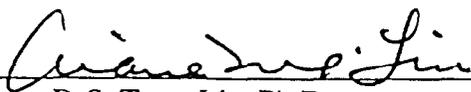


Restasis® as indicated would not lead to levels of CsA at or above 0.1 micrograms per milliliter in any tissue of the body.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on: October 22, 2003



Diane D-S. Tang-Liu, Ph.D.
Vice President of Pharmacokinetics and
Drug Metabolism

Attachment 6

DECLARATION OF H. DWIGHT CAVANAGH, M.D., Ph.D.

H. Dwight Cavanagh, M.D., Ph.D. makes the following declaration:

1. I am currently the Dr. W. Maxwell Thomas Chair, Professor and Vice-Chairperson of Ophthalmology, as well as Medical Director and Associate Dean for Clinical Services, Zale Lipshy University Hospital/The University of Texas Southwestern Medical Center at Dallas. I previously served on the full-time academic medical faculty of Johns Hopkins University, Harvard University, Emory University (F. Phinizy Calhoun, Sr., Professor and Chair of Ophthalmology, 1978-1987), and Georgetown University. I have also served as a past president of the Contact Lens Association of Ophthalmologists (CLAO) and the Castroviejo Corneal Society (CCS), executive director of the Association for Research in Vision and Ophthalmology (ARVO), and as a member (chair) of the Visual Sciences A and Neurosciences and Biobehavioral Sciences Study Sections of the National Institutes of Health. I served a six-year term as Editor-in Chief of the journal *Cornea* (1989-1995), and currently serve as Editor-in Chief of the *Eye & Contact Lens Journal* (formally the *CLAO Journal*). I have a longstanding interest in both corneal and contact-lens related research. A full statement of my education and professional accomplishments is contained in my curriculum vitae, which is attached as Exhibit A to this declaration.

2. I have been asked to comment both on the clinical use of Restasis eye drops (cyclosporine ophthalmic emulsion 0.05%) and whether Restasis is used for

treating eye infections. I specialize in diseases of the cornea and the external surface of the eye, including dry eye disease. In my specialty practice, which includes many dry eye patients, I have treated greater than 100 dry eye patients with Restasis. I was a clinical investigator for the Restasis phase III clinical trials, which studied Restasis as dry eye therapy.

3. Restasis is an eye drop preparation of cyclosporine A given twice daily for the treatment of moderate and severe dry eye disease. Generally, patients begin dry eye therapy with artificial tear eye drops applied to the eyes as needed to supplement their deficient tear production. Patients who are not adequately managed with artificial tear preparations are frequently candidates for Restasis therapy. The daily dose of Restasis is one drop twice daily to the affected eye, and a course of Restasis therapy typically lasts several months.

4. Although the exact mechanism of action of Restasis in dry eye disease is unknown, its therapeutic effect is thought to occur from the suppression of T-lymphocytes, not from any anti-infective properties. In fact, the T-lymphocyte suppressive effect of Restasis actually makes a patient's eye more susceptible to infection, and, as stated in the Restasis labeling, the use of Restasis is contraindicated in patients with active ocular infections.

5. As noted above, I have served and currently am serving as Editor-in Chief of a peer review scientific journal. My professional time is divided between patient care and active scientific research. As an active scientist, I am thoroughly abreast of the scientific ophthalmic literature. There are no data showing the clinical utility of

cyclosporine as an anti-infective. Any references in the literature to antifungal uses associated with Restasis, on examination, refer not to antifungal activity of the drug but rather to it being less likely than corticosteroids to encourage fungal growth after corneal transplant for certain corneal fungal infections. I have treated many fungal corneal ulcers, and would not consider Restasis as a therapy for this condition or any other ocular infection.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on: Oct 23 2003


H. Dwight Cavanagh, M.D., Ph.D. *FICS*
Professor and Vice Chairman of the
Department of Ophthalmology at the
University of Texas Southwestern Medical
Center.

Attachment 7

MEMORANDUM OF MEETING

Between: Division of Antibiotics
and
Division of New Drugs

November 7, 1962

Present: Dr. Donald C. Grove, DA
Mr. William Jester, DA
Dr. Ralph C. Smith, BM
Mr. Julius Hauser, BM
Dr. Earl L. Meyers, BM
Mr. Robert W. Jennings, BM
Miss Lee Geismar, BM

Purpose of the meeting was to discuss the handling of antibiotic new drug applications in the interim period extending from the present to May 1, 1963, when all antibiotics will come under certification by the Division of Antibiotics.

A proposal made November 1, 1962, by DND outlining a possible procedure was accepted in toto by the representatives of D.A. The points proposed were:

1. DND will continue to send new human antibiotic new drug applications to D.A. for review and comment as has been done in the past. This may aid D.A. in obtaining information for drafting regulations for publication at the time the drugs become subject to certification.
2. DND will continue to send antibiotic samples submitted with new drug applications to D.A. for biological testing. Previously samples have been sent to District Laboratories for verification for methods other than biological assays. However, D.A. may now want to check these other methods in connection with establishing methods suitable for certification regulations.
3. If correspondence is submitted for an application which has already been forwarded to D.A., DND will request the return of that application in order to answer the correspondence.
4. DND will continue to send to D.A. inactive human antibiotic new drug applications as they become available.

With regard to point (2) above, D.A. would like to receive all samples. It was settled that all samples submitted with a human antibiotic new drug application will routinely be sent to D.A. for verification of all methods and not to the District Laboratories.

The question of how to handle NDA 14008, Lyovac, Merck Sharp & Dohme, was raised.

1. Should DND handle the application completely at this time because 180 days are up before May 1, 1963?
2. Will it be sufficient to send the NDA to the MD assigned to D.A. for

Cont'd Memo of Meeting

comment on clinical data so that he will be able to continue the handling of the NDA after May 1, 1963?

3. Will this NDA come under Section 507 of the Act at all? The drug fulfills the requirements of the definition of an antibiotic as defined in the Act, however, because of its toxicity, its therapeutic use is restricted to antineoplastic action and is not utilized for antibiotic activity in infections.

It was suggested that it might be well to keep track of an anti-cancer drug like this by means of certification. It was also pointed out that many other cancer drugs are handled by New Drug procedure.

Dr. Grove pointed out that Dr. Lewis and his staff are already overburdened, and that comments on NDA's submitted might be delayed for a long time.

4. It was decided to submit this question of whether Lyovac should come under 507 or 505 to the Commissioner for a ruling.

Mr. Hauser thought it might be advisable to certify 50 or so batches of this drug, and then exempt it from certification if warranted.

An _____, which would also fit the definition of an antibiotic was also discussed. Dr. Meyers and Mr. Hauser felt that _____ should definitely be handled under 505, but this question should also be submitted to the Commissioner.

Final Conclusions reached:

1. November 1, 1962 proposal by DND to be used as a guideline for handling Antibiotic NDA's.
2. All antibiotic samples to be sent to D.A. for verification of all methods.
3. Lyovac and _____ questions to be submitted to the Commissioner for an opinion.

cc BM
LGeismar/pev
11/8/62
R/D init by:
ELMeyers

Lee Geismar, DND, BM

Attachment 8

Meractinomycin Chronology

- 5/1/63 Meractinomycin transferred to certifiable antibiotic status.
- 5/28/63 Final printed labeling received
- 5/31/63 Letter from W. B. Ronkin to Robert Dole of U. S. House of Representatives stating that there is no bar to the firm's continuing to supply the drug to qualified physicians.
- 7/10/63 Final printed labeling approved.
- 7/30/63 FDA received an inquiry from office of Senator Simpson concerning a complaint the Senator had received from a physician. The complaining physician indicated that MS&D had informed him that under the regulations of June 7, 1963 they could no longer supply the material. Mr. Kingham of the Senator's office was informed that as of May 1, 1963, this drug became a certifiable antibiotic and that DA was working with MS&D defining adequate methods and specifications for the product.
- 7/31/63 MS&D telephone Dr. Ruskin and was informed by him that as of May 1, 1963 this drug became a certifiable antibiotic
- 7/31/63 NDA sent to DA endorsed as ready for drafting of regulations after completion of review by DAD.
- 8/9/63 Letter from Commissioner Larrick to Senator Simpson stating that FDA is willing to certify this antibiotic for commercial marketing by firm employing appropriate controls. In the interim period, FDA will not object if firm continues to distribute the drug to those medical experts who have been investigating the drug.

Upon review of the drug, DA adopted necessary controls and standards within guidelines of the antibiotic certification program. In the absence of a submission for a toxicity test and due to the toxic nature of the drug, DA decided to require the full LD₅₀ mice test submitted in the NDA until further experience shows that it can safely be adopted to a toxicity test. It was decided that a test for histamine was unnecessary because the low concentration of the dosage form (0.5 mg) it would have to contain 20% histamine for a response as great as the histamine standard.

9/30/63 Letter from DA to MS&D to advise firm of the following:

- (1) Progress in establishing certification tests and methods of assay.
- (2) Need for additional samples needed by DA to verify controls.
- (3) Need to establish a master standard and working standard with assigned potencies.

10/14/63 Dr. Sinotte came in without appointment to discuss letter of 9/30/63.

- (4) DA concern for safety in handling the material in the laboratory.

11/4/63 MS&D submitted the following:

- (1) Samples requested on 9/30/63
- (2) Material to establish a master and working standard.
- (3) An agreement to the following proposals of letter of 9/30/63: a membrane filtration sterility test developed (and verified for this drug) by DA; the dosage for the pyrogen test; the conditions for the over moisture test.
- (4) Stability data and a request for a 24 month expiration.
- (5) A request for release of batches pending certification.

11/19/63 DA sent a reply to MS&D to letter of 11/4/63 stating batches will not be released until controls are complete.

11/21/63 DA sent a memorandum to DP concerning the hazards for laboratory personnel in meractinomycin assays after meeting with DAD on this subject.

1/2/64 DA received a memorandum from DP advising use of gloves and separate glassware and cautioning that this material is quite corrosive and highly toxic and that extreme caution should be exercised in the handling of this drug.

1/2/64 DA telephoned MS&D concerning safety precautions for handling of this drug in the laboratory.

1/2/64 Precautions submitted by telephone from MS&D sent to DAD for review.

- 1/3/64 DA received reply from DAD concerning the precautions.
- 1/3/64 Written confirmation sent to DA from MS&D concerning precautions suggested on 1/2/64 by telephone and testing of material received.
- 1/16/64 Telephone conversation between Dr. Nielsen (FDA) and Dr. Peck (MS&D) concerning toxicity testing of meractinomycin.
- 2/13/64 Meractinomycin chronology dated(2/7/64) submitted by MS&D at interview between MS&D personnel and W. B. Rankin to discuss three drugs, one of which is meractinomycin.
- 2/27/64 A copy of proposed regulations submitted to MS&D by DA including a microbiological activity test developed in the laboratory of DA in place of a submission in the NDA with an admitted error of 20 percent.
- 3/3/64 Letter from Dr. Jerome AMA to Dr. Wright stating that USAN council has agreed to name of Dactinomycin as the generic name for this substance ~~of~~ meractinomycin. The new name was suggested strongly by Dr. Waksman, the discoverer.
- 3/11/64 The Commissioner has designated the standard for dactinomycin.

Attachment 9

UNITED STATES GOVERNMENT

Memorandum

TO : Dr. C. N. Lewis

DATE: July 10, 1963

FROM : Dr. R. E. Barzilai

SUBJECT: "Cosmegen" (Merck Sharp & Dohme)

I. General information =

"Cosmegen" is the brand-name for Meractinomycin (also known as Actinomycin-D). This substance is one of closely related compounds designated as actinomycin A, B, C, D, I, J and X and obtained in various mixtures from a soil actinomyces (*Streptomyces Antibioticus*). "Cosmegen" however is obtained from *Streptomyces Parvullus* which yields the purest possible form of Actinomycin-D. All actinomycins are too toxic to be used as clinical antibiotics but their marked cytotoxicity is being utilized here in the palliation of certain neoplasms.

II. Toxicology-Pharmacology =

Animal toxicity studies have shown that this compound is "highly corrosive", has a narrow margin between lethal and therapeutic dosages and that it presents a marked degree of "cumulative toxicity". On the other hand, this drug had been considered and investigated as an antitumor agent because of this toxicity. Extensive human trials have established a certain range of "relative safety" in terms of indications, dosage schedules, route of administration, etc. This drug is being introduced as an adjunct palliative agent in the treatment of highly lethal malignancies and since it will be used only "under appropriate supervision of hospitalized patients", we believe that the factor of clinical relative safety should outweigh the factor of pharmacological absolute toxicity. Our Division of Pharmacology seems to agree with these general lines (memo of January 25, 1963).

III. Quality controls and procedures =

Several questions on quality controls and procedures were raised by Dr. W. W. Wright and Mr. R. W. Jennings (see appropriate memos and correspondence exchanged with firm). All these questions were answered satisfactorily in a letter dated April 5, 1963 and signed by Dr. L. P. Sinotte for the company. Miss L. Geismar's report of

Memo

To: Dr. C. N. Lewis

From: Dr. R. E. Barzilai

Subject: "Cosmegen" (Merck Sharp & Dohme) - 7/10/63

April 11, 1963 considers all controls and procedures as acceptable and makes no further request.

This drug will be the first antibiotic certified for antineoplastic uses. It is appropriate to mention here that our certification regulations will provide only for standards of antibiotic characteristics (= identity, microbiological bioassays, etc.). At present, no direct reliable and practical laboratory test to standardize antineoplastic activity is available. Therefore, despite the new indication proposed for this antibiotic drug, the same quality control methods are followed here as with any antimicrobial agent. A standardized control procedure of evaluating directly the antitumor activity of an antibiotic (= in fact, of any type of drug) will be a most welcome addition to our certification standards. The so-called ascites tumor cell plating technic is of some value for screening chemotherapeutic agents and its further uses are still under experimentation.

IV. Clinical studies =

These have been reviewed in detail by Dr. A. Ruskin (DND) who handled the NDA (# 14008) from its original submission on October 18, 1962 to May 1, 1963 when it was referred to us. In addition to our own review of clinical data, we discussed with Dr. Ruskin on July 5, 1963 the quantitative and/or qualitative value of all clinical studies and proposed labeling and it was generally agreed that we can safely approve the marketing of this drug under certain labeling changes. Most of these changes were requested in Dr. Ruskin's letter of April 15, 1963, and appeared in the revised brochure submitted by firm on May 23, 1963. All labeling may be now considered as satisfactory.

Conclusions

1. On the basis of the pre-clinical and data submitted in NDA # 14008 for "Cosmegen" (brand name for: Meractinomycin - Actinomycin-D), it is recommended that this drug be considered for certification.
2. Since this drug is the first antibiotic substance to become certified as an antineoplastic agent, it is suggested to follow and

Memo

To: Dr. C. N. Lewis

From: Dr. R. E. Barzilai

Subject: "Cosmegen" (Merck Sharp & Dohme) - 7/10/63

evaluate carefully all clinical experience with the marketed drug.

3. The "primary" indications approved in the labeling are: Wilm's tumor, rhabdomyosarcoma, and carcinoma of the testis and uterus (embryonal, teratocarcinoma, choriocarcinoma). All other indications in the brochure must remain listed as "experimental" until, of course, further convincing experience could modify our position.
4. The metabolic disposition of all actinomycins is still under investigation in various specialized research centers here and abroad. Experts anticipate interesting and possibly surprising results from these intensive studies. We should be alert for such scientific developments.

Attachment 10

Merck, Sharp & Dohme
Philadelphia Pa (AP 4-715)

August 9, 1953

Honorable Willard L. Simpson
United States Senate
Washington, D. C. 20510

Dear Senator Simpson:

This replies to your letter enclosing a copy of the communication
sent to you on July 22 by _____

_____ regarding actinocycin-D.

Dr. _____ state that they have been using actinocycin-D for investigational purposes but that recently the Merck, Sharp & Dohme drug firm notified them that because of Federal regulations actinocycin-D can no longer be distributed. For the reasons stated below, we wonder if there is not some misunderstanding about the position that the firm has taken.

Actinocycin-D has been the subject of a number of medical investigations and knowledge concerning this drug has reached the point where we are willing to permit its commercial marketing by firms who employ appropriate manufacturing and control procedures and label the article with proper information for its use by physicians. The Merck, Sharp & Dohme firm is aware of this decision and is consulting with members of our scientific staff with the goal of having the firm's actinocycin-D preparation certified by our Division of Antibiotics and released for commercial marketing. During the interim period, we will not object if the firm continues to distribute actinocycin-D to those medical experts who have been investigating the drug.

If Dr. _____ are still having difficulty in obtaining actinocycin-D from Merck, Sharp & Dohme, we would appreciate their sending the details to us. Neither the law nor our administration of it is intended to place obstacles in the way of legitimate research conducted by physicians of the calibre of Dr. _____

_____ We will be glad to take any proper action to help Merck, Sharp & Dohme resolve any problems which the firm may feel arise because of regulations promulgated by us.

what is status of product?
By [unclear]

[Handwritten initials]

Incidentally, you may wonder why actinomycin-D, intended for use in treating a form of cancer, requires certification as an antibiotic. This arises from the fact that actinomycin-D is produced by a microorganism and is an "antibiotic drug" within the definition of that term as used in the Food, Drug, and Cosmetic Act.

We hope these comments prove helpful. Please call on us if we can be of further service.

Sincerely yours,

Geo. F. Larrick
Commissioner of Food and Drugs

cc:
Congressional Liaison Officer
?
DND - Miss McEniry
DA - Dr. DiLorenzo
Mrs. Pendleton

MLYakowitz:cc 8-7-63
bb 8-9-63

R/D init:MCY
KLN
GPL

Attachment 11

MEETING MINUTES

MEETING DATE: August 16, 1999 **TIME:** 3:00 pm **LOCATION:** Conf. Rm. G

NDA 50-778

Meeting Request Submission Date: July 29, 1999

DRUG: ELLENCE (epirubicin hydrochloride)

SPONSOR/APPLICANT: Pharmacia & Upjohn

TYPE of MEETING:

Special Considerations – "old" antibiotic classification

FDA PARTICIPANTS:

Dr. Murray Lumpkin – Director, Office of Review Management

Dr. Robert Temple – Associate Director for Policy

Ms. Christine Rogers – Regulatory Counsel

Mr. David Fox – General Attorney

Dr. Renata Albrecht – Acting Deputy Director, ODE IV

Dr. Tom Hassell – Asst. Dep. Reg. Health, ODE IV

Dr. Lillian Gavrilovich – Deputy Director, DAIDP

Dr. James King – Microbiologist, DAIDP

Dr. Jim Timper – Chemistry Reviewer, DAIDP

Dr. Hasnukh Patel – DNDC I

Dr. John Simmons – Director DNDC I

Dr. Grant Williams – Medical Team Leader

Ms. Leslie Vaccari – Assistant to the Director, DODP

Mr. Patrick Guinn – Project Manager

INDUSTRY PARTICIPANTS:

Larry Moore – Pharmacia and Upjohn

Ken King – Pharmacia and Upjohn

Daniel Mannix – Pharmacia & Upjohn

Nancy Bue – Bue and Beardsley

Michael Berstein – Bue and Beardsley

BACKGROUND:

Pharmacia & Upjohn submitted a New Drug Application (NDA) on December 15, 1998, for epirubicin hydrochloride. Upon receipt of the application, epirubicin was assigned as NDA 21-010 and during the review process, epirubicin was noted to be an antibiotic and was reassigned as NDA 50-778. Once the NDA was reassigned as an antibiotic, it was also determined that epirubicin would be considered an "old" antibiotic according to The Guidance for Industry and Reviewers: Repeal of Section 507 of the Federal Food, Drug and Cosmetic

Act. This guidance document states that an antibiotic application received by the Secretary, on or before November 20, 1997, is considered an "old" antibiotic. An application for epirubicin was originally submitted on _____, by _____, and subsequently, received a Not Approvable. Pharmacia & Upjohn chose not to address the NA issues. Additional studies were performed and the new data was submitted as a new application.

Upon learning that the classification of epirubicin as an "old" antibiotic represented a barrier to Waxman/Hatch exclusivity, Pharmacia & Upjohn requested that the Agency reconsider the classification of epirubicin as an "old" antibiotic. The sponsor has submitted several documents that provided additional information for our consideration.

In addition, Pharmacia & Upjohn had filed for orphan drug designation on December 11, 1998, and recently received a letter denying that request. Upon appeal of the decision, Pharmacia & Upjohn was informed that the original decision not to designate epirubicin an orphan drug for the treatment of stage II node-positive and stage III breast cancer would remain unchanged. Pharmacia & Upjohn is still interested in pursuing this issue further.

Currently, NDA 50-778 for ELLENCE (epirubicin hydrochloride) Injection is under review. The application received a priority review status and was originally due June 15, 1999, however, the Agency received a major amendment June 9, 1999, and the User Fee Date was extended to September 15, 1999.

MEETING OBJECTIVES:

To discuss the policy on antibiotic classification, what constitutes an "old" antibiotic and in particular, how this relates to epirubicin.

DISCUSSION and DECISIONS REACHED:

Pharmacia & Upjohn believes that they deserve some economic protection rights for the development of epirubicin. At this time, there are two options that could be considered. The first option would be for the Agency to reconsider its judgement that epirubicin is an antibiotic, leading to 5 years exclusivity under Waxman/Hatch. The second option is for the Agency to reconsider its denial of the orphan drug application, leading to 7 years exclusivity.

- There was a lengthy discussion pertaining to the interpretation of the term "antibiotic drug".

According to 201(jj) of the Federal Food, Drug and Cosmetic Act, "The term 'antibiotic drug' means any drug (except drugs for use in animals other than humans) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline,

chloramphenicol, bacitracin, or any other drug intended for human use containing any quantity of any chemical substance which is produced by a micro-organism and which has the capacity to inhibit or destroy micro-organisms in dilute solution (including a chemically synthesized equivalent of any such substance) or any derivative thereof."

Both Pharmacia & Upjohn and the Agency agreed that the definition of an "antibiotic drug" could be interpreted in various ways. At this time epirubicin is designated as an "antibiotic drug", however, the Agency will consider the points raised during the meeting, by Pharmacia & Upjohn, on how the definition could be interpreted and make a final decision on its classification.

- There was brief discussion pertaining to orphan drug designation

[

It was agreed that the Division of Oncology Drug Products would discuss this issue with the Office of Orphan Products Development. The Agency has agreed to contact Pharmacia & Upjohn after our internal meeting and will provide information on how Pharmacia & Upjohn will need to proceed.

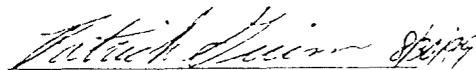
- It was agreed that if epirubicin receives orphan drug designation, Pharmacia & Upjohn will formally rescind their request, in writing, pertaining to the reconsideration of epirubicin being classified as an "old" antibiotic. In addition, the orphan drug designation must proceed the Action Letter. However, if epirubicin does not receive orphan drug designation, the Agency will need to formally provide the decisions, in writing, pertaining to orphan drug designation and "old" antibiotic classification.
- If Pharmacia & Upjohn receives some exclusivity, the outstanding Chemistry issues will need to be addressed before the Agency can take an Approval Action. However, if the exclusivity issues are not resolved before the User Fee Date of September 15, 1999,

Pharmacia & Upjohn has requested that the Agency issue an Approvable Letter.

ACTION ITEMS:

1. The Agency will consider the points raised during the meeting, by Pharmacia & Upjohn, on how the definition of an antibiotic could be interpreted and make a final decision on its classification.
2. An internal meeting between the Division of Oncology Drug Products and the Office of Orphan Products Development will be scheduled. The Agency will contact Pharmacia & Upjohn on how to proceed with this application.
3. The official meeting minutes will be forwarded to Pharmacia & Upjohn from the Agency.

The meeting was concluded at 4:15 pm. There were no unresolved issues or discussion points.


Patrick Guinn, Project Manager
Minutes preparer

Concurrence Chair:  9/1/94
Grant Williams, M.D.
Medical Team Leader

NDA 50-778
Meeting Minutes
Page 5

cc:

Original NDA 50-778
HFD-150/Div File
 /DPease
 /DSpillman

electronic only cc:

MLumpkin
RTemple
CRogers
DFox
RALbrecht
THassell
LGavrilovich
JKing
JImper
HPatel
JSimmons
RJustice
JBeitz
GWilliams
SHonig
RWood
SKim
LVaccari
DPease
DSpillman
PGuinn

MEETING MINUTES

Attachment 12

Drug jacket

MEMO RECORD	AVOID ERRORS PUT IT IN WRITING	DATE 8/16/82
FROM: Lee Ripper		OFFICE
TO: NDA 50-574 and 50-573		DIVISION
SUBJECT: Telecon with Mr. R. Raffa, Sandoz		
SUMMARY		
<ol style="list-style-type: none"> 1. Cyclosporin will be handled administratively as a Form 5, antibiotic. HFD-150 will handle xxx medical and pharmacological aspects. HFD-140 will handle M&C = microbiological aspects. All the samples must be submitted before the clock starts running. National Center for Antibiotic Certification must clear it before the monograph can be written; the monograph must be written before the NDAs can be approved. 2. NDA ≠ IND progress report. Some kind of progress report should be submitted even though the NDAs will be submitted this year. 3. When submitting something to more than one IND, please submit four copies if going to 2 INDs, five copies if addressed to 3 INDs. 4. Is Basel doing any work on cyclosporin for _____! Raffa did not know, apparently there is little or no work in this area due to the third and fourth world status of the countries where _____ is endemic. 5. Mr. Raffa stated that their recent pharmacology pre-NDA submission did not contain the acute tox info and appendix 8. They hope to have this ready soon. 		
<p>The firm is aiming for an October submission date, if not, it will be submitted in November. Basel has been informed for the need of cyclosporin B and C, etc. and are accumulating samples. We discussed a possible presentation to the ODAC in late January.</p>		
<p style="text-align: right;"><i>L Ripper</i></p>		
SIGNATURE	DOCUMENT NUMBER	