TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

October 9, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate [redacted] gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for UVB data

NC

Dear Dr. Wilkin:

Reference is made to NDA 50-782 for Clindagel™(Clindamycin Phosphate [redacted] gel) 1% for the once a day treatment of acne vulgaris submitted to FDA on January 27, 2000, and to the October 2, 2000 fax request of Ms. Indira Kumar in which she requested UVB data.

On behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate, the attached information in response to the October 2, 2000 request. Please be advised that this information is located in NDA 50-782 Volume 1.5 pages 254-257. The Clindagel formulation, Lot 4CL-7A listed in the Absorbance Spectra report is the same as the to be marketed formulation of Clindagel.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Jill A. Powers, RAC
Manager, Regulatory Affairs

APPEARS THIS WAY
ON ORIG

DUPLICATE

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Clindagel, LLC	October 9, 2000
TELEPHONE NO. (Include Area Code)	**FACSIMILE (FAX) Number (Include Area Code)**
707-793-2600	707-793-0145
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* **IF APPLICABLE**
4189 Chaparral Court Santa Rosa, CA 95409	Target Research Associates 554 Central Avenue New Providence, NJ 07974 Telephone: 908-464-7500 Fax: 908-464-3529

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 50-782

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY	CODE NAME *(If any)*
1% Clindamycin Phosphate, USP	Clindagel	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*		
Clindamycin 2-(dihydrogen phosphate)		

DOSAGE FORM: Topical gel	STRENGTHS: 1% clindamycin phosphate	ROUTE OF ADMINISTRATION: Topical

(PROPOSED) INDICATION(S) FOR USE: Once a day treatment for acne vulgaris

APPLICATION INFORMATION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) ☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☒ 505 (b)(2)

IF AN ANDA, or 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug Cleocin-T gel Holder of Approved Application Pharmacia & Upjohn

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

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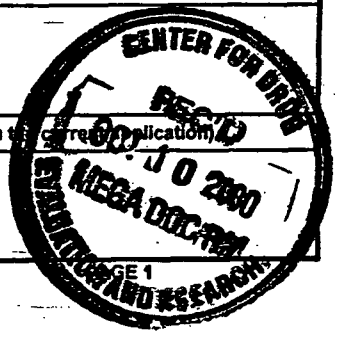
All sites ready for inspection



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- ☐ 18. User Fee Cover Sheet (Form FDA 3397)
- ☐ 19. Financial Information (21 CFR Part 54)
- ☒ 20. OTHER *(Specify)* Response to FDA request for additional information

CERTIFICATION

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2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
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7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Robert J McCormack /qp	Robert J. McCormack, Ph.D., VP, Regulatory Affairs Target Research Associates	October 9, 2000

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
554 Central Avenue New Providence, NJ 07974	(908)-464-7500

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Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

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FDA/Target Research Associates/Fax Memo

Date: October 2, 2000

To: **Jill Powers/Manager, Regulatory Affairs**
(908) 464-7500 (P)
(908) 464- 3529 (F)

From: Indira Kumar, Regulatory Project Manager

Subject: NDA 50-782 Clinical Information Request – UVB data

Dear Ms. Powers,

So that we may evaluate the need for clinical phototoxicity and photosensitivity testing, please submit a UV absorption spectrum for the drug product in the 280 to 700 nm range.

If you have questions, please call **Indira Kumar** at **(301) 827-2020.**

APPEARS THIS WAY
ON ORIGINAL

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Jim A. Powers, RAC
Manager, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

BEST POSSIBLE COPY

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FOOD AND DRUG ADMINISTRATION

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CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*
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CODE NAME *(If any)*

DOSAGE FORM: Topical gel	STRENGTHS: 1% clindamycin phosphate	ROUTE OF ADMINISTRATION: Topical

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Name of Drug: Cleocin-T gel — Holder of Approved Application: Pharmacia & Upjohn

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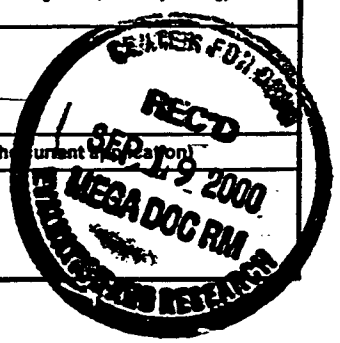

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NDA ORIG AMENDMENT

September 14, 2000

Jonathan K. Wilkin, MD
Director
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9201 Corporate Boulevard
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RE: NDA 50-782
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Clindagel™ (Clindamycin Phosphate — gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional pharmacokinetic information

BP

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate — gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the August 23, 2000 conference call between the agency and sponsor representatives in which additional information relating to study CGEL-005 was requested by biopharmaceutics personnel.

On behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate the following information in response to the August 23, 2000 request:

- The calculated individual proportions and % total dose of clindamycin in urine from study CGEL-005. Analyses were carried out for both AUC and the sum of 0-12 hr and 12-24 hr urinary excretion (total excretion).
- Raw data used in the above calculations.
- The statistical analysis output.
- Summary of results.
- Electronic files containing the calculated proportions and the raw data.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

ORIGINAL

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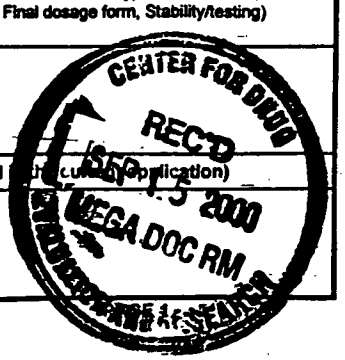

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- ☐ 19. Financial Information (21 CFR Part 54)
- ☒ 20. OTHER *(Specify)* Response to FDA request for additional information

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Robert J. McCormack, Ph.D.	Robert J. McCormack, Ph.D., VP, Regulatory Affairs Target Research Associates	September 14, 2000

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
554 Central Avenue New Providence, NJ 07974	(908)-464-7500

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

August 21, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate —— gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional pharmacokinetic information

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate —— gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the August 17, 2000 telephone request of Ms. Indira Kumar for clarifications concerning pharmacokinetic information previously submitted.

On behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate, the following information in response to the August 17, 2000 request. Listed below is the FDA request for information (in boldface type) followed by the response (*in italics*):

1. **What do the Urinary Excretion values (ng/ml) given in Table 6 of the CGEL-005 report represent compared to the Urine AUC values submitted in Clindagel response to FDA dated August 18, 2000?**

   Both the urinary excretion value and the AUC value are variables which estimate the concentration of clindamycin in urine but are determined using different methods of calculation.

   The urinary excretion values estimate the mean concentration (ng/ml) of clindamycin in urine from 0 to 24 hrs for both Clindagel™ and Cleocin-T® groups. This estimate is calculated by taking the individual means (0 to 12 hrs and 12 to 24 hrs) and combining them to estimate the concentration of clindamycin in urine from 0 to 24 hrs.

   The calculated urinary AUC values are an estimate of the concentration of clindamycin in urine from 0 to 24 hrs using the linear assumption of time vs. concentration.

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Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

August 16, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate — gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional pharmacokinetic information

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate — gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the August 3, 2000 fax request of Ms. Indira Kumar for additional pharmacokinetic information.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate the following information in response the August 3, 2000 request:

- Individual calculated AUC urine and plasma values from study CGEL-005.
- The statistical output used for the analysis of the individual pharmacokinetic parameters.

Please be advised that the statistical output contains information needed to compute the power of the test. We could not compute the power of the test for this response since we do not know what the biopharmaceutics reviewer considers a clinically meaningful difference in mean AUC values between treatment groups.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

(B)

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

15

FDA/Target Research Associates/Fax Memo

Date: August 3, 2000

To: Jill Powers/Manager, Regulatory Affairs
(908) 464-7500 (P)
(908) 464- 3529 (F)

From: Indira Kumar, Regulatory Project Manager

Subject: [redacted] Pharmacokinetic Information Request – Table of Individual AUC Values.

Dear Ms. Powers,

The reviewing pharmacokineticist wanted the following comments forwarded to you (This is for your NDA submission).

Biopharm Comments:

The information request submitted in response to the telephone contact of Ms. Indira Kumar on July 11, 2000 on behalf of the biopharm reviewer is acknowledged. However, as also noted on your cover letter (dated July 17th, 2000) attached to the information request, the request was for the Individual AUC urine and plasma values used for the statistical analysis of Study CGEL-005 entitled "An Open-Label Randomized Study of the Comparative Absorption of Clindagel™ (QD) versus Cleocin T (BID) in Subjects with Acne Vulgaris". The information you have submitted is the Individual urine and plasma concentration values and not the calculated Individual AUC (i.e. pharmacokinetic parameter) values. Please submit a table of the Individual pharmacokinetic parameters (which in your study report was specified as the AUC) used for the statistical analysis and, the statistical analysis output which should include information on the power of the test as well as the parameter estimates.

If you have questions, please call **Indira Kumar** at **(301) 827-2020.**

APPEARS THIS WAY
ON ORIGINAL

TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

July 31, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate [redacted] gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional statistical information

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate [redacted] gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the July 26, 2000 fax request of Ms. Indira Kumar for additional statistical information.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate, two new statistical tables, S7 and S8, attached, in the absence of a strong rationale for testing the ratio rather than the difference between pairs of treatment means.

In response to FDA Question 1:

Table 7, Summary results of noninferiority testing on percent change from baseline of inflammatory, non-inflammatory and total lesion count at week 12 (per protocol), contains the least squares means for the Clindagel QD, Clindagel BID, and Cleocin T BID treatment groups, along with the two-sided 95% confidence intervals for the differences between means comparing each Clindagel group to the Cleocin T group. Since percent change from baseline is a negative quantity in this study, noninferiority is based on the upper bound of the confidence interval for the difference between means rather than the lower bound of the confidence interval. Noninferiority of Clindagel to Cleocin T will be asserted if the upper confidence bound for difference in mean percent change from baseline between treatment groups is less than 10%.

By this rule, Clindagel QD and Clindagel BID are both noninferior to Cleocin T BID with respect to percent change from baseline at week 12 in inflammatory lesion count and total lesion count, though not in noninflammatory lesion count.

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In response to FDA Question 2:

Table S8, Summary results of noninferiority testing on patients with grade 0 or 1 in physician's global severity assessment at week 12 (per protocol), contains the proportions of success for the Clindagel QD, Clindagel BID, and Cleocin T BID treatment groups, along with the two-sided 95% confidence intervals for the difference between proportions between each Clindagel group and the Cleocin T group. The lower bounds of the two-sided 95% confidence intervals are equivalent to the 97.5% lower confidence bounds that were requested. Noninferiority of Clindagel to Cleocin T will be asserted if the lower confidence bound for the difference in proportions is greater than –15%.

By this rule, Clindagel QD and Clindagel BID are both noninferior to Cleocin T BID with respect to the proportion of patients with success, defined as physician's Global Severity Assessment score of 0 or 1 at Week 12.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

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ON ORIGI

TABLE S7
SUMMARY RESULTS OF NONINFERIORITY TESTING ON PERCENT CHANGE FROM BASELINE OF INFLAMMATORY, NONINFLAMMATORY AND TOTAL LESION COUNT AT WEEK 12
(PER PROTOCOL)

	TREATMENT GROUP						95% CONFIDENCE INTERVAL			
	Clindagel QD (T1) (N=139)		Clindagel BID (T2) (N=140)		CleocinT BID (T5) (N=140)		T1 - T5		T2-T5	
	LS MEAN	SE	LS MEAN	SE	LS MEAN	SE	LB	UB	LB	UB
INFLAMMATORY LESION	-54.47	2.710	-55.76	2.695	-53.21	2.722	-8.66	6.12	-9.94	4.83
NONINFLAMMATORY LESION	-27.50	3.491	-32.13	3.471	-34.58	3.508	-2.42	16.60	-7.04	11.97
TOTAL LESION	-40.75	2.484	-43.26	2.470	-43.14	2.494	-4.40	9.14	-6.89	6.64

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ON ORIGINAL

PERCENT CHANGE=100*(POST-BASE)/BA...
TWO-SIDED 95% CI FOR DIFFERENCE BETWEEN LS MEANS IN % CHANGE FROM BASELINE (CLINDAGEL - CLEOCINT)
THE UPPER BOUND MUST BE < 10% TO DECLARE NONINFERIORITY.
ANALYSIS BASED ON ANOVA WITH TREATMENT AND INVESTIGATOR AS FACTORS
INVESTIGATORS 11 AND 12 WERE POOLED

TABLE S8
SUMMARY RESULTS OF NONINFERICRITY TESTING ON PATIENTS WITH GRADE 0 OR 1
IN PHYSICIAN'S GLOBAL SEVERITY ASSESSMENT AT WEEK 12
(PER PROTOCOL)

	TREATMENT GROUP						95% CONFIDENCE INTERVAL			
	Clindagel QD (T1)		Clindagel BID (T2)		CleocinT BID (T5)		T1 - T5		T2 - T5	
	N	%	N	%	N	%	LB	UB	LB	UB
N	139		140		140		-.134	0.066	-.102	0.102
GSA = 0 OR 1	31	(22.3%)	36	(25.7%)	36	(25.7%)				
GSA > 1	108	(77.7%)	104	(74.3%)	104	(74.3%)				

APPEARS THIS WAY
ON ORIGINAL

TWO-SIDED 95% CONFIDENCE INTERVAL FOR DIFFERENCES IN PROPORTION OF PATIENTS WITH GSA OF 0 OR 1, I.E., (CLINDAGEL - CLEOCINT)
THE LOWER BOUND MUST BE > -.15 TO DECLARE NON-INFERIORITY.

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

September 6, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate —— gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional pharmacokinetic information

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate —— gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the August 23, 2000 conference call between the agency and sponsor representatives in which additional information relating to study CGEL-005 was requested by biopharmaceutics personnel.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate the following information in response the August 23, 2000 request:

- The calculated individual proportions and % total dose of clindamycin in urine from study CGEL-005. Analyses were carried out for both AUC and the sum of 0-12 hr and 12-24 hr urinary excretion (total excretion).
- The statistical analysis output.
- Summary of results.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Jill A. Powers, RAC
Manager, Regulatory Affairs

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THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

12 Pages

(A)

FDA/Target Research Associates/Fax Memo

Date: **July 26, 2000**

To: **Jill Powers/Manager, Regulatory Affairs**
(908) 464-7500 (P)
(908) 464- 3529 (F)

From: Indira Kumar, Regulatory Project Manager

Subject: [redacted] Statistical Information Request - Relative to the non-inferiority testing.

Dear Ms. Powers,

The reviewing statistician wanted the following comments forwarded to you (This is for your NDA submission).

Statistical:

1. Please provide a rational for using the confidence interval for the ratio of Clindagel divided by Cleocin T gel instead of the confidence interval for the difference between Clindagel and Cleocin T gel. (For therapeutic non-inferiority, the standard approach is using the confidence interval for the difference between the new drug and the reference drug).

In the absence of a strong rationale for using the ratio, the use of the difference is indicated.

Please provide the following two tables:

1. A table similar to Table 13 on page 260 of Volume 1.1 of the Statistical Report. The new table should provide the lower bound of the one-sided 97.5% confidence interval for the difference between least square means (Clindagel-Cleocin), instead of the ratio of least square means (Clindagel/Cleocin).

2. A table similar to Table 14 on page 261 of the same volume with results of non-inferiority testing on the proportion of patients with grades 0 or 1 in the Physician's Global Severity Assessment at Week 12 instead of the two-category improvement. The new table should provide the lower bound of the one-sided 97.5% confidence interval for the difference of proportions between Clindagel and Cleocin T (Clindagel-Cleocin) instead of the ratio of proportions (Clindagel/Cleocin).

If you have questions, please call **Indira Kumar** at **(301) 827-2020.**

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ON ORIGINAL

TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

July 20, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate [redacted] gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional statistical information

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate [redacted] gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the July 18, 2000 fax request of Ms. Indira Kumar for additional statistical information.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate, the following information:

- A summary table similar to Table 13 on page 260 in volume 1.1 of NDA 50-783 but with the lower bound in the one-sided 97.5% Confidence Interval. This table is designated S6.

- A summary table similar to Table 14 on page 261 in volume 1.1 of NDA 50-783 but with results of non-inferiority testing on the proportion of patients with grades 0 or 1 in the Physician's Global Severity Assessment at Week 12 instead of a two-category improvement and the lower bound in the one-sided 97.5% Confidence Interval. This table is designated S5.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Clindagel, LLC	July 20, 2000
TELEPHONE NO. (Include Area Code)	**FACSIMILE (FAX) Number (Include Area Code)**
707-793-2600	707-793-0145
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
4189 Chaparral Court Santa Rosa, CA 95409	Robert J. McCormack, Ph.D. Target Research Associates 554 Central Avenue New Providence, NJ 07974 Telephone: 908-464-7500 Fax: 908-464-3529

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 50-782

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
1% Clindamycin Phosphate, USP	Clindagel

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*
Clindamycin 2-(dihydrogen phosphate)

CODE NAME *(If any)*

DOSAGE FORM: Topical gel	STRENGTHS: 1% clindamycin phosphate	ROUTE OF ADMINISTRATION: Topical

(PROPOSED) INDICATION(S) FOR USE: Once a day treatment for acne vulgaris

APPLICATION INFORMATION

APPLICATION TYPE
(check one) ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☒ 505 (b)(2)

IF AN ANDA, or 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug: Cleocin-T gel Holder of Approved Application: Pharmacia & Upjohn

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

IF A SUBMISSION OR PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION FDA request for additional information

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED ~~N/A~~ THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability/testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See attachment

All sites ready for inspection

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

See attachment

This application contains the following items: *(Check all that apply)*

☐	1. Index		
☐	2. Labeling *(check one)*	☐ Draft Labeling	☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50(c))		
☐	4. Chemistry section		
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)		
☐	B. Samples (21 CFR 314.50(e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)		
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)		
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)		
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)		
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))		
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)		
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)		
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)		
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)		
☐	12. Case report forms (e.g., 21 CFR 314.50(f)(2); 21 CFR 601.2)		
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))		
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355(b)(2) or (j)(2)(A)		
☐	15. Establishment description (21 CFR Part 600, if applicable)		
☐	16. Debarment certification (FD&C Act 306(k)(1))		
☐	17. Field copy certification (21 CFR 314.50(k)(3))		
☐	18. User Fee Cover Sheet (Form FDA 3397)		
☐	19. Financial Information (21 CFR Part 54)		
☒	20. OTHER *(Specify)* FDA request for additional information		

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Robert J. McCormack, Ph.D.	Robert J. McCormack, Ph.D., VP, Regulatory Affairs Target Research Associates	July 20, 2000
ADDRESS *(Street, City, State, and ZIP Code)* 554 Central Avenue New Providence, NJ 07974		TELEPHONE NUMBER (908)-464-7500

(C)

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

4

JUL 18

FDA/Target Research Associates/Fax Memo

Date: July 18, 2000

To: Jill Powers/Manager, Regulatory Affairs
(908) 464-7500 (P)
(908) 464- 3529 (F)

From: Indira Kumar, Regulatory Project Manager

Subject: NDA ——— Statistical Information Request

Dear Ms. Powers,

The reviewing statistician wanted the following comments forwarded to you (This is for your NDA submission).

Statistical:

1. Please submit an additional table similar to Table 13 on page 260 in Volume 1.1 of the Statistical Report. The only change is the following: the lower bound in the one-sided 97.5% Confidence Interval instead of the lower bound in the one-sided 95% Confidence Interval.

2. Please provide us a table similar to Table 14 on page 261 of Volume 1.1 of the Statistical Report. The new table should differ from Table 14 in the following:

   a. The new table provides summary results of non-inferiority testing on the proportion of patients with grades 0 or 1 in the Physician's Global Severity Assessment at Week 12 instead of a two-category improvement.
   b. The new table provides the lower bound in the one-sided 97.5% Confidence interval instead of the 95% Confidence interval.

If you have questions, please call **Indira Kumar** at **(301) 827-2020.**

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TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

July 17, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: **NDA 50-782**
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate [redacted] gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate [redacted] gel), 1% for the once a day treatment of acne vulgaris submitted to FDA on January 27, 2000, and to the July 11, 2000 telephone contact of Ms. Indira Kumar during which she requested additional information on behalf of the Biopharm reviewer.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting, in duplicate, the following information requested by Ms. Kumar:

- Individual AUC urine and plasma values used for the statistical analysis of Study CGEL-005 entitled "An Open-Label Randomized Study of the Comparative Absorption of Clindagel™ (QD) versus Cleocin T (BID) in Subjects with Acne Vulgaris".

Please let me know if you have any questions or require additional information.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Clindagel, LLC	July 17, 2000
TELEPHONE NO. (Include Area Code)	**FACSIMILE (FAX) Number (Include Area Code)**
707-793-2600	707-793-0145
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
4189 Chaparral Court Santa Rosa, CA 95409	Robert J. McCormack, Ph.D. Target Research Associates 554 Central Avenue New Providence, NJ 07974 Telephone: 908-464-7500 Fax: 908-464-3529

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 50-782

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
1% Clindamycin Phosphate, USP	Clindagel

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
Clindamycin 2-(dihydrogen phosphate)	

DOSAGE FORM: Topical gel	STRENGTHS: 1% clindamycin phosphate	ROUTE OF ADMINISTRATION: Topical

(PROPOSED) INDICATION(S) FOR USE: Once a day treatment for acne vulgaris

APPLICATION INFORMATION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☒ 505 (b)(2)

IF AN ANDA, or 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug: Cleocin-T gel Holder of Approved Application: Pharmacia & Upjohn

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRECUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

IF A SUBMISSION OR PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION FDA request for additional information

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED ~~N/A~~	THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See attachment

All sites ready for inspection

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, EMFs, and DMFs referenced in the current application)

See attachment

This application contains the following items: *(Check all that apply)*

☐	1. Index
☐	2. Labeling *(check one)* ☐ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50(c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50(e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50(f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355(b)(2) or (j)(2)(A)
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306(k)(1))
☐	17. Field copy certification (21 CFR 314.50(k)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☒	20. OTHER *(Specify)* FDA request for additional information

CERTIFICATION

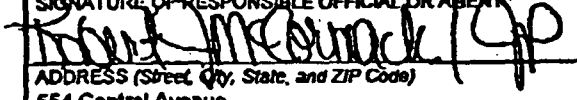
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Robert J. McCormack, Ph.D., VP, Regulatory Affairs Target Research Associates	July 17, 2000
ADDRESS *(Street, City, State, and ZIP Code)* 554 Central Avenue New Providence, NJ 07974		TELEPHONE NUMBER (908)-464-7500

(D)

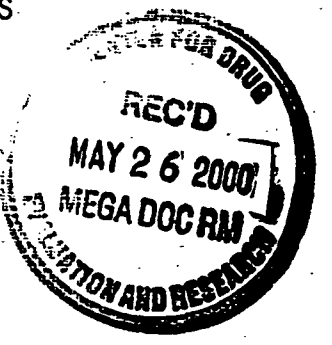
THIS SECTION WAS DETERMINED NOT TO BE RELEASABLE

12

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

NDA ORIG AMENDMENT



May 25, 2000

Jonathan K. Wilkin, MD
Director
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

BS

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate [redacted] gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional statistical information

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate —— gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to the May 15, 2000 fax request of Ms. Indira Kumar for additional statistical information.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting in duplicate, the following information:

- Summary tables containing results of the requested analyses. Please be advised that the tables are numbered to correspond to the question number of the fax request.
- Statistical tables containing data used for the summary tables. Each statistical table is numbered to correspond to the appropriate summary table.
- Diskette containing one SAS file and one output file for each statistical table.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Robert J McCormack/gp

ORIGINAL

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page.

FOR FDA USE ONLY
APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT
Clindagel, LLC

DATE OF SUBMISSION
May 25, 2000

TELEPHONE NO. *(Include Area Code)*
(707) 793-2600

FACSIMILE (FAX) Number *(Include Area Code)*
(707) 793-0145

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*:

4189 Chaparral Court
Santa Rosa, CA 95409

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

Robert J. McCormack, Ph.D.
Target Research Associates
554 Central Avenue
New Providence, NJ 07974
Telephone: 908-464-7500
Fax: 908-464-3529

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
MAY 26 2000
MEGA DOC RM

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME (*e.g., Proper name, USP/USAN name*)
1% Clindamycin Phosphate, USP

PROPRIETARY NAME (*trade name*) IF ANY
Clindagel

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (*If any*)
Clindamycin 2-(dihydrogen phosphate)

CODE NAME (*If any*)

DOSAGE FORM:
Topical gel

STRENGTHS:
1% clindamycin phosphate

ROUTE OF ADMINISTRATION:
Topical

)POSED) INDICATION(S) FOR USE:
Once a day treatment of acne vulgaris

APPLICATION INFORMATION

APPLICATION TYPE
(check one) ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☒ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION
(check one) ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION

☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT

☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY, MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

REASON FOR SUBMISSION
Submission of additional statistical information

PROPOSED MARKETING STATUS (check one) ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1

THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at this site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See Attachment

s References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

See Attachment

This application contains the following items: *(Check all that apply)*	
	1. Index
	2. Labeling (check one) ☐ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
X	19. OTHER (Specify) Submission of additional statistical information

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense. U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Robert J. McCormack, Ph.D. Vice President, Regulatory Affairs Target Research Associates	May 25, 2000

ADDRESS (*Street, City, State, and ZIP Code*)	Telephone Number
Target Research Associates 554 Central Avenue New Providence, NJ 079747	(908) 464-7500

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 531-H
Independence Avenue, S.W.
hington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

(E)

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

4

TARGET
RESEARCH
ASSOCIATES

IICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

May 16, 2000

Indira Kumar
Regulatory Project Manager
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate ——— gel), 1%
Indication: Once a day treatment of acne vulgaris
Response to FDA request for additional copies of the Clindagel package insert

Dear Ms. Kumar:

erence is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate ——— gel), 1% for the once a day treatment of acne vulgaris which was submitted to FDA on January 27, 2000 and to your May 15, 2000 telephone contact. During the call you requested that an additional five copies of the Clindagel package insert be submitted to FDA in both paper and electronic format.

Therefore, on behalf of Clindagel, LLC, Target Research is hereby submitting five copies of the annotated and unannotated package insert for Clindagel™ (Clindamycin phosphate ——— gel), 1%. In addition this submission contains a diskette that contains both the annotated (file name: package insert final annotated) and unannotated (file name: package insert final) versions of the document.

Please let me know if you have any questions regarding the contents of this submission.

Sincerely,

Robert J. McCormack

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

ntral Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

HFD-540 / Kumar

FDA/Target Research Associates/Fax Memo

Date: May 15, 2000

To: Jill Powers/Manager, Regulatory Affairs
(908) 464-7500 (P)
(908) 464- 3529 (F)

From: Indira Kumar, Regulatory Project Manager

Subject: NDA——— Statistical Information Request

Dear Ms. Powers,

The reviewing statistician wanted the following comment forwarded to you (This is for your NDA submission).

Statistical:

Please provide the results of the efficacy analysis in the Phase 3 study comparing Clindagel QD versus Vehicle QD in all ITT patients at Endpoint (LOCF) relative to the following dichotomized variables:

1. Proportion of patients with the grade 0 in the Investigator's Global Severity Assessment at the final visit;
2. Proportion of patients with the grades 0 or 1 in the Investigator's Global Severity Assessment at the final visit.

In other words, we need a table that is similar to Table 8 on page 254 of Volume 1, but uses the above definitions of success in the Investigator's Global Severity Assessment.

Also please submit a Table similar to Table 14 on page 261 of Volume 1 with the only difference that we want comparisons relative to the following dichotomized variables:

1. Proportion of patients with the grade 0 in the Investigator's Global Severity Assessment at the final visit;
2. Proportion of patients with the grades 0 or 1 in the Investigator's Global Severity Assessment at the final visit.

If you have questions, please call **Indira Kumar at (301) 827-2020.**

APPEARS
ON OR

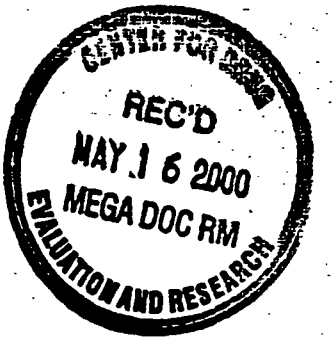
TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

April 28, 2000

NDA ORIG AMENDMENT

Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850



BM

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate ___ gel), 1%
Indication: Once a day treatment of acne vulgaris
Submission of dermal carcinogenicity data sets

Dear Dr. Wilkin:

Reference is made to NDA 50-782, for Clindagel™ (Clindamycin Phosphate ___ gel), 1% for the once a day treatment of acne vulgaris which was submitted on January 27, 2000 and to the pre-NDA meeting held on November 15, 1999. At the pre-NDA meeting the division stated that the data from dermal carcinogenicity study # 451293 would be required to be submitted to the division in a format that would enable analysis of the data by the statistician.

Therefore, on behalf of Clindagel, LLC, we are submitting in duplicate, two diskettes which contain data and information pertaining to the above mentioned dermal carcinogenicity study. The diskettes contain the following information:

- Dermal carcinogenicity data sets formatted as SAS (v6.09) transport files
- Dataset transfer documents formatted in Word 97 which describe the aforementioned SAS transport files

For your convenience a printout of the dataset transfer documents is also included with this submission.

Please let me know if you have any questions about the enclosed information.

Sincerely,

ORIGINAL

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

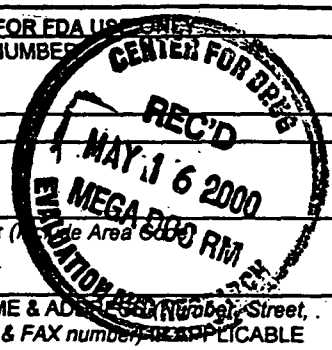
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page.

FOR FDA USE ONLY
APPLICATION NUMBER



APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Clindagel, LLC	April 28, 2000
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
(707) 793-2600	(707) 793-0145

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code; and U.S. License number if previously issued)*:	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
4189 Chaparral Court Santa Rosa, CA 95409	Robert J. McCormack, Ph.D. Target Research Associates 554 Central Avenue New Providence, NJ 07974 Telephone: 908-464-7500 Fax: 908-464-3529

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 50-782

ESTABLISHED NAME (*e.g., Proper name, USP/USAN name*)	PROPRIETARY NAME (*trade name*) IF ANY
1% Clindamycin Phosphate, USP	Clindagel

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (*If any*)	CODE NAME (*If any*)
Clindamycin 2-(dihydrogen phosphate)	

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Topical gel	1% clindamycin phosphate	Topical

(PROPOSED) INDICATION(S) FOR USE:
Once a day treatment of acne vulgaris

APPLICATION INFORMATION

APPLICATION TYPE
(check one) ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☒ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION
(check one) ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY, MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

REASON FOR SUBMISSION
Submission of dermal carcinogenicity study data sets

PROPOSED MARKETING STATUS (check one) ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED N/A

THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at this site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See Attachment

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

See Attachment

This application contains the following items: *(Check all that apply)*	
	1. Index
	2. Labeling (check one) ☐ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
X	19. OTHER (Specify) Submission of dermal carcinogenicity data sets

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to he following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Robert J McCormack/cpp	Robert J. McCormack, Ph.D. Vice President, Regulatory Affairs Target Research Associates	April 28,2000

ADDRESS (*Street, City, State, and ZIP Code*)	Telephone Number
Target Research Associates 554 Central Avenue New Providence, NJ 079747	(908) 464-7500

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RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

April 28, 2000

Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
North 214
Rockville, MD 20850

NDA ORIG AMENDMENT

RE: NDA 50-782
Clindagel, LLC, Santa Rosa, CA
Clindagel™ (Clindamycin Phosphate [redacted] gel), 1%
Indication: Once a day treatment of acne vulgaris
Submission of stability data update

BC

Dear Dr. Wilkin:

Reference is made to NDA 50-782 for Clindagel™ (Clindamycin phosphate [redacted] gel), 1% for the once a day treatment of acne vulgaris submitted on January 27, 2000, and the commitments made within.

The commitment made in the CMC section of this NDA, volume 1.5, page 010, was to submit 12 month primary stability data (protocol 115-G) and 9 month primary stability data (protocol 140-G) to the agency within 3 months, post submission. Based on the commitment, the following stability data are submitted:

- Primary stability study 115-G, month 12 stability tables and interim report. A copy of the protocol and all protocol amendments to date has also been included for reference.

- Primary stability study 140-G, month 12 stability tables and interim report. A copy of the protocol and all protocol amendments to date has also been included for reference. The commitment in the NDA was to submit month 9 data however, we were able to finalize the month 12 testing to include in this supplement.

Also committed in the CMC section of this NDA, volume 1.5, page 011, was to submit 18 month auxiliary stability data (protocols 087 and 091) to the agency within 3 months, post submission. Based on that commitment, the following stability data are submitted:

- Auxiliary stability study 087, month 18 stability tables and interim report. A copy of the protocol and all protocol amendments to date has also been included for reference.

ORIGINAL

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515