CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76067

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

#: 76-067 SPONSOR: Clay-Park Labs, Inc.

DRUG AND DOSAGE FORM: **Mometasone Furoate Ointment, USP**

STRENGTH (S): **0.1%**

TYPES OF STUDIES: Pilot (Vasoconstrictor) and Pivotal (Bioequivalence) Studies.

CLINICAL STUDY SITE (S):

ANALYTICAL SITE (S): N/A

STUDY SUMMARY: Pilot and pivotal studies are acceptable.

DISSOLUTION: N/A

DSI INSPECTION STATUS

Inspection needed: NO	Inspection status:	Inspection results:
First Generic No New facility _____ For cause _____ Other _____	Inspection requested: (date) Inspection completed: (date)	

PRIMARY REVIEWER : CHANDRA S. CHAURASIA, Ph. D. BRANCH : I

INITIAL : /S/ DATE : 5/30/2001

TEAM LEADER : YIH-CHAIN HUANG, Ph. D. BRANCH : I

INITIAL : /S/ DATE : 5/31/2001

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : /S/ DATE : 6/13/2001

Mometasone Furoate Ointment USP,
0.1%
ANDA #76-067
Reviewer: Chandra S. Chaurasia

Clay-Park Labs, Inc.
Bronx, NY 10457
Submission date:
December 21, 2000

Review of a Pilot Dose Response Study and a Pharmacodynamic Bioequivalence Study

I. Introduction

Clay-Park Labs is seeking approval to market its Mometasone Furoate Ointment USP, 0.1%. The firm has submitted pilot dose-response and pivotal in vivo bioequivalence studies based on the OGD guidance "*Topical Dermatologic Corticosteroids: In Vivo Bioequivalence, June 2, 1995*".

Type of Submission: Original ANDA: **First Generic**

Reference Listed Drug: Elocon® (NDA #19543, April 30, 1987; manufactured by Schering)

Indications: Mometasone Furoate USP, 0.1% is a medium potency corticosteroid indicated for the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Financial Disclosure: Form FDA 3454 was submitted. The firm certifies that it has not entered into any financial arrangement with clinical investigators and that its certification is in compliance with 21 CFR part 54 and 54.2(d) [Vol. 1.2, pp. 65].

II. Pilot Study – Dose-Response Study of Mometasone Furoate Ointment USP, 0.1% (Vasoconstrictor Assay: Study No. 9916922)

A. Objective:

To determine the dose-response relationship for Elocon® Ointment 0.1% to be used to estimate the ED_{50} of D1 and D2 parameters for use in a full bioequivalence study.

B. Study Information:

Clinical Site:

Principal Investigator:

Clinical Dates: February 12-13, 2000 (Vol. 1.5, pp. 1164)

Subjects: Twenty normal healthy non-tobacco-using (for 30 days prior to dosing) Caucasian female subjects between 18 and 23 years of age, weighing between 109 and 172 lbs. (Vol. 1.5, pp. 1234) were enrolled in the study. All the 20 subjects completed the study.

Inclusion/Exclusion Criteria: Listed in vol. 1.5, pp. 1174.

Subject Selection:

Subject selection for this study was carried out according to the procedure described in the OGD guidance (*Topical Dermatologic Corticosteroids: In Vivo Bioequivalence, June 2, 1995)*. Potential study participants were screened to determine blanching response to Elocon® Ointment (mometasone furoate ointment) 0.1%. A 10 µL of the ointment was applied to the upper arm (above the forearm), and left in place for 45 minutes (± 5 minutes). The site was evaluated visually approximately 6-9 hours after application. All subjects were selected based on a demonstrated blanching response and the absence of any clinically significant findings on the medical history or clinical assessment . Selected subjects had no history of allergy or hypersensitivity to any corticosteroids or to any topical products. They had no skin condition or coloration that would interfere with the placement of test sites or the response or assessments of skin blanching. All subjects tested negative on a urine pregnancy test (Vol. 1.2, pp. 1162).

Dosing Procedures:

Drug Treatment:	Elocon® Ointment (Mometasone Furoate Ointment) 0.1%
Manufacturer:	Schering
Lot No.:	#9UHK404
Expiration Date:	June, 2001

Study Design: One Period, Randomized, Vasoconstrictor Study

Confinement/Restrictions: Described in Vol. 1.5, pp. 1164. The subjects were dosed on 02/12/00 and completed the study approximately 28 hours after first application.

Application and Removal: Listed in Vol. 1.5, pp. 1235-1236.

The sponsor has followed the *staggered application and synchronized removal methodology* in this study.

Eleven circular (approximately 1.6 cm diameter) application sites were designated on the flexor surface of each forearm between the wrist and the elbow. The sites were marked with numbers 1-11 on the right arm from wrist to elbow and 12-22 on the left arm from wrist to elbow for ease of identification. Care was taken that sites were not placed within 3 cm of the wrist or antecubital fossa. Of the eleven sites, nine were assigned as treatment sites as determined by the randomization schedule (Vol. 1.5, pp. 1182). Two untreated reference sites were also randomly assigned on each arm as ChromaMeter and visual reference sites.

After baseline chromameter and visual readings, an open washer was positioned over each site and taped to the forearm using hypo-allergenic paper tape on the sides of the washer so that the treated area was not occluded. The washers were not closer than 2 cm apart center-to-center. Using a 250 uL glass syringe, a 10 uL application of Elocon 0.1% ointment was applied to the 9 assigned sites on each arm at times according to the randomization schedule. Two sites on each arm were left untreated.

Elocon® ointment 0.1% was applied to 9 sites on both arms at 3, 6, 15, 30 and 45 minutes and 1, 2, 3 and 4 hours prior to removal. The applied ointment was spread evenly over the skin surface at each site with the conical tip of a 1.5-mL microcentrifuge tube.

All applications were removed at the same time point (0.0 hour), with the shortest duration removed first. The washers were detached and the residual surface treatment was removed by gently wiping several times with a cotton ball. The untreated site on each arm was similarly wiped with a clean cotton ball.

Dermal Assessment:

The ChromaMeter CR-300 was used in this study to measure the reflective colors from the skin surface.

ChromaMeter operators and visual evaluators assessed the degree of blanching response at each site prior to treatment application and at 0, 2, 4, 6, 8, 10,12, 20, and 24 hours after removal. All sites were assessed under standard fluorescent lighting and at room temperature. All assessments were made within 5 minutes of their scheduled time. Prior to the study, precision of the ChromaMeter operators were evaluated (please see below).

The chromameter operators and visual evaluators were blinded as to the duration of application at each site. Chromameter assessments were based on a-scale measurements. Visual scoring used the following rating scale:

0 = No pallor; no change from surrounding area.
1 = Mild pallor; slight or indistinct outline of application site.
2 = Moderate pallor; discernable outline of application site.
3 = Intense pallor; clean, distinct outline of application site.

Precision of ChromaMeter (Method Validation):

Data Evaluation: Areas under the response curve for the ChromaMeter assessments were determined from the a-scale reading. The methodology is summarized below:

- The post-dose chromameter a-scale reading at each site and assessment time was first adjusted by subtracting the average value of the duplicate pre-dose (baseline) readings at the site. This baseline adjustment normalized the chromameter readings for variations in skin tone between the different sites on each subject's forearms.

- To compensate for skin tone changes that occur over time, the average baseline-adjusted value for the untreated sites on each arm was subtracted from the baseline-adjusted chromameter value for each site on the same arm at each assessment time. These "corrected, baseline-adjusted" chromameter values were used in all subsequent analysis.

- The sponsor has calculated chromameter areas-under-the-effect curve (AUEC) from 0-24 hours from the corrected, base-line adjusted readings by the linear trapezoidal method. To conform to the usual form of the Emax model, all chromameter areas were multiplied by –1 before fitting and statistical analyses.

- The ED50 and Emax parameters were estimated using a population fitting technique.

C. Study Results:

Protocol Deviations: The firm has stated the following minor protocol deviations related to the drug removal from the application site:

All subjects' 0-hour visual assessment was performed +1 minute outside $\pm$ 5 minute window. Subjects 5 through 20, ten-hour visual assessments were performed +1 minute outside $\pm$ 5 minute window. Subjects 19 and 20, 20-hour hour visual assessments were performed +1 minute outside $\pm$ 5 minute window (Vol.1.5, pp.1165).

The firm notes that subject #13 was +5 lbs. over the 20% weight criteria required by the protocol. The PI approved the subject for dosing.

Adverse Events: None of the subjects reported any adverse events during the study.

Pharmacodynamic Data Analysis:

- The firm estimated ED_{50} and Emax parameters using a population fit of the chromameter results by means of version 1.5 (Vol. 1.5, pp. 1166). The firm 's population fit of chromameter data are provided in Vol. 1.5, 1167-1168.

- The Division of Bioequivalence also analyzed the AUEC vs. dose duration data based on the non-linear mixed effect modeling method using The results of population analyses performed by the Division and the firm are summarized below. The population model results using log-normalized and normal data are given in Figures 1 and 2, respectively.

Table 1: Estimation of Pharmacodynamic Parameters Using Nonlinear Mixed Effect Modeling (N=20)

ED50 Distribution	Data Analyst	Population Parameters	
		ED50 (%CV)	Emax (%CV)
Normal	Sponsor	25.1 (69.3)	40.6 (26.7)
	DBE	29.8 (73.2)	42.1 (26.4)
Log-Normal	DBE	41.7 (135.9)	49.5 (16.2)

The firm's analyses were based on the use of a heteroscedastic error variance with normal distribution for ED_{50}. The ED_{50} value calculated by DBE using the same error variance is similar to the one reported by the firm. However, based on exploratory graphic analyses of the model output, DBE determined that the ED_{50} was log-normally distributed (Figures 1 and 2). Therefore the analyses were repeated using the same error variance but log-normal distribution for ED_{50}. Based on that analysis the ED_{50} value was found to be 41.7 minutes.

D. Conclusion:

The Division's estimate for the ED_{50} for Elocon® ointment is 41.70 minutes. The value reported by the firm is 25.1 minutes based on chromameter results. Based on the pilot study results, the sponsor has used dose duration of 30 minutes for the pivotal bioequivalence study. The testing at 30-minutes duration of application would provide evaluation in the sensitive region of the dose-response curve, based on the Emax model (Singh et. al, *Clinical Pharmacology and Therapeutics*. 66; 347-56, 1999). In addition, the Guidance accepts a demonstration of dose duration-response based on D1 within 0.25-0.5 times the observed ED50 and D2 within 2-4 times the observed ED50.

A lower duration of application (D1) at 15 minutes and a higher duration (D2) at 60 minutes were included to establish eligibility for BE comparisons.

E. Comment:

The ED_{50} duration (30 min) and the use of D1 (15 min) and D2 (60 min) are acceptable.

III. Pivotal Study: Bioequivalence of Mometasone Furoate Ointment, 0.1% Study No. 10016924

A. Objective:

To demonstrate *in vivo* bioequivalence between Clay-Park's Mometasone Furoate Ointment, 0.1% and Schering's Elocon® Ointment, 0.1%.

B. Study Information:

Clinical Site:

Principal Investigator:

Dosing Dates: (Vol.1.2, pp. 93)

Group 1: September 23, 2000 (Subject # 01-21)
Group 2: September 30, 2000 (Subject # 22-42)
Group 3: October 07, 2000 (Subject # 43-60)
Group 4: October 21, 2000 (Subject # 61-82)

Subjects: Eighty-two normal healthy female subjects (38 Caucasian, 2 Asian and 1 Indian) between 18 and 44 years of age, weighing between 105 and 188 lbs. were enrolled in the study (Vol. 1.2, pp. 139). All 82 subjects completed the study.

Inclusion/Exclusion Criteria: Listed in Vol. 1.2, pp. 103.

Subject Selection: Same as that given for the pilot study.

Product Information: The following drug products were used in this study:

Test: Mometasone Furoate Ointment USP, 0.1%, Clay-Park Labs, Inc., Lot #RX081, Mfg. Date: 08/01/00; Batch Size: Bio Batch kg, Scale-up Batch kg

Reference: Elocon® (Mometasone Furoate) Ointment, 0.1%, Schering Corporation, Lot #9UHK404, Exp. Date: 06/01 (same as used in the Pilot Study).

Study Design: The pivotal study was conducted as one-period study involving randomized applications of the test formulations to both arms along with the replicate applications of the calibrator doses (D1 and D2) of the reference product.

Randomization: The ointments were applied to 6 sites on the flexor surface of each forearm determined by the randomization schedule listed in Vol. 1.2, pp. 111-112. Consistent with the Agency guidance, the treatment randomization provided complementary applications on left and right arms. Two untreated (control) sites were also randomized on each arm.

Application and Removal: The arms of each subject were washed with a mild soap and gently dried at least 2 hours prior to initial dosing.

The sponsor has followed the *staggered application and synchronized removal methodology* in this study.

- Eight circular (approximately 1.6 cm diameter) application sites were designated on the flexor surface of each forearm between the wrist and the elbow. The sites were marked with numbers (1-8) on the right arm and 9-16 on the left arm from wrist to elbow for ease of identification. After baseline chromameter (in duplicate) and visual readings, an open washer was positioned over each site and taped to the forearm using hypo-allergic paper tape on the sides of the washer so that the treated area was not occluded.

- Using a 250 uL glass syringe with a 'Repeating Dispenser", a 10 uL application of each formulation was applied to the assigned sites on each arm according to the randomization schedule. The test and reference products were each applied to 2 sites on each arm. The reference product was also applied to 2 additional sites on each arm for D1 and D2 duration. Two sites on each arm were left untreated. All applications were spread evenly over the skin surface at each site with the tip of a 1.5-mL polypropylene microcentrifuge tube. The Guidance On Topical Corticosteroids (June 2, 1995) recommends two sites per arm for untreated control treatments and one site per arm for the RLD D1 and D2 treatments.

- Baseline assessments were started approximately 2 hours prior to first application. The test and reference products were applied to 6 sites on each arm; these treatments were applied 15 (reference product only), 30 (test and reference products) and 60 (reference product only) minutes prior to removal. All sites were on, or staggered about, the midline axis of the subject's forearm and at least 3 cm form the wrist or antecubital fossa. A schedule of the actual dosing (application) times, removal times and treatment sites is provided in Vol. 1.2, pp. 142-145.

- All applications were removed at the same time point (0 hour). The washers were detached and the residual surface treatment was removed by gently wiping the application site at least 3 times with separate cotton balls. The untreated site on each arm was similarly wiped with a clean cotton ball.

Housing and Meals: Described on page Vol. 1.2, pp. 93.

Confinement/Restrictions: Described on page Vol. 1.2, pp. 93.

Dermal Assessment: Same as that provided for the pilot study.

Precision of the ChromaMeter Operators (WSB, YIW, MLG, RC, RWM and LMT) Validation: Same as described above for the pilot study.

The degree of skin blanching was determined both by chromameter and visual assessments at each site prior to treatment application, and at 0, 2, 4, 6, 8, 10, 12, 20 and 24 hours after drug removal (Vol. 1.2, pp. 92). The 0-hour assessments were made within 15 minutes of their scheduled time and the 2- through 24-hour assessments were made within + 5 minutes of their scheduled time. All assessments were made under standard fluorescent lighting and at room temperature with the ChromaMeter assessment always preceding the visual evaluation.

Data Evaluation: Described on page 94, Vol. 1.2

- The post-dose chromameter a-scale reading at each site and assessment time was obtained as described in the pilot study.

- Chromameter areas under the effect curve (AUEC) from 0-24 hours were calculated from the corrected, baseline-adjusted readings by the linear trapezoidal method.

- The firm has also submitted visual scores data. The DBE does not use visual score data for BE evaluations. The visual assessment data were, therefore, not reviewed.

- The ratio of the mean area under the response curve for the reference 60-minute duration (D2) to that of the 15-minute duration (D1) was calculated for each subject. Subjects whose D2/D1 ratio was at least 1.25 were considered qualified for inclusion in the statistical analysis. If a subject showed no vasoconstrictor response for the D1 (where, D1 is equal to or less than 0 and D2 is greater than 0) duration, but the response ratio for the D2 duration to the ED50 duration was at least 1.25, then the subject also qualified for inclusion in the bioequivalence evaluation. The firm states that the data from 50 subjects qualified for inclusion within these criteria using ChromaMeter results.

- method for calculating confidence intervals was applied to the chromameter area results from qualifying subjects.

C. Study Results:

Eighty-two (82) subjects entered and all of them completed the study.

Protocol Deviations: Minor deviations noted (Vol. 1.1, pp. 94).

Adverse Events: A total of six mild adverse events were reported by the firm. Of these 5 events of headache (Subject #10, 17, 21, 27 and 33) were judged remotely related to the study drugs, and one event of redness to the left of site #01, subject 47 pre-dose was judged unrelated to the study drugs (Vol. 1.1, pp. 146).

Pharmacodynamic Data Analysis:

1. Based on the D2/D1 ratio criterion of 1.25, 41 subjects qualified for the chromameter results.

2. The firm also accepted the subjects whose mean D1 values indicated no blanching but whose D2 showed blanching if the ratio of her D2 duration to the ED_{50} for the reference was at least 1.25. Based on this, 9 additional subjects (#2, 7, 37, 47, 64, 70, 71, 74 and 75) were qualified for chromameter data. These subjects were included by the firm in the statistical analysis for the evaluation of the bioequivalence for the test and reference products. Thus, the firm's chromameter data analysis is based on a total of 50 subjects. The reviewer, in consultation with Dr. Gur Jai Pal Singh, DBE/OGD also included these subjects for the statistical analysis since the AUEC of these subjects were in the order of D2>R>D1 (Figure 3).

3. Mean $AUEC_{(0\text{-}24)}$ for the 50 evaluable subjects for the test and reference products are shown in Table 2 below.

4. method for calculating confidence intervals was applied to the chromameter data from the qualifying subjects. The results are given in Table 3A below. Results based on method calculations performed by the sponsor are represented in Table 3B.

5. The firm has also submitted visual scores data. The OGD guidance does not require documentation of bioequivalence based on both chromameter and visual assessment of vasoconstriction. The visual assessment data were, therefore, not reviewed.

Table 2. Mean AUEC Test and Reference and Ratios of Mean AUEC D2/Mean AUEC D1

Sub #	Test Mean	Ref Mean	Mean D1	Mean D2	D2/D1
2	11.75	13.34	-5.47	24.38	-4.46
3	28.15	17.48	2.67	30.46	11.41
6	12.39	7.60	6.13	16.16	2.64
7	9.52	5.13	-1.94	10.15	-5.24
8	16.71	24.27	17.89	26.86	1.50
9	31.03	24.74	28.48	39.45	1.39
12	35.72	39.46	10.81	27.70	2.56
13	9.20	8.29	1.56	8.34	5.35
14	6.31	8.40	9.78	20.55	2.10
16	25.12	28.95	20.75	57.20	2.76
17	23.67	23.94	2.51	58.94	23.48
20	-0.11	6.00	0.23	28.08	122.07
21	19.13	21.38	17.46	31.23	1.79
23	12.09	19.80	10.13	32.08	3.17
24	23.41	17.65	11.86	27.38	2.31
25	18.04	16.80	17.16	34.11	1.99
29	-3.23	-0.10	3.05	28.65	9.39
32	8.90	2.74	2.45	16.77	6.86
33	16.10	20.90	14.84	60.40	4.07
34	-3.75	-3.43	6.32	15.93	2.52
35	24.69	36.25	14.58	50.74	3.48
37	15.28	18.35	-3.74	23.91	-6.39
38	2.38	1.96	3.96	10.92	2.76
39	8.14	3.09	7.05	29.08	4.12

40	26.71	41.92	14.47	48.69	3.36
42	14.19	15.16	7.29	49.09	6.74
43	5.83	6.00	6.96	9.35	1.34
44	1.64	0.77	9.43	13.22	1.40
46	21.68	31.12	22.92	28.98	1.26
47	6.65	3.92	-4.55	6.24	-1.37
48	14.68	16.94	4.51	54.83	12.16
56	18.98	22.71	3.12	31.67	10.17
58	-5.14	-0.01	2.53	24.24	9.58
59	11.87	32.41	6.16	30.13	4.89
61	18.06	10.94	9.63	18.41	1.91
62	20.95	20.21	2.60	36.87	14.21
64	15.45	10.00	-3.25	22.95	-7.06
65	5.80	14.38	6.73	18.69	2.78
67	2.24	11.50	6.93	20.92	3.02
68	25.98	24.00	12.25	27.78	2.27
69	18.27	7.96	14.62	65.29	4.47
70	21.47	14.73	-3.22	48.30	-15.02
71	3.23	1.97	-1.32	12.66	-9.63
72	5.73	10.05	1.80	10.85	6.04
73	1.48	2.68	5.70	14.73	2.58
74	-3.95	4.12	-2.46	23.33	-9.48
75	7.49	3.90	-1.03	10.13	-9.83
76	13.57	10.52	4.90	18.05	3.68
79	-8.54	-1.00	5.59	16.19	2.90
81	23.57	13.86	13.17	21.89	1.66

Table 3A. Mean results for chromameter evaluation of Clay-Park's test ointment vs. Elocon® Ointment using Method (**as calculated in the Division**).

		Mean Area Under the Curve		T/R (%)	Confidence Intervals	
Assessment Method	N	Test	Reference		Low	High
Chromameter	50	12.770	13.874	92.04	80.6	105.3

Table 3B. Mean results for chromameter evaluation of Clay-Park's test ointment vs. Elocon® Ointment using Method (***as reported by the sponsor***: Vol. 1.2, pp. 324).

		Mean Area Under the Curve		T/R (%)	Confidence Intervals	
Assessment Method	N	Test	Reference		Low	High
Chromameter	50	12.770	13.874	92.04	81.9	103.4

IV. Formulation. Components and composition of the test and the reference products are given in the Table below:

Table 4. Comparative Formulations (Not to be released under FOI):

Ingredients	Test, %w/w	Reference, %w/w*	Type
Mometasone Furoate, USP			Active
Hexylene Glycol, NF			Inactive
Phosphoric Acid, NF			Inactive
Propylene Glycol Monostearate,			Inactive
White Beeswax			Inactive
White Petrolatum, USP			Inactive
Purified water			Inactive

*%w/w based on values as reported in COMIS for NDA 19543

All inactive ingredients used in the test products are within the IIG range for topical dermatologic route of administration.

V. Comments:

1. The firm has conducted pilot and pivotal dose response studies according to OGD Guidance *Topical Dermatologic Corticosteroids: In Vivo Bioequivalence, June 2, 1995* on topical corticosteroids.

2. Based on the chromameter evaluation of skin blanching, test product's $AUEC_{(0-24)}$ was % lower than the reference product. The 90% confidence intervals for chromameter results are within the 80-125% range. The study is acceptable.

3. There was no severe medical event reported during pilot and pivotal studies.

VI. Recommendations

The in vivo bioequivalence study conducted by Clay-Park Labs, Inc., on its Mometasone Furoate Ointment USP, 0.1%, Lot #RX081 comparing it to the reference product, Elocon® (mometasone furoate) Ointment 0.1%, Lot #9UHK404, has been found acceptable by the Division of Bioequivalence. The results of this vasoconstriction study demonstrate that Clay-Park's Mometasone Furoate Ointment USP, 0.1% is bioequivalent to the reference product, Elocon® 0.1% ointment manufactured by Schering.

The firm should be informed of the above recommendations.

/S/

Chandra S. Chaurasia
Review Branch I
Division of Bioequivalence

Date: 5/30/2001

RD INITIALED YHUANG
FT INITIALED YHUANG /S/ Date: 5/31/2001

Concur: /S/ Date: 6/13/2001
Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

for

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANTS

ANDA: 76-067 APPLICANT: Clay-Park Labs, Inc.

DRUG PRODUCT: Mometasone Furoate Ointment USP, 0.1%

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these regulatory reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation in not approvable.

Sincerely yours,

/S/

for Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CC: ANDA 76-067
ANDA DUPLICATE
DIVISION FILE
HFD-652/Bio Secretary-Bio Drug File
HFD-650/C.Chaurasia

Endorsements: (Draft and Final with Dates)
HFD-652/CS Chaurasia 5/25/2001 5/30/2001
HFD-655/Gur J.P. Singh 5/28/01
HFD-652/YC Huang 5/31/2001
HFD-617/KScardina 6/14/01
HFD-650/Dale Conner 6/13/2001

Printed in ~~Draft~~ Final on 05/~~25~~30/2001 5/30/2001

BIOEQUIVALENCY – **Acceptable**

Submission Dates:
12/21/2000

1. **Other Options** — **Strength: 0.1%**
Bio study
Pilot Study — Outcome: **AC**

2. **Other Options** — **Strength: 0.1%**
Bio study
Pivotal Study — Outcome: **AC**

Outcome Decisions:
AC - Acceptable
NC - No Action
UN - Unacceptable
IC - Incomplete

WinBio Comments:

- Pilot and pivotal studies on mometasone furoate ointment 0.1% are acceptable.