CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 74-579

CHEMISTRY REVIEW(S)

12/14/95

/S/

COMPOSITION OF THE DRUG

Include the composition of the drug stating the name and amount of each ingredient whether active or not, contained in a stated quantity of the drug in the form in which it is distributed:

BETAMETHASONE DIPROPIONATE CREAM USP, 0.05%

INGREDIENTS:	% w/w	mg/g	Variations*
Mineral Oil USP XXII			within IIG range
Petrolatum USP XXII			within IIG range
Cetyl Alcohol,			other IIG range
Phosphoric Acid			other IIG range
Ceteth			within IIG range
Monobasic Sodium Phosphate			within IIG range
Propylene Glycol,			other IIG range
Betamethasone Dipropionate USP XXII	0.066	0.66***	3% excess
Stearyl Alcohol,			other IIG range
Chlorocresol			within IIG range
Water, Purified			

NOTES:

* Excess is within allowable limits
** Brand of polyethylene Glycol 1000 Cetyl Ether (Ceteth
*** Equivalent to 0.05% of Betamethasone plus excess of 3% (0.0515%)

These amounts are accurate for each gram of material packaged in any size container.

SECTION VI

1. CHEMISTRY REVIEW NO. 4

2. ANDA # 74-579

3. NAME AND ADDRESS OF APPLICANT

Clay-Park Labs, Inc.
Attention: Mr. Gabriel Lebovic
1700 Bathgate Avenue
Bronx, NY 10457

4. BASIS OF SUBMISSION
The ANDA is based on the approved listed drug, Diprosone Cream 0.05%, the subject of NDA 17-536, held by Schering Corporation. There is no remaining patent or marketing exclusivity for Diprosone Cream 0.05%.

5. SUPPLEMENT(s) N/A 8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

6. PROPRIETARY NAME
None.

7. NONPROPRIETARY NAME
Betamethasone Dipropionate Cream USP, 0.05%

9. AMENDMENTS AND OTHER DATES:

12/01/94 Original ANDA.
04/20/95 NA letter.

10/11/95 Minor amendment (chemistry and labeling).
10/24/95 Telecon from Angela Payne to firm.
11/12/95 Final printed inserts.
01/25/96 NA letter - chemistry only.

10/29/96 Chemistry minor amendment.
11/01/96 Gratuitous labeling telephone amendment - corrected color printed carton labeling.
11/20/96 **First telecon** requesting chemistry information.
11/21/96 Minor chemistry amendment responding to telecon of 11/20/96.
12/06/96 **Second telecon** requesting chemistry information.
12/12/96 Minor chemistry amendment responding to telecon of 12/06/96.
12/17/96 **Third telecon** requesting chemistry information.
12/18/96 Minor chemistry amendment responding to telecon of 12/17/96.
01/09/97 **Fourth telecon** requesting chemistry information.
01/10/97 Minor chemistry amendment responding to telecon of 01/09/97.

01/14/97 **Fifth telecon** requesting chemistry information.
01/15/97 Minor chemistry amendment responding to telecon of 01/14/97.
01/17/97 **Sixth telecon** requesting chemistry information.
01/17/97 Minor chemistry amendment responding to telecon of 01/17/97. **This amendment contained a commitment to submit impurities limits for the DS and DP as a CBE supplement before marketing the product.**
05/20/97 NA-Minor letter for GMP problems.

09/12/97 N/AA amendment: APET results were submitted as a follow-up to Clay-Park's letter to FDA dated 12/18/96. The results are acceptable.
10/17/97 Minor amendment in response to NA letter of 5/20/97. GMP problems have been remedied.
11/10/97 Minor telephone amendment - commitment to make viscosity a part of the release and stability specs.

10. PHARMACOLOGICAL CATEGORY

A synthetic adrenocorticosteroid for dermatologic use. Indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses.

11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s) For DMFs, see checklist.

13. DOSAGE FORM Cream 14. STRENGTH 0.05%

15. CHEMICAL NAME AND STRUCTURE

$C_{28}H_{37}FO_7$ 504.59 *CAS-5593-20-4*

Pregna-1,4-diene-3,20-dione, 9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-,(11β,16β)

9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate

16. RECORDS AND REPORTS N/A

17. COMMENTS

All CMC deficiencies have been resolved.

The following Points have been completed and are satisfactory:

31. Samples and Results
32. Labeling
33. Establishment Inspection
34. Bioequivalence Status

18. CONCLUSIONS AND RECOMMENDATIONS

ANDA 74-579 CAN BE APPROVED.

19. REVIEWER:	DATE COMPLETED:	DATE REVISED:
Eugene L. Schaefer, Ph.D.	11/7/97	11/17/97

Endorsed by P.Schwartz, Ph.D.

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Chemistry

1. CHEMISTRY REVIEW NO. 3

Completed (AP) 1/17/97.

2. ANDA # 74-579

Revised (NA-Minor) 4/11/97.

3. NAME AND ADDRESS OF APPLICANT

Clay-Park Labs, Inc.
Attention: Ms. Tsion Bellete
1700 Bathgate Avenue
Bronx, NY 10457

4. BASIS OF SUBMISSION

The ANDA is based on the approved listed drug, Diprosone Cream 0.05%, the subject of NDA 17-536, held by Schering Corporation. There is no remaining patent or marketing exclusivity for Diprosone Cream 0.05%.

5. SUPPLEMENT(s) N/A 8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

6. PROPRIETARY NAME

None.

7. NONPROPRIETARY NAME

Betamethasone Dipropionate Cream USP, 0.05%

9. AMENDMENTS AND OTHER DATES:

12/01/94 Original ANDA.
04/20/95 NA letter.

10/11/95 Minor amendment (chemistry and labeling).
10/24/95 Telecon from Angela Payne to firm.
11/12/95 Final printed inserts.
01/25/96 NA letter - chemistry only.

10/29/96 Chemistry minor amendment.
11/01/96 Gratuitous labeling telephone amendment - corrected color printed carton labeling.
11/20/96 **First telecon** requesting chemistry information.
11/21/96 Minor chemistry amendment responding to telecon of 11/20/96.
12/06/96 **Second telecon** requesting chemistry information.
12/12/96 Minor chemistry amendment responding to telecon of 12/06/96.
12/17/96 **Third telecon** requesting chemistry information.
12/18/96 Minor chemistry amendment responding to telecon of 12/17/96.
01/09/97 **Fourth telecon** requesting chemistry information.
01/10/97 Minor chemistry amendment responding to telecon of 01/09/97.

01/14/97 **Fifth telecon** requesting chemistry information.
01/15/97 Minor chemistry amendment responding to telecon of 01/14/97.
01/17/97 **Sixth telecon** requesting chemistry information.
01/17/97 Minor chemistry amendment responding to telecon of 01/17/97.

10. PHARMACOLOGICAL CATEGORY

A synthetic adrenocorticosteroid for dermatologic use. Indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses.

11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s) For DMFs, see checklist.

13. DOSAGE FORM Cream 14. STRENGTH 0.05%

15. CHEMICAL NAME AND STRUCTURE

$C_{28}H_{37}FO_7$ 504.59 *CAS-5593-20-4*

Pregna-1,4-diene-3,20-dione, 9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-,(11β,16β)

9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate

16. RECORDS AND REPORTS N/A

17. COMMENTS

Deficiencies in the following points have been resolved:

20. Components and Composition
28. Laboratory Controls - Finished Dosage Form
29. Stability

The following Points have been completed and are satisfactory:

32. Labeling
34. Bioequivalence Status

The following Point **has not been completed** for ANDA 74-579:

33. Establishment Inspection

The applicant's facility will not be ready for inspection until 12/97, so Shirnette Ferguson found the facility to be **unacceptable** on 4/10/97.

18. CONCLUSIONS AND RECOMMENDATIONS

ANDA 74-579 CAN NOT BE APPROVED, because the applicant's facility is not ready for inspection and thus is unacceptable.

19. REVIEWER:	DATE COMPLETED:	DATE REVISED:
Eugene L. Schaefer, Ph.D.	1/17/97	4/11/97
Endorsed by P.Schwartz, Ph.D.	1/22/97	

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Chemistry

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 74-579

3. NAME AND ADDRESS OF APPLICANT

Clay-Park Labs, Inc.
Attention: Ms. Tsion Bellete
1700 Bathgate Avenue
Bronx, NY 10457

4. BASIS OF SUBMISSION

The ANDA is based on the approved listed drug, Diprosone Cream 0.05%, the subject of NDA 17-536, held by Schering Corporation. There is no remaining patent or marketing exclusivity for Diprosone Cream 0.05%.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME

None.

7. NONPROPRIETARY NAME

Betamethasone Dipropionate Cream USP, 0.05%

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

9. AMENDMENTS AND OTHER DATES:

12/01/94 Original ANDA.
04/20/95 NA letter.
10/11/95 Minor amendment (chemistry and labeling).
10/24/95 Telecon from Angela Payne to firm.
11/12/95 Final printed inserts.

10. PHARMACOLOGICAL CATEGORY

A synthetic adrenocorticosteroid for dermatologic use. Indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses.

11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s) For DMFs, see checklist.

13. DOSAGE FORM

Cream

14. POTENCY

0.05%

15. CHEMICAL NAME AND STRUCTURE

$C_{28}H_{37}FO_7$ 504.59 *CAS-5593-20-4*

Pregna-1,4-diene-3,20-dione, 9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-,(11β,16β)

9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate

16. RECORDS AND REPORTS N/A

17. COMMENTS

ANDA 74-579 is **deficient** in the following Points:

20. Components and Composition
28. Laboratory Controls - Finished Dosage Form
29. Stability

The following Points **have not been completed** for ANDA 74-579:

33. Establishment Inspection
34. Bioequivalence Status

The labeling is **satisfactory.**

18. CONCLUSIONS AND RECOMMENDATIONS

The ANDA is **NOT APPROVED - MINOR AMENDMENT.**

19. REVIEWER: DATE COMPLETED:

Eugene L. Schaefer, Ph.D. 12-7-95
Endorsed by P.Schwartz, Ph.D. 12-27-95

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Chemistry

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 74-579

3. NAME AND ADDRESS OF APPLICANT

Clay-Park Labs, Inc.
Attention: Jay Jadeja
1700 Bathgate Avenue
Bronx, NY 10457

4. BASIS OF SUBMISSION

The ANDA is based on the approved listed drug, Diprosone Cream 0.05%, the subject of NDA 17-536, held by Schering Corporation. There is no remaining patent or marketing exclusivity for Diprosone Cream 0.05%.

A debarment certification is provided in Section XXI.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME

None.

7. NONPROPRIETARY NAME

Betamethasone Dipropionate Cream USP, 0.05%

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

9. AMENDMENTS AND OTHER DATES:

12/01/94 Original ANDA.

10. PHARMACOLOGICAL CATEGORY

A synthetic adrenocorticosteroid for dermatologic use. Indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses.

11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s) For DMFs, see checklist.

13. DOSAGE FORM

Cream

14. POTENCY

0.05%

15. CHEMICAL NAME AND STRUCTURE

$C_{28}H_{37}FO_7$ 504.59 *CAS-5593-20-4*

Pregna-1,4-diene-3,20-dione, 9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-,(11β,16β)

9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate

16. RECORDS AND REPORTS N/A

17. COMMENTS

ANDA 74-579 is **deficient** in the following Points:

20. Components and Composition
23. Raw Material Controls - Other Ingredients
26. Container
28. Laboratory Controls - In-Process
28. Laboratory Controls - Finished Dosage Form
29. Stability
32. Labeling

The following Points **have not been completed** for ANDA 74-579:

33. Establishment Inspection
34. Bioequivalence Status

An **acknowledgement** will be requested from the applicant regarding:

28. Laboratory Controls - In-process (100% packaging of exhibit lots in future)

18. CONCLUSIONS AND RECOMMENDATIONS

The ANDA is **NOT APPROVED - MINOR AMENDMENT.**

19. REVIEWER: DATE COMPLETED:

Eugene L. Schaefer, Ph.D. 4-12-95
Endorsed by P.Schwartz, Ph.D. 4-12-95

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