CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40251

CHEMISTRY REVIEW(S)

DIVISION APPROVAL SUMMARY

ANDA: 40-251 **DRUG PRODUCT:** Trihexyphenidyl Hydrochloride Elixir, USP

FIRM: Mikart, Inc.

DOSAGE: Elixir **STRENGTH:** 2 mg/5 mL

CGMP STATEMENT/EIR UPDATE STATUS:
CGMP: Statement provided on page 450 (vol 1.1).
EIR: Acceptable dated 4/14/99.

BIO STUDIES/BIOEQUIVALENCE STATUS:
Bio waiver granted on 9/23/97.

METHODS VALIDATION:
Field had picked up samples (on their own) and conducted methods verification and found them suitable. Results filed in volume 1.1.

STABILITY (conditions, containers and methods):
Bio batch was setup on stability in the proposed container/closure systems and data reported. The following are the firm's tests and specifications.

Organoleptic test	Clear liquid with a lime-peppermint aroma
pH	2.0-3.0
Assay (USP XXIII)	90-110%
Methylparaben	%
Propylparaben	%
Alcohol	%
Assay related substances	Individual NMT %
	Total NMT %
Antimicrobial effectiveness Testing*	Conforms
Average Fill volume	NLT %
Microbial limits	USP <61>
Total plate count	NMT cfu/mL
Yeast/mold	NMT /mL
Salmonella etc.	Absent

* To be conducted at initial and expiry test stations on the first three production lots.

LABELING REVIEW STATUS:
Acceptable dated 12/10/98.

STERILIZATION VALIDATION (If Applicable):
NA

BATCH SIZES:
Bio batch (identity #, drug substance source):
The drug substance supplier is
is used for the manufacture of bio batch. The bio batch size is L.

STABILITY BATCH (different from bio batch, manu. Site, process):
Stability batch is the same as bio batch.

PROPOSED PRODUCTION BATCH:
L is proposed for commercial scale. Reprocessing statement is enclosed on page 486.

COMMENTS:
None.

CHEMISTRY REVIEWER: Radhika Rajagopalan, Ph.D. /S/
DATE: 7/21/99 9/22/99

/S/ 9/22/99

1. CHEMISTRY REVIEW NO: 3

2. ANDA # 40-251

3. NAME AND ADDRESS OF APPLICANT
Mikart, Inc.
Attention: Ms. Cerie B. McDonald
1750 Chattahoochee Av., N.W.
Atlanta, GA 30318-2112

4. LEGAL BASIS FOR SUBMISSION
The applicant certifies, that to the best of their knowledge there are no patents referenced in the "orange book", 16th Edition. Also, no exclusivity exists for the listed drug Artane® elixir manufactured by Lederle Laboratories.

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Trihexyphenidyl Hydrochloride Elixir, USP

8. SUPPLEMENTS PROVIDED FOR
N/A

9. AMENDMENTS AND OTHER DATES
Firm
March 10, 1997-- Original Submission
May 13, 1997-- ANDA original amendment
November 9, 1998 -- ANDA Major amendment
July 9, 1999-- ANDA Minor amendment
August 31, 1999--Amendment

FDA
April 22, 1997-- Refusal to file letter
May 19, 1997-- Date accepted for filing by FDA
May 27, 1997-- Date of communication of the above by FDA
July 7, 1998-- Chemistry & Labeling deficiencies
September 23, 1997-- Bio waiver granted
December 10, 1998-- Acceptable label review
June 24, 1999-- Minor Deficiency fax (Chemistry)
August 3, 1999-- Phone call by PM for clarifications on Chemistry issues

10. PHARMACOLOGICAL CATEGORY
Adjunct treatment for all forms of Parkinsonism

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(S)
-- Type DMF -
NDA # N06773
Refer to section 37 for all Type DMFs

13. DOSAGE FORM
Elixir

14. POTENCY
2 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
Trihexyphenidyl Hydrochloride

$C_{20}H_{30}NO.HCl$; M.W. = 337.94

16. RECORDS AND REPORTS
N/A

17. COMMENT
None.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval recommended.

19. REVIEWER:

Radhika Rajagopalan, Ph.D.

/S/

DATE COMPLETED:

7/21/99; 9/21/99

9/22/99