

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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) for filling the 25 mg (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 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 s the maximum production batch size.

Specifications for active ingredient: Under #23A

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

CHEMIST: Maria C. Shih *MCS* **DATE:** 4/18/00 *4/24/00*

SUPERVISOR: R. Adams *R.C. Adams* **DATE:** *4/25/00*

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. NONPROPRIETARY NAME
Cyclosporine Capsules USP (modified)
8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

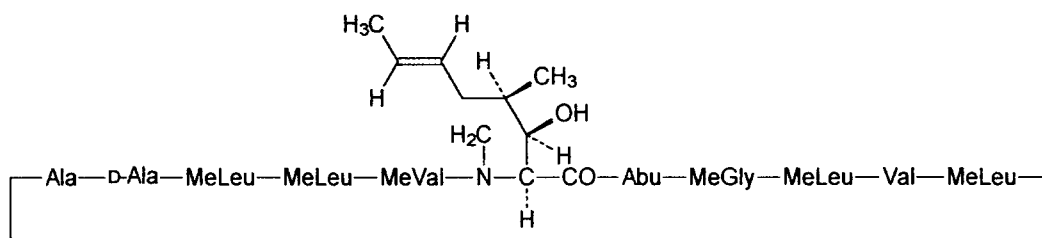
9. AMENDMENTS AND OTHER DATES:

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; C₆₂H₁₁₁N₁₁O₁₂. 1202.64 59865-13-3.



[R[R*,R*-(E)]]-Cyclic(L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-3-hydroxy-N,4-dimethyl-L-2-amino-6-octenoyl-L-α-aminobutyryl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl). CAS [59865-13-3].

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.

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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

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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,

for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

AUG 19 1998

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38. Chemistry Comments to be Provided to the Applicant

ANDA: #65-003APPLICANT: Abbott LaboratoriesDRUG PRODUCT: Cyclosporine Capsules, 25 mg, 50 mg and 100 mg

The deficiencies presented below represent MAJOR deficiencies

Chemistry Deficiencies:

Sincerely yours,

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