Forms for this meningitis study. The relevant corrections in data, referred to as "Errata," was provided to the Office of Compliance as part of our response to the 483 which addresses these observations. A copy of this Errata is provided in **Enclosure #1.**

Upon examination o (b)(4) files, we recently noted that on rare occasions (less than 5% of all tables in the NDA), blank lines were inadvertently substituted for lines of text in portions of tables (typically one to three lines, or occasionally, more in a few very large tables). This occurred during the ASCII → PDF conversion steps. We have identified a particular characteristic contained in the files in which these blank lines appeared. We then scanned our entire NDA and subsequently identified 333 tables in our original application and 11 tables in our 4-month Safety Update with this characteristic. Approximately 50% of these blank lines appeared in areas of the table that do not contain data (e.g., table header, lines separating header from body of table, or footer).

Enclosure #2 provides a listing of these tables and depicts the page(s) within each table that was affected. As discussed with Dr. Leissa and Ms. Fogarty, corrected pages for these tables will be provided for both the archive (b)(4) [redacted]

We will also be making additional corrections to complete or replace other sections of the Esub in which we have found additional errors. A list of the affected tables is provided in **Enclosure #3**.

Additional case report forms that should have been included will be provided in the upcoming (b)(4) update. A list of these case report forms is enclosed (**Enclosure #4**).

We believe that none of the errors noted have contributed to incorrect conclusions regarding the safety or efficacy of Trovan. Arrangements to deliver this amendment will be made in the near future.

Desk copies of this submission are being provided to Ms. Fogarty for distribution to all seven Medical Reviewers (Drs. R. Albrecht, R. Alivisatos, P. Coyne, D. Davis, B. Leissa, M. Makhene and R. Roca), herself, and Dr. Philip Colangelo, Pharmacological Reviewer.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

APPEARS THIS WAY ON ORIGINAL

Sincerely yours,

Ronald I. Trust

Ronald I. Trust. Ph.D., MBA
Associate Director II
Regulatory Affairs Department

lab
Enclosures
Desk Copies (9 complete): Ms. P. Fogarty
Serial No. 42 NDA-20,759
43 NDA-20,760 *(Cover letter only)

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Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

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Central Research

SU
NDA ORIG AMENDMENT

Department of Clinical Research

April 28, 1997

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Dear Doctor Feigal:

RE: NDA-20-759 - TROVAN® TABLETS (TROVAFLOXACIN MESYLATE)
NDA-20-760* - TROVAN® I.V. (ALATROFLOXACIN MESYLATE INJECTION)
FOUR MONTH SAFETY UPDATE

Reference is made to our pending New Drug Applications, NDA-20-759 and NDA-20-760 submitted December 30, 1996. Reference is also made to a January 28, 1997 teleconference with the Division and to our February 4, 1997 Four Month Safety Update proposal. On February 7, 1997 the Division agreed with this proposal.

Pursuant to 314.50 vi(b), we are submitting a Four Month Safety Update for the above referenced NDAs. As stated in the proposal, Pfizer is submitting Case Report Forms (CRFs) for safety discontinuations and serious adverse events. Please note that the CRFs are being provided electronically and all other information is being provided both hardcopy and electronically as in the original submission. Please also note that there are no new data for I.V.-only studies. Therefore, only oral treatment, which also includes I.V.-to-oral data, has been updated.

A desk copy of this submission is being provided to Dr. Philip Coyne, Primary Medical Reviewer and a cover letter to Ms. Pauline Fogarty, Project Manager. If you have any questions or need any additional information, please contact the undersigned at (860) 441-6991.

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ RCAL ☐ MEMO
CSO INITIALS

Sincerely yours,

Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

/s/ [redacted] 4/28/97

law
Enclosures
Desk Copies: Dr. Philip Coyne (Complete)
Ms. Pauline Fogarty (Cover Letter)
Serial No. 30 NDA-20-759
30 NDA-20-760 *(Cover letter only)

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Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

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Central Research

NEW CORRESPONDENCE

April 25, 1997

Department of Clinical Research

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug
Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Feigal:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to a March 18, 1997 discussion with Dr. Brad Leissa, Medical Team Leader.

Dr. Leissa had requested that Pfizer provide a revised contact list to include Dr. David Luke as the contact for the surgical studies (query #73). A revised contact list was forwarded to Dr. Leissa's attention via facsimile on March 19, 1997. In the interim, this list has been revised again to add Ms. Kristi Helmbold's pager number, Mr. Michael DeBari, Pfizer Email Contact, Dr. Daphne Lin, Biostatistics Reviewer, Dr. David Feigal, Acting Director and Kjeld Molvig, Division Systems Support.

A revised list is being submitted to our NDAs to complete our records. A desk copy of this submission is being provided to Dr. Leissa, Dr. Philip Coyne, Primary Medical Reviewer and Ms. Pauline Fogarty, Project Manager.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information in our files for NDA-20-759 and NDA-20-760.

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☑ N.A.L. ☐ MEMO
CSO INITIALS /s/ [redacted] DATE

Sincerely yours,

Linda Wypacki for:
Ronald I. Trust, Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

APPEARS THIS WAY ON ORIGINAL

law
Enclosure
Desk Copy: Ms. P. Fogarty
Dr. P. Coyne
Dr. B. Leissa
Serial No.: 29 NDA-20-759
29 NDA-20-760 *(Cover letter only)

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
APR 28 1997
MEGA DOC RM

Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

Central Research

BC

ORIG AMENDMENT

Department of Clinical Research

April 3, 1997

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug
Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Feigal:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our pending New Drug Applications, submitted December 30, 1996.

(b)(4)

(b)(4)

A desk copy of this submission is being provided to Dr. B.V. Shetty, Chemistry Reviewer and a copy of this cover letter is being provided to Ms. Fogarty, Project Manager.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information for our file for NDA-20-759 and NDA-20-760.

APPEARS THIS WAY ON ORIGINAL

Sincerely yours,

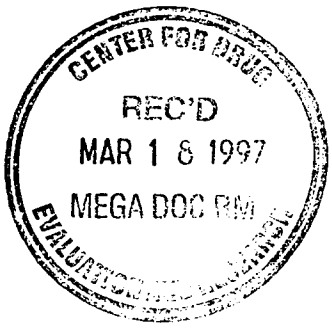
Linda Wysocki for:
Ronald I. Trust, Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

law
Enclosures
Desk Copies: Dr. B.V. Shetty (Complete)
Ms. Pauline Fogarty (Cover Letter)
Serial No.: 23 NDA-20-759
23 NDA-20-760 *Cover letter only

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO
CSO INITIALS /s/ 4/9/97 DATE

Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 860 441 4100

ORIGINAL



Central Research

Department of Clinical Research

March 17, 1997

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug
Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Feigal:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to a February 19, 1997 discussion with Ms. Pauline Fogarty, Project Manager. Ms Fogarty had indicated that the Environmental Safety Officer, Ms. Nancy Sager, had completed her review and had a few comments.

Enclosed are Ms. Sager's questions followed by our responses (Queries #48 and #49). A desk copy of this submission is being provided to Ms. Sager, Ms. Fogarty and Dr. B.V. Shetty, Chemistry Reviewer. If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991.

Please include this information for our files for NDA-20-759 and NDA-20-760.

APPEARS THIS WAY ON ORIGINAL

Sincerely yours,

Linda Wypocki for:
Ronald I. Trust, Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

law
Enclosures
Desk Copies (3): Ms. Nancy Sager (Complete)
Ms. Pauline Fogarty (Complete)
Dr. B.V. Shetty (Complete)
Serial No.: 20 NDA-20-759
20 NDA-20-760 *Cover letter only

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO

CSO INITIALS /s/ 3/19/97 DATE

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 203 441 4100

#1

Central Research

Department of Clinical Research

February 10, 1997

BC

NDA ORIG AMENDMENT

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

Dear Doctor Feigal:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
INFORMATION AMENDMENT- CHEMISTRY, MANUFACTURING AND CONTROL
GENERAL CORRESPONDENCE

Pursuant to 21 CFR 312.31, we are submitting an amendment to NDA-20-759 and NDA-20-760. Reference is made to our December 30, 1996 submission of NDA-20-759 and NDA-20-760. Reference is also made to our January 15, 1997 teleconference with Dr. B.V. Shetty, Chemistry Reviewer.

We are currently submitting information on manufacturing and testing sites in preparation for the pre-approval inspections for trovafloxacin mesylate and trovafloxacin mesylate tablets (100 and 200 mg) (**Enclosure #1**) and alatrofloxacin mesylate and alatrofloxacin mesylate injection (b)(4) as trovafloxacin/vial) (**Enclosure #2**). This information was previously provided by facsimile on January 23, 1997.

A desk copy of this cover letter is being provided to Ms. Pauline Fogarty, Project Manager. If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information for our files for NDA-20-759 and NDA-20-760.

Sincerely yours,

APPEARS THIS WAY ON ORIGINAL

Linda Wysocki for:
Ronald I. Trust. Ph.D.
Associate Director II
Regulatory Affairs Department

law
Desk Copy: Ms. Pauline Fogarty (Cover letter only)
Serial No. 11 NDA-20-759
11 NDA-20-760 (*Cover letter only)

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO

CSO INITIALS /s/ 1/9/97 DATE

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 203 441 4100

#1

Central Research

Department of Clinical Research

February 10, 1997

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

NEW CORRESPONDENCE

APPEARS THIS WAY ON ORIGINAL

Dear Doctor Feigal:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our December 30, 1996 submission of NDA-20-759 and NDA-20-760. Reference is also made to our December 6, 1996 meeting with the Division and our January 15, 1997 teleconference with Ms. Pauline Fogarty, Project Manager.

The Division had requested a list of Pfizer counterparts the Division reviewers can contact directly for minor clarifications. Enclosed is a chart listing the names, phone numbers, facsimile numbers and Email addresses for both the Division reviewers and their Pfizer counterparts. A desk copy of this submission is being provided to Ms. Fogarty and Dr. Philip Coyne, Primary Medical Reviewer.

Queries #10 and #20 have been completed with the submission of this information. If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information for our file for NDA-20-759 and NDA-20-760.

APPEARS THIS WAY ON ORIGINAL

Sincerely yours,

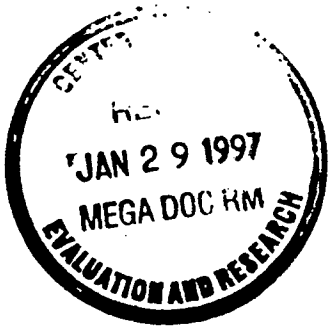
Linda Wypocki for:
Ronald I. Trust, Ph.D.
Associate Director II
Regulatory Affairs Department

law
Desk Copies: Ms. Pauline Fogarty
Dr. Philip Coyne
Serial No. 10 NDA-20-759
10 NDA-20-760 (*Cover letter only)

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO
CSO INITIALS /s/ [redacted] DATE 2/19/97

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 203 441 4100



Central Research

Department of Clinical Research

January 28, 1997

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

BM

NDA ORIG AMENDMENT

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Dear Doctor Feigal:

RE: NDA-20-759 - TROVAN® TABLETS (TROVAFLOXACIN MESYLATE)
NDA-20-760* - TROVAN® I.V. (ALATROFLOXACIN MESYLATE INJECTION)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to teleconferences with Dr. Matthew Thomas, Division of Scientific Investigations on September 4 and December 6 and 9, 1996. Reference is also made to our pending NDA submissions of December 30, 1996.

To assist Dr. Thomas in preparing for clinical study site inspections, he has requested the following information:

- A list of site locations and number of subjects enrolled for each pivotal study, by site.
- A table showing overall subject randomization, treatment with study drug, evaluability and completion status, including those evaluated for adverse events and discontinuations.
- A copy of the study report synopsis for each pivotal study.

In response to these requests we are providing the following:

- A copy of the cover letter to the NDAs, including all attachments (**Enclosure #1**). Please note that Attachment #6 contains a table outlining all pivotal studies by indication along with the basic study design of each.
- For each pivotal study we are providing the following (**Enclosure #2**):
  - A table outlining sites that randomized subjects, separated by country.
  - The study report synopsis.
  - The following tables from each study report:
    - Table 1.1 "Subject Disposition"
    - Table 1.2 "Study Evaluation Groups: Randomized Subjects"

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO

CSO INITIALS /s/ 2/3/97 DATE

- Table 1.3 "Number of Subjects Enrolled by Center: Randomized Subjects"

Please note that the pivotal study information provided in Enclosure #2 is presented in the order of Attachment #6 to the cover letter. We hope that this information provides sufficient information to help Dr. Thomas prepare for the site inspections.

Dr. Thomas also requested evaluability, discontinuation and safety information by site. We will be analyzing our data using these analysis parameters and will provide this information at a later date.

In addition, we will also be providing a list of study sites that were audited during the conduct of the studies. Please note that we did not exclude any clinical information from analysis as a result of any audit findings.

Enclosed is our Query Tracking Chart that describes the status of our NDA queries to date (**Enclosure #3**). Queries with completed responses have been shaded. We have designated Dr. Thomas' request as Queries #1 and #2.

A desk copy of this submission is being provided to Dr. Thomas and a copy of this cover letter is being provided to Ms. Pauline Fogarty, CSO. If you have any questions or need any additional information, please contact the undersigned at (860) 441-6991.

Sincerely yours,

APPEARS THIS WAY ON ORIGINAL

Linda Wypochi for:
Ronald I. Trust. Ph.D., M.B.A.
Associate Director II
Regulatory Affairs Department

law
Enclosures
Desk Copies: Dr. Matthew Thomas (Complete)
Ms. Pauline Fogarty (Cover Letter)
Serial No. 5 NDA-20-759
5 NDA-20-760 *(Cover letter only)

APPEARS THIS WAY ON ORIGINAL

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 203 441 4100

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS
DATE

#1

Central Research

BP
NDA ORIG AMENDMENT

January 20, 1997

Department of Clinical Research

noted
/s/ [redacted]
3/14/97

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug
Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JAN 21 1997
HFD-

Dear Doctor Feigal:

RE: NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made to our pending New Drug Applications, submitted December 30, 1996. Reference is also made to a December 30, 1996 discussion with Dr. Terry Peters, Pharmacology Reviewer and her request that Pfizer provide "raw data" of histopathology information, by animal, for studies of 3 months duration or greater, if not available in the study reports.

In response to her request please note that there were three studies of 3 months duration or greater, that study reports for these studies have been submitted to (b)(4) [redacted] NDA-20-759, and NDA-20-760 and that the histopathology data can be found in a study report appendix. For ease of review, we are providing (b)(4) [redacted] and page references for the studies:

- Study **93-783-16**: entitled "CP-99,219-27 6 Month Gavage Study In Beagle Dogs @ 7.5, 15, (7.5 bid), and 50 (25 bid) mg/kg" (b)(4) [redacted] Individual pathology data begins on page 144.

- Study **93-783-17**: entitled "CP-99,219-27 6 Month Oral Gavage Study In Sprague-Dawley Rats @ 25, 75, and 200 (100 bid) mg/kg" (b)(4) [redacted] Individual pathology data begins on page 194.

- Study **94-783-23**: entitled " CP-99,219-27 Six Month Oral Gavage Reversibility Study In Beagle Dogs @ 50 (25 BID) mg/kg/day (b)(4) [redacted] Individual pathology data begins on page 84 (this is liver data only).

Desk copies of this submission are being provided to Ms. Pauline Fogarty, CSO and to Dr. Peters. Please note that this query is query #4 on our enclosed tracking chart. All completed queries are shaded for ease of review.

If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information for our file for NDA-20-759 and NDA-20-760.

Sincerely yours,

APPEARS THIS WAY ON ORIGINAL

Linda Wypocki for:
Ronald I. Trust. Ph.D., M.B.A.
Associate Director I
Regulatory Affairs Department

law
Enclosures
Desk Copies (2): Ms. Pauline Fogarty
Dr. Terry Peters
Serial No.: 4 NDA-20-759
4 NDA-20-760 *Cover letter only

APPEARS THIS WAY ON ORIGINAL

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 203 441 4100

#1

Pfizer

Central Research

January 20, 1997

NEW CORRESPONDENCE

Department of Clinical Research

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug
Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

Dear Doctor Feigal:

RE: **NDA-20-759- TROVAN® Tablets (Trovafloxacin Mesylate)**
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate Injection)
RESPONSE TO FDA REQUEST FOR INFORMATION

Reference is made our December 30, 1996 submission of NDA-20-759 and NDA-20-760. Reference is also made to a December 20, 1996 discussion with Ms. Pauline Fogarty, Project Manager and our discussion regarding training the NDA reviewers on use of the Esub.

Enclosed please find a revised list of suggested reviewers to receive Esub training. This list supersedes the list provided to Ms. Addie Evans, CSO Support by facsimile on December 30, 1996. This request is Query #3. Enclosed is an updated tracking chart containing all queries received to date. Completed queries have been shaded for ease of review.

Arrangements have been made to provide training on use of the Esub for Dr. Philip Coyne (completed on January 6, 1997) and with other DAIDP staff (completed on January 14, 1997). We appreciate the opportunity to provide this orientation for electronic review of our Applications.

A desk copy of this submission is being provided to Ms. Fogarty. If you have any questions regarding this submission, please contact the undersigned at (860) 441-6991. Please include this information for our file for NDA-20-759 and NDA-20-760.

APPEARS THIS WAY ON ORIGINAL

Sincerely yours,

Linda Wysocki for:
Ronald I. Trust, Ph.D.
Associate Director I
Regulatory Affairs Department

law

Desk Copy: Ms. Pauline Fogarty
Serial No. 3 NDA-20-759
3 NDA-20-760 (*Cover letter only)

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO

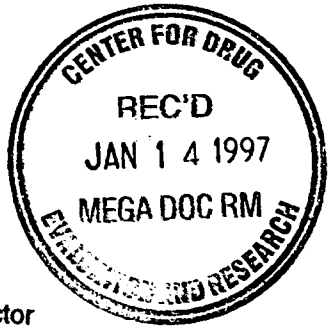
/s/ 1/22/97
CSO INITIALS DATE

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JAN 21 1997
HFD-

ORIGINAL

Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340
Tel 203 441 4100

NDA 20-760



Central Research

Department of Clinical Research

January 13, 1997

David Feigal, M.D., Acting Director
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research HFD #520
Office of Drug Evaluation IV
ATT: DOCUMENT CONTROL ROOM #12B-30
5600 Fishers Lane
Rockville, MD 20857

CONFIDENTIAL/TRADE SECRET INFORMATION SUBJECT TO 18-USC-1905 AND TO WHICH ALL CLAIMS OF PRIVILEGE AND CONFIDENTIALITY ARE ASSERTED IN BOTH STATUTORY AND COMMON LAW. FURTHER DISSEMINATION MAY ONLY BE MADE WITH THE EXPRESS WRITTEN PERMISSION OF PFIZER INC.

BP

NDA ORIG AMENDMENT

Dear Doctor Feigal:

RE: NDA-20-759 - TROVAN® Tablets (TROVAFLOXACIN MESYLATE)
NDA-20-760*- TROVAN® I.V. (Alatrofloxacin Mesylate)
(b)(4) [redacted]

Reference is made to our pending New Drug Applications for TROVAN® Tablets and TROVAN® I.V., submitted on December 20, 1996. Pursuant to 21 CFR 312.30 and 314.60 we are submitting, in triplicate, and in duplicate respectively, an amendment to our investigational New Drug Application for TROVAN® Tablets, Oral and an amendment to our New Drug Application for TROVAN® Tablets and TROVAN® I.V.

We are enclosing the following preclinical report conducted by the Department of Drug Safety Evaluation, Pfizer Central Research, Groton, Connecticut:

Study No. 96-783-32- *In Vitro* Cytogenetic Photomutagenicity Studies

In order to be consistent with our IND process, we will submit all Information Amendments for Pharmacology and Toxicology and Clinical Data to NDA-20-759, with cross-reference with NDA-20-760. If you have any questions, please contact the undersigned at (860) 441-6991.

APPEARS THIS WAY ON ORIGINAL [redacted]

Sincerely yours,

Ronald I. Trust

Ronald I. Trust. Ph.D., M.B.A.
Associate Director I
Regulatory Affairs Department

law
Enclosure
Serial No. 265 (b)(4) [redacted]
002 NDA-20-759
002 NDA-20-760 *(Cover Letter Only)

REVIEWS COMPLETED
CSO ACTION
☐ LETTER ✓ MEMO
/s/ [redacted]
CSO INITIALS DATE