

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-076

CHEMISTRY REVIEW(S)

NDA 22-076

**Locoid® (hydrocortisone butyrate) Lotion, 0.1%
Ferndale Laboratories, Inc.**

Tarun Mehta, M.Sc.

ONDQA Pre Approval Marketing Division II, Branch III

CHEMISTRY REVIEW

Chemistry Review Data Sheet

Table of Contents

Table of Contents.....	2
Chemistry Review Data Sheet.....	3
The Executive Summary	6
I. Recommendations.....	6
A. Recommendation and Conclusion on Approvability.....	6
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable.....	6
II. Summary of Chemistry Assessments.....	6
A. Description of the Drug Product(s) and Drug substance(s).....	6
B. Description of How the Drug Product is Intended to be Used.....	7
C. Basis for Approvability or Not-Approval Recommendation.....	7
III. Administrative.....	8
A. Reviewer's Signature.....	8
B. Endorsement Block.....	8
Chemistry Assessment.....	9
I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data.....	9
S DRUG SUBSTANCE [Name, Manufacturer].....	9
P DRUG PRODUCT [Name, Dosage form].....	14
A APPENDICES.....	44
R REGIONAL INFORMATION.....	44
II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1.....	44
A. Labeling & Package Insert.....	44
B. Environmental Assessment Or Claim Of Categorical Exclusion.....	52
III. List Of Deficiencies Communicated.....	53
Appendix 1: Deficiencies.....	53
Appendix 2: EES Reports.....	54
Appendix 3: Letter for DMF.....	56

b(4)

CHEMISTRY REVIEW

Chemistry Review Data Sheet

Chemistry Review Data Sheet

1. NDA #: 22-076
2. REVIEW #: 1
3. REVIEW DATE: 15-May-2007
4. REVIEWER: Tarun Mehta
5. PREVIOUS DOCUMENTS: Original NDA: 26- JUNE-2006

6. SUBMISSION(S) BEING REVIEWS:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	June 26, 2006
Original amendment	December 21, 2006
Original amendment	March 16, 2007

7. NAME & ADDRESS OF APPLICANT:

Name: Ferndale Laboratories, Inc.
Address: 780 W. 8 Mile Road
Ferndale, MI 48220
Representative: Richard A. Hamer, VP Regulatory/Clinical & QA
Telephone: 248-548-0900 X 433

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: LOCOID
- b) Non-Proprietary Name (USAN): Hydrocortisone Butyrate
- c) Code Name/# (ONDQA only): NA
- d) Chem. Type/Submission Priority (ONDQA only):
- Chem. Type: 3
 - Submission Priority: Standard
9. LEGAL BASIS FOR SUBMISSION: FD&C Act 505 b (1)

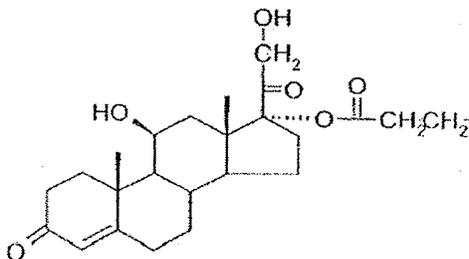
CHEMISTRY REVIEW

Chemistry Review Data Sheet

10. PHARMACOL. CATEGORY: Corticosteroid
11. DOSAGE FORM: Lotion (Proposed)
12. STRENGTH/POTENCY: 0.1% w/w
13. ROUTE OF ADMINISTRATION: Topical
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM): -
 SPOTS product – Form Completed
 Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: Pregn-4-ene-3, 20-dione, 11, 21 – dihydroxy -17-[(1-oxobutyl) oxy (11B)-]



Chemical Structure:

Molecular weight: 432.56
Molecular formula: C₂₅H₃₆O₆

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ₁	STATUS ¹	DATE REVIEW COMPLETED	COMMENTS
—	II	—	—	1	Adequate	10-April-2007	Reviewed by Tarun Mehta



CHEMISTRY REVIEW



Chemistry Review Data Sheet

—	III	—	—	1	Adequate	6-Mar-2007	Donald Klein
—	III	—	—	4	Adequate		Tarun Mehta
—	III	—	—	4	Adequate		Tarun Mehta
—	III	—	—	3	No changes made in — since 1992 Appendix - 2	9/1/2003	Reviewed by Craig Bertha

b(4)

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF is not review, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

18. STATUS:

ONDQA:

CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES- Ferndale Lab	Acceptable	Sept. 21, 2006	S. Fergusons (HFD-322)
EES - —	Acceptable	Sept. 19, 2006	J.D.Ambrogio (HFD-322)

b(4)

CHEMISTRY REVIEW

Chemistry Assessment Section

The Chemistry Review for NDA 22-076

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Due to the unresolved issue on the nomenclature for the dosage form, from the Chemistry, Control, and Manufacturing standpoint, this NDA is recommended for "Approvable".

B. Recommendation on Phase 4 (Post-Marketing) Commitments

None

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug substance

The drug product "Locoid® (Hydrocortisone Butyrate, USP) 0.1% Lotion is an _____ formulation containing 0.1% (1mg/g) of _____ hydrocortisone butyrate-17. Drug substance is well dispersed in emulsion. Locoid lotion is white to off white smooth homogenous lotion and indicated for the atopic dermatitis.

b(4)

Hydrocortisone butyrate is widely used as a drug substance in marketed topical drug products, and is also listed under USP monograph.

Ferndale Laboratories currently markets the locoid family of products, which include cream, leprocream, ointment, and solution. The proposed lotion formulation is _____

b(4)

Although the sponsor proposed "lotion" designation for this product, based on its physical properties (rheology), it should be designated as "Cream", and this has been communicated to the sponsor, but no corrective response has been submitted.

The applicant's Ferndale, MI sites have conducted product development, manufacturing of the clinical supply and will manufacture to-be-marketed drug product. During the product development, the applicant has successfully completed process parameters ranging study to establish ruggedness of manufacturing process and controls. Drug product composition for the clinical supply and proposed commercial formulation are

CHEMISTRY REVIEW

Chemistry Assessment Section

identical. A commercial size _____ batch at proposed scale-up site using the proposed manufacturing process and equipments was successfully completed. b(4)

Various tests such as description, pH, viscosity, hydrocortisone butyrate ID, assay, related substances, assay of preservative agents and microbial growth are listed in specifications to control the quality of the drug product at the time of release and during the shelf life. The specifications deemed satisfactory.

Drug product is packaged in 4g _____ for professional sampling. Trade samples are supplied in 2oz and 4 oz _____ Information provided for the proposed container/closure deemed adequate for regulatory requirements. However, concern is raised about difficulty of delivering approximately 20% of deliverable amount of prescribed product from proposed container due to rheology of drug product. Sponsor was made aware of this fact during tele-con conducted on May 10, 2007. b(4)

Stability results derived from the three bulk stability batches packaged in the proposed container/closure concluded that the drug product meet the shelf life specifications up to 30 months for 25°C/60% RH condition in the to-be-marketed container system. Based on the stability results, sponsor's request for 24 months expiration for drug product can be granted.

The drug substance (hydrocortisone butyrate, USP) is a _____ and manufactured by _____. The Chemistry, Manufacturing, and Control information of the drug substance is provided in DMF _____ which deemed adequate to support this application. b(4)

B. Description of How the Drug Product is Intended to be Used

Locoid lotions, 0.1% applies as a thin film to the affected skin areas by rubbing gently, two _____ times daily. Locoid lotion may be used in adult and pediatric patients 3 months of age or older. Locoid lotion, 0.1% indicated for the relief of the _____. b(4)

C. Basis for approvable recommendation:

CMC information for Locoid lotion 0.1% adequately assures Ferndale laboratories' capability to manufacture the quality drug product. In support of its robust manufacturing capability applicant has provided adequate manufacturing process and ruggedness data. The drug product quality and safety is monitored by the adequate specifications throughout the drug product life cycle. Marketed container/closure made up of widely used _____ material, the packaging design is relatively simple to use. Adequate stability data support 24-months of expiry date and the quality of product during the shelf life. b(4)

CHEMISTRY REVIEW

Chemistry Assessment Section

However, upon close examination of the clinical supply samples' physical appearance and drug product's rheology data, ONDQA recommends that proposed dosage should be labeled as "Cream" and not "Lotion".

NDA is deemed "Approvable" due to this incorrect dosage form.

The final recommendation from the Office of Compliance for the drug product and drug substance manufacturer is **ACCEPTABLE** (see Attachment).

III. Administrative

A. **Reviewer's Signature:** Electronically entered in the DFS

B. **Endorsement Block:**

Chemist Name/Date:	Tarun Mehta, M.Sc,
Branch Chief:	Moo-Jhong Rhee, Ph.D
Project Manager:	Melinda Bauerlien

48 Page(s) Withheld

X Trade Secret / Confidential (b4)

 Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

Withheld Track Number: Chemistry- 1

**This is a representation of an electronic record that was signed electronically and
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/s/

Tarun Mehta
5/15/2007 03:28:58 PM
CHEMIST

Moo-Jhong Rhee
5/15/2007 03:42:36 PM
CHEMIST
Chief, Branch III