APPLICATION NUMBER:
65003

CHEMISTRY REVIEW(S)
ANDA APPROVAL SUMMARY

ANDA #: 65-003  FIRM: Abbott Laboratories

DRUG PRODUCT: Cyclosporine Capsules USP (modified)

DOSAGE: Capsules  STRENGTH: 25 mg, 50 mg and 100 mg

CAMP STATEMENT/EIR UPDATE STATUS: Acceptable (10/22/99)

BIO STUDY: Acceptable (5/28/99; 4/17/00)

METHOD VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
Not requested (USP drug)

STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION): The container/closure system used in the stability is the same as those described in the container section.

LABELING: Acceptable 1/14/00

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?): See below

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?): In Amendment 5/24/99, the executed batch records for capsule premix Lot 45-997-AR-03 and premix Lot 45-998-AR-03, and 50 mg (Lot 45-999-AR-03, and premix Lot 45-001-AR-03) for the 100 mg capsules. capsules and capsules are provided (see also page 843). capsules, capsules and capsules are filled for the 25 mg, 50 mg and 100 mg strengths, respectively (about 100% yield for each strength).

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?): The proposed production batch size is the maximum production batch size.

Specifications for active ingredient: Under #23A

Specifications for the finished product: Under #28 and #29

CHEMIST: Maria C. Shih  DATE: 4/18/00

SUPERVISOR: R. Adams  DATE: 4/18/00
1. CHEMIST'S REVIEW NO. #4

2. ANDA #65-003

3. NAME AND ADDRESS OF APPLICANT

Abbott Laboratories
Attention: Rebecca A. Welch
D-491, AP6B-1
100 Abbott Park Road
Abbott Park, IL 60064-3537

Phone: 847-937-8971
Fax: 847-937-8002

4. LEGAL BASIS FOR SUBMISSION

The reference listed drug is Neoral® (cyclosporine capsule for microemulsion) by Novartis (Sandoz' NDA #50-715).

The firm certifies that to the best of its knowledge, no other patent and no exclusivity period in force for the above referenced drug product.

5. SUPPLEMENT(S) N/A

6. PROPRIETARY NAME

Gengraf™ Capsules

7. NONPROPRIETY NAME

Cyclosporine Capsules USP (modified)

8. SUPPLEMENT(S) PROVIDE(S) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Original application: 12/19/97
Amendment 3/3/98 for Refuse to File 2/3/98
FDA acknowledgment: 3/19/98
New Correspondence: 5/13/98 (capsule dimpling)
Bio study (3/31/99 and 4/23/99)
Amendment 5/28/99 to N/A (MAJOR) letter 8/19/98
Amendment 12/7/99 to N/A (FAX) letter 11/15/99
Telephone Amendment 1/27/00
Amendments (Bio) 2/10/00, 2/17/00 and 3/1/00
Amendment 3/30/00 to N/A (FAX) letter 3/17/00

10. PHARMACOLOGICAL CATEGORY

Immunosuppressive agent for the prophylaxis of organ rejection in allogeneic transplants.
11. **Rx or OTC**  
**Rx**

12. **RELATED IND/NDA/DMF(s)**  
See under #37 **DMF CHECKLIST**

13. **DOSAGE FORM**  
Capsules

14. **POTENCY**  
25 mg, 50 mg and 100 mg

15. **CHEMICAL NAME AND STRUCTURE**  
Cyclosporine USP; C_{62}H_{111}N_{11}O_{12}.  1202.64  59865-13-3.

\[
\text{Ala} \text{ d-Ala} \text{ MeLeu} \text{ MeLeu} \text{ MeVal} \text{ N} \text{ C} \text{ CO} \text{ Abu} \text{ MeGly} \text{ MeLeu} \text{ Val} \text{ MeLeu}
\]


16. **RECORDS AND REPORTS**  
N/A

17. **COMMENTS**  
A. This application is a second generic version of cyclosporine capsules for microemulsion. The reference listed drug is Neoral® (cyclosporine capsule for microemulsion) by Novartis (formerly Sandoz), which is a soft-gel capsule. Abbott's product is manufactured by filling a homogeneous liquid into a hard capsule shell, and a gelatin band is subsequently applied.

A copy of specifications from Novartis on Neoral® Capsules (NDA #50-715) is attached in this review.
Redacted 2

pages of trade secret and/or confidential commercial information Chem #4
Status Summary for #65-003:

Labeling: Acceptable 1/14/00
EER: Acceptable 10/22/99
Sample: Not requested (USP drug)
Bio: Acceptable 4/17/00

18. CONCLUSIONS AND RECOMMENDATIONS
Approval recommended

19. REVIEWER: DATE COMPLETED:
Maria C. Shih 4/18/00
Redacted 16

16 pages of trade secret and/or confidential commercial information Chem
38. Chemistry Comments to be Provided to the Applicant

ANDA:  #65-003  APPLICANT:  Abbott Laboratories

DRUG PRODUCT:  Cyclosporine Capsules USP (Modified), 25 mg, 50 mg and 100 mg

The deficiencies presented below represent FAX deficiencies:

Chemistry Deficiencies:
Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
38. Chemistry Comments to be Provided to the Applicant

ANDA: #65-003  

APPLICANT: Abbott Laboratories

DRUG PRODUCT: Cyclosporine Capsules, 25 mg, 50 mg and 100 mg

The deficiencies presented below represent MAJOR deficiencies

Chemistry Deficiencies:
Sincerely yours,

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Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research