

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022503Orig1s000

CHEMISTRY REVIEW(S)

NDA 022-503

Metaxalone Tablet

Corepharma, LLC

Xiaobin Shen, Ph.D.
for

Division of Pulmonary, Allergy, and Rheumatology Products

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Chemistry Review Data Sheet

1. NDA 22-503
2. REVIEW #: 3
3. REVIEW DATE: 21-Apr-2015
4. REVIEWER: Xiaobin Shen, Ph.D.
5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original Submission	20-Aug-2009
Amendment 0001	26-Oct-2009
Amendment 0003	30-Nov-2009
Amendment 0006	22-Mar-2010
Amendment 0008	28-Apr-2010
Amendment 0016	18-Jun-2013

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Amendment 0019	15-Dec-2014
Amendment 0020	19-Mar-2015
Amendment 0021	19-Mar-2015
Amendment 0023	30-Mar-2015

Other amendments dated older than the last listed do not have CMC related information for review.

7. NAME & ADDRESS OF APPLICANT:

Name: CorePharma, LLC

Chemistry Review Data Sheet

Address: 215 Wood Avenue,
Middlesex, New Jersey 08846

Representative Kimberly D. Ernst, Senior Director, Regulatory Affairs /
(Agent): Quality Assurance R&D

Telephone: 732-667-6009

Fax: 732-805-5643

Email: Kimberly.ernst@corepharma.com

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: None
- b) Non-Proprietary Name (USAN): Metaxalone
- c) Code Name/# (ONDC only): N/A
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 5
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: NDA 505(b)(2)**10. PHARMACOL. CATEGORY: Not established****11. DOSAGE FORM: Tablet****12. STRENGTH/POTENCY: 640 mg/tablet****13. ROUTE OF ADMINISTRATION: Oral**

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

Chemistry Review Data Sheet

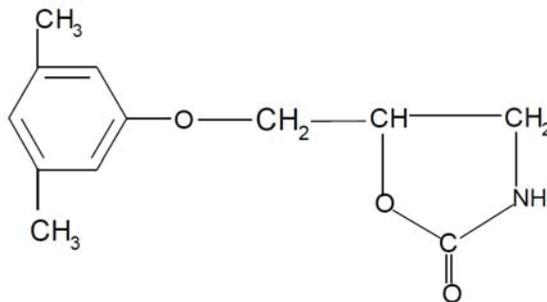
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: 5-(3,5-dimethylphenoxy)methyl-2-oxazolidone

United States Adopted Name (USAN): Metaxalone

Compendial name: Metaxalone

Chemical structure:

Molecular Formula: C₁₂H₁₅NO₃Molecular Weight: 221.2^(b)₍₄₎

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	1	Adequate	09-Sep-2014	There has been no further updates
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

Chemistry Review Data Sheet

		(b) (4)				
--	--	---------	--	--	--	--

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, 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)

B. Other Documents:

None relevant in this resubmission.

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biopharmaceutics	Approval	4/7/2015	Haritha Mandula, Ph.D.
EES	Approval	2/17/15	Linda Ng, Ph.D.
Pharm/Tox	Approval	4/20/10	Jay Chang, Ph.D.
Clinical	Approval	10/10/13	Keith M. Hull, MD, Ph.D.
Clinical Pharm.	Approval	11/20/13	Agarwal Sheetal, Ph.D.
Methods Validation	Not needed	4/27/10	Elsbeth Chikhale, Ph.D.
DMEPA	Approval	8/21/13	Teresa McMillan, Ph.D.
EA	Approval	4/27/10	Elsbeth Chikhale, Ph.D.

The Chemistry Review for NDA 022-503

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the chemistry, manufacturing and controls standpoint, the NDA is recommended for approval.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

PMC: Provide comparative dissolution data (determined by f2 metrics) between the (b) (4) tablets (b) (4) using the approved dissolution method. (b) (4)

II. Summary of Chemistry Assessments

A. Description of the Drug Substance and Drug Product

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

Refer to Chemistry Review #1 completed by Dr. Elsbeth Chikhale on 27-Apr-2010 for the two sections above.

C. Basis for Approvability or Not-Approval Recommendation

The prior review cycles completed by both Drs. Elsbeth Chikhale and Edwin Jao deemed the NDA approvable pending satisfactory overall EES status and a finalized package insert and labeling information.

In this review cycle, the overall EES status has been deemed satisfactory by Dr. Linda Ng. The package insert and labeling information are separately evaluated and edited in collaboration with the clinical division prior to taking the final action. As such, the NDA is approvable.

Executive Summary Section

III. Administrative**A. Reviewer's Signature**

Xiaobin Shen -A Digitally signed by Xiaobin Shen -A
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA,
ou=People, cn=Xiaobin Shen -A,
0.9.2342.19200300.100.1.1=2000423313
Date: 2015.04.21 09:06:57 -04'00'

Xiaobin Shen, Ph.D.
Review Chemist, Branch IV, ONDP

B. Endorsement Block

Julia C. Pinto -A Digitally signed by Julia C. Pinto -A
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People,
cn=Julia C. Pinto -A, 0.9.2342.19200300.100.1.1=1300366849
Date: 2015.04.21 10:39:48 -04'00'

Julia Pinto, Ph.D.
Chief, Branch IV, ONDP

C. CC Block

Chemistry Assessment Section

Chemistry Assessment**I. Review Of New Information Included in the Resubmission**

The resubmission includes three categories of information. It is listed below and separately evaluated.

The first is to notify the Agency that the facilities previously not ready for inspection have been inspected and found acceptable. Dr. Linda Ng has evaluated the facility inspection results and made an overall recommendation of approval from OPF's perspective.

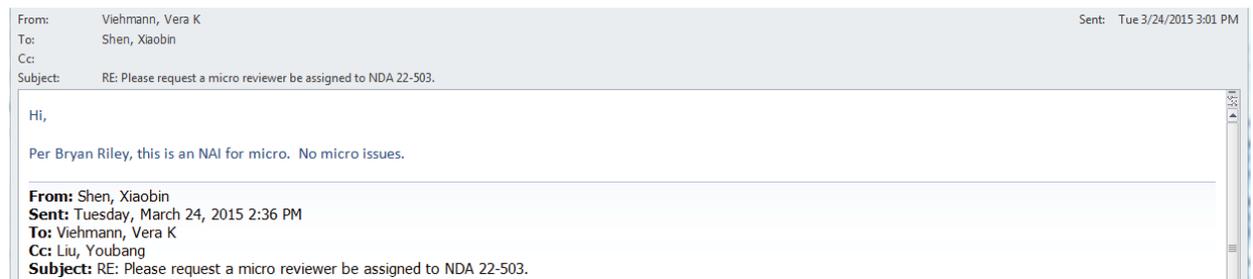
The second is to add an additional acceptance limit to the dissolution data. The addition is justified with data and citing the Agency's guidance. Biopharmaceutics reviewer Dr. Haritha Mandula completed the review and recommended the NDA for approval from the biopharmaceutics perspective.

The third is to update the NDA with additional real time stability data of a total of 6 batches, all completed up to 36 months. All results met specifications already evaluated and deemed acceptable in previous quality reviews completed by Drs. Elsbeth Chikhale and Edwin Jao in 2010 and 2013 respectively. The assay, impurities and water content test results showed no meaningful change over 36 months. The dissolution results trended lower over time but all reported results were still within the acceptance limits. Biopharmaceutics reviewer Dr. Haritha Mandula has recommended approval.

The registration batch tablets (b) (4)

Therefore they made a post marketing commitment to provide comparative dissolution data (determined by f2 metrics) between (b) (4) tablets (b) (4) using the approved dissolution method to support the change.

Additionally, the NDA does not perform microbial burden testing as in process control or at release. It has not provided any justification for not including the test either. The Microbiology review team has deemed this not an issue. The micro communication is reproduced below.



Evaluation: Acceptable. The prior pending EES status has been resolved. The submitted new information are acceptable and support a product expiry of 36 months.

II. Review Of Labeling & Package Insert**A. Labeling & Package Insert**

The bottle label images are reproduced below.

Chemistry Assessment Section

(b) (4)

The applicant stated that the bottles will not be further packaged in cartons.

Evaluation: Acceptable. The labels have all required information displayed acceptably from CMC perspective.

Package Insert

Refer to details of the package insert in Section 1.14.1.3 of the eCTD.
The SPL is provided with the required details.

Evaluation: Acceptable. The package insert will be revised, separately and in collaboration with other disciplines of the review team, to meet the requirements listed below.

Chemistry Assessment Section

III. EES Report

Overall Manufacturing Inspection Recommendation

NDA 022503-Orig1-Resubmission/Class 2(19)

[Task Details](#)**Task Data**[Open Issues](#)[Approvals | More ▾](#)**Facility Inspection - Overall Application Recommendation**

Facility Inspection - Overall Application Recommendation

Approve

Facility Inspection - Overall Application Re-evaluation Date

8/12/16 **Linda Ng** marked this as Done and made **3 other updates**.Feb 17 at 10:28 am - [Comment](#)

-  Updated **Facility Inspection - Overall Application Recommendation** to **Approve**.
-  Updated **Facility Inspection - Overall Application Re-evaluation Date** to **8/12/16**.

IV. Approved Commercial Specifications



CHEMISTRY REVIEW TEMPLATE



Chemistry Assessment Section

Drug Substance Specifications –

		RAWMATERIAL CERTIFICATE OF ANALYSIS		
RAWMATERIAL METAXALONE		SAMPLE AMOUNT REQUIRED (b) (4)	RM CODE NO. RM-523	LOT NO.
VENDOR NAME		MFG. LOT NUMBER		QTY. ON HAND
MFG. EXPIRATION DATE		RETEST DATE		[<input checked="" type="checkbox"/>] FULL TESTING [N/A] REDUCED TESTING
PREPARED BY (b) (4)	DATE 03/18/2009	QC APPROVAL (b) (4)	DATE 03/19/09	REGULATORY APPROVAL DATE 03/18/09
TEST	METHOD	SPECIFICATION	RESULT	REFERENCE
APPROVED MANUFACTURER	1. Manufacturer's Certificate Of Analysis	(b) (4)		
DESCRIPTION	2. Bulk Container Label And Markings VISUAL	White to off white crystalline powder		
IDENTIFICATION	A. USP/NF <197K> B. QCM 135	A. Infrared Absorption B. The R.Time of the Metaxalone peak in the assay sample should correspond to that of the standard preparation	Std. R.T. = min. Sample R.T. = min.	
MELTING RANGE	USP/NF<741>	Between (b) (4) and (b) (4)		
LOSS ON DRYING	USP/NF <731>	NMT (b) (4)		
RESIDUE ON IGNITION	USP/NF <281>	NMT 0.3%		
RESIDUAL SOLVENTS	QCM 234	(b) (4) NMT (b) (4) ppm (b) (4) NMT (b) (4) ppm		
REVISION HISTORY: Page 1 of 2 4 Rev 03/09	REMARKS:			



CHEMISTRY REVIEW TEMPLATE



Chemistry Assessment Section

		RAWMATERIAL CERTIFICATE OF ANALYSIS		
RAWMATERIAL METAXALONE		SAMPLE AMOUNT REQUIRED (b) (4)	RM CODE NO. RM-523	LOT NO.
VENDOR NAME		MFG. LOT NUMBER		QTY. ON HAND
MFG. EXPIRATION DATE		RETEST DATE		<input checked="" type="checkbox"/> FULL TESTING <input type="checkbox"/> [N/A] REDUCED TESTING
PREPARED BY (b) (4)	DATE 03/18/2009	QC APPROVAL (b) (4)	DATE 03/19/09	REGULATORY APPROVAL
TEST	METHOD	SPECIFICATION		RESULT
HEAVY METALS	USP/NF <231>, Method-II	NMT (b) (4) %		
ASSAY BY HPLC	QCM 135	NLT (b) (4) % and NMT (b) (4) % calculated on (b) (4) basis		
IMPURITY ASSAY BY HPLC	QCM 135			
Specified Identified Impurity				
3,5-Dimethylphenol (3,5-xylenol)		NMT 0.05%		
Individual UnSpecified Unidentified Impurity		NMT 0.05% (Report impurities >0.03%		
Total Impurities		NMT 0.5%		
BULK DENSITY	SOP#24-010	(b) (4) g/mL		
TAP DENSITY	SOP#24-010	(b) (4) g/mL		
PARTICAL SIZE ANALYSIS (BY SIEVE)	QCM 12	<u>Sieve #</u>	<u>% Retained</u>	
		(b) (4)	NMT (b) (4) %	
			NMT (b) (4) %	
			NMT (b) (4) %	
REMARKS:				
REVISION HISTORY:		QC AUDIT VERIFICATION _____ DATE _____		
Page 2 of 2		CONCLUSION:		
4 Rev 03/09		[] THIS LOT MEETS ALL OF THE ABOVE TEST SPECIFICATIONS AND IS THEREFORE APPROVED FOR RELEASE		
		[] THIS LOT DOESNOT MEET ALLONE OF THE ABOVE TEST SPECIFICATIONS AND IS THEREFORE NOT APPROVED FOR RELEASE		
		QUALITY CONTROL APPROVAL _____ DATE _____		



CHEMISTRY REVIEW TEMPLATE



Chemistry Assessment Section

(b) (4) Drug Substance Specifications –

PCOREPHARMA LLC		RAWMATERIAL CERTIFICATE OF ANALYSIS		
RAWMATERIAL	SAMPLE AMOUNT REQUIRED	CODE NO.	LOT NO.	
METAXALONE (b) (4)	(b) (4)	RM-192		
VENDOR NAME	MFG. LOT NUMBER	QTY. ON HAND		
MFG. EXPIRATION DATE	RETEST DATE	[<input checked="" type="checkbox"/>] FULL TESTING [<input type="checkbox"/>] REDUCED TESTING		
PREPARED BY (b) (4)	DATE 03/18/2009	QC APPROVAL (b) (4)	DATE 03/19/09	REGULATORY APPROVAL <i>CBeltre</i> DATE 03/18/09
TEST	METHOD	SPECIFICATION	RESULT	REFERENCE
APPROVED MANUFACTURER	1. Manufacturer's Certificate Of Analysis 2. Bulk Container Label And Markings	(b) (4)		
DESCRIPTION	VISUAL	White to off white crystalline powder		
IDENTIFICATION	A. USP/NF <197K> B. QCM 135	A. Infrared Absorption B. The R.Time of the Metaxalone peak in the assay sample should correspond to that of the standard preparation	Std. R.T. = min. Sample R.T. = min.	
MELTING RANGE	USP/NF <741>	Between (b) (4) and (b) (4)		
LOSS ON DRYING	USP/NF <731>	NMT (b) (4) (b) (4)		
RESIDUE ON IGNITION	USP/NF <281>	NMT 0.3%		
RESIDUAL SOLVENTS	QCM 234	(b) (4) NMT (b) (4) ppm (b) (4) NMT (b) (4) ppm		
REVISION HISTORY: Page 1 of 2 8 rev 03/09	REMARKS:			



CHEMISTRY REVIEW TEMPLATE



Chemistry Assessment Section

		RAWMATERIAL CERTIFICATE OF ANALYSIS			
RAWMATERIAL METAXALONE (b) (4)		SAMPLE AMOUNT REQUIRED (b) (4)		CODE NO. RM-192	LOT NO.
VENDOR NAME			MFG. LOT NUMBER		QTY. ON HAND
MFG. EXPIRATION DATE			RETEST DATE		[<input checked="" type="checkbox"/>] FULL TESTING [N/A] REDUCED TESTING
PREPARED BY (b) (4)	DATE 03/18/2009	QC APPROVAL (b) (4)	DATE 03/19/09	REGULATORY APPROVAL <i>C. Bette</i>	DATE 03/18/09
TEST	METHOD	SPECIFICATION		RESULT	REFERENCE
HEAVY METALS	USP/NF <231>, Method-II	NMT (b) (4) %			
ASSAY BY HPLC	QCM 135	NLT (b) (4) % and NMT (b) (4) % calculated on dried basis			
IMPURITY ASSAY BY HPLC	QCM 135				
Specified Identified Impurity					
3,5-Dimethylphenol (3,5-xyleneol)		NMT 0.05%			
Individual UnSpecified Unidentified Impurity					
Total Impurities		NMT 0.5%			
BULK DENSITY	SOP#24-010	(b) (4) g/mL			
TAP DENSITY	SOP#24-010	(b) (4) g/mL			
PARTICLE SIZE ANALYSIS	M1208.01	(b) (4) % of the particles (d ₁₀): NMT (b) (4) μ			
		(b) (4) % of the particles (d ₅₀): NMT (b) (4) μ			
		(b) (4) % of the particles (d ₉₀): NMT (b) (4) μ			
REMARKS:					
REVISION HISTORY:					
		QC AUDIT VERIFICATION		DATE	
CONCLUSION:					
[<input type="checkbox"/>] THIS LOT MEETS ALL OF THE ABOVE TEST SPECIFICATIONS AND IS THEREFORE APPROVED FOR RELEASE					
[<input type="checkbox"/>] THIS LOT DOES NOT MEET ALL/ONE OF THE ABOVE TEST SPECIFICATIONS AND IS THEREFORE NOT APPROVED FOR RELEASE					
		QUALITY CONTROL APPROVAL		DATE	

Chemistry Assessment Section

Drug Product Specifications –



Exhibit 45-039A
Product Specification Template

	Product Specification		Page
			1 of 2
	Specification #	PS-0324-01	
	Specification Effective Date	N/A	
Prepared By: (b) (4)	Date:		N/A

Product Information	
Product Description: Metaxalone Tablets 640mg Peach colored, oval shaped compressed tablets. Debossed on one side with cor 324 and plain on the other side. Free from any visible defects.	Product Code: 324
DEA Classification: None	

Manufacturing Site
CorePharma; 215 Wgod Ave, Middlesex, New Jersey 08846

Release Test Requirements		
Test	Test Method	Specification
Appearance	24-037	Peach colored, oval shaped compressed tablets. Debossed on one side with cor 324 and plain on the other side. Free from any visible defects.
Identification A	QCM 640 OR QCM 324-0002	The retention time of the Metaxalone peak in the chromatogram obtained from the assay preparation should correspond to that of the Metaxalone peak obtained from standard preparation.
Identification B	24-661 OR QCM 324-0002	The infrared absorption spectrum of a (b) (4), (b) (4), obtained from the tablet preparation exhibits maxima only at the same wavelength as that of a similar preparation of Metaxalone RS.
Water Content	USP/NF<921>Method 1a	NMT (b) (4)%
Dissolution	24-642 OR QCM 324-0003	30 Minutes : (b) (4) % ¹ 90 Minutes : Q = (b) (4) % ² ¹ USP <711> Acceptance Table 2 Criteria ² USP <711> Acceptance Table 1 Criteria
Uniformity of Dosage by Weight Variation	QCM 640 OR QCM 324-0002	Meets the requirements of USP/NF <905> AV≤15.0
Assay	QCM 640 OR QCM 324-0002	(b) (4)

Printed on: 30 Mar 2015, 01:02:08 pm; Printed by: (b) (4). This copy expires on 02 Apr 2015 at 01:03:08 pm.

Chemistry Assessment Section

InfoCard Number: PS-0324-00 Revision: 01 Effective Date:

	Product Specification		Page
			2 of 2
	Specification #	PS-0324-01	
Specification Effective Date	N/A		

Release Test Requirements		
Test	Test Method	Specification
Impurity Assay	QCM 640 OR QCM 324-0001	(b) (4) NMT (b) (4) %
		Individual Unspecified Unidentified Impurity: NMT 0.10% Total Impurities: NMT 0.50%
(b) (4)		

Stability/Shelf Life Test Requirements		
Test	Test Method	Specification
Package Integrity	24-037	The bottle and cap are free from visible defects. The liner is intact.
Appearance	24-037	Peach colored, oval shaped compressed tablets. Debossed on one side with cor 324 and plain on the other side. Free from any visible defects.
(b) (4)		
Dissolution	24-642 OR QCM 324-0003	30 Minutes : (b) (4), % ¹
		90 Minutes : Q = (b) (4) % ²
¹ USP <711> Acceptance Table 2 Criteria ² USP <711> Acceptance Table 1 Criteria		
Assay	QCM 640 OR QCM 324-0002	(b) (4)
Impurity Assay	QCM 640 OR QCM 324-0001	(b) (4) NMT (b) (4) %
		Individual Unspecified Unidentified Impurity: NMT 0.10% Total Impurities: NMT 0.50%

Revision History	
Rev #	Description
00	New Specification created
01	Refer to CR-0027. Revised Appearance test specifications. For Dissolution test removed (b) (4) min. time point and revised specification for 30 min. time point from NMT (b) (4) % to (b) (4) % and added footnotes 1 and 2 for reference to USP <711> acceptance tables.

NDA 22-503

Metaxalone Tablets

Corepharma LLC

Chemistry Review #2

November 21, 2013

Edwin Jao, Ph.D.

**ONDQA/Division III/Branch VIII
for**

Division of Pulmonary, Allergy, and Rheumatology Products

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B. Description of How the Drug Product is Intended to be Used	9
C. Basis for Approvability or Not-Approval Recommendation.....	9
III. Administrative.....	9
A. Reviewer's Signature.....	9
B. Endorsement Block.....	9
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Chemistry Assessment	10
I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data.....	10
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P DRUG PRODUCT [Tradename, Tablets].....	17
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A. Labeling & Package Insert	43
B. Environmental Assessment Or Claim Of Categorical Exclusion	43
III. List Of Information Requests Communicated	N/A

Chemistry Review Data Sheet

1. NDA 22-503
2. REVIEW #: 2
3. REVIEW DATE: 21-Nov-2013
4. REVIEWER: Edwin Jao, Ph.D.
5. PREVIOUS DOCUMENTS:
 - Original: 18-AUG-2009
 - Amendment to original1: 20-OCT -2009
 - Amendment to original2: 25-NOV -2009
 - Amendment to original3: 19-MAR -2010
 - Amendment to original4: 27-APR -2010

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed
resubmission

Document Date
18-Jun-2013

7. NAME & ADDRESS OF APPLICANT:

Name: Corepharma LLC
Address: 215 Wood Avenue
Middlesex, NJ 08846
Representative: N.A.
Telephone: (732) 805- 5642

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: NA
- b) Non-Proprietary Name (USAN): metaxalone
- c) Code Name/#:
- d) Chem. Type/Submission Priority:
 - Chem. Type: 5 (new formulation)
 - Submission Priority: Standard

9. LEGAL BASIS FOR SUBMISSION: This NDA is submitted as a 505(b)(2) application. The reference listed drug is Metaxalone Tablets, 800 mg, NDA 13-217, from King Pharmaceuticals, Inc.

10. PHARMACOL. CATEGORY:

Metaxalone is indicated for the relief of discomforts associated with acute musculoskeletal conditions. Its mechanism of action has not been established.

11. DOSAGE FORM: Tablet

12. STRENGTH/POTENCY: 640 mg/tablet

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: Rx OTC

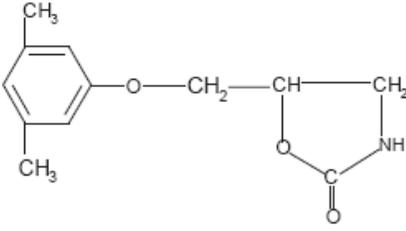
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product Form Completed
 Not a SPOTS product

Chemistry Review Data Sheet

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

Metaxalone:

Structural Formula	
Molecular Formula	C ₁₂ H ₁₅ NO ₃
Molecular Weight	221.2 ^(b) ₍₄₎

Chemical name: 5-(3,5-dimethylphenoxy)methyl]-2-oxazolidone

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	1	Adequate	January 25, 2010	Reviewed by Elsbeth Chikhale, Ph.D.
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no relevant revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other:

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

Chemistry Review Data Sheet

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	13-217	Skelaxin (metaxalone) Tablets, 800 mg, RLD, King Pharmaceuticals, Inc
(b) (4)		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biowaiver	N/A		
Biopharmaceutics			
Biometrics	N/A		
EES	withhold	10/24/13	Robert H. Wittorf, PharmD
Pharm/Tox	Approval	4/20/10	Jay Chang, Ph.D.
CDRH	N/A		
Clinical	Approval	10/10/13	
Clinical Pharmacology	approval	11/20/13	Dr. AGARWAL, SHEETAL
Methods Validation	FDA revalidation is not needed	4/27/10	Elsbeth Chikhale, Ph.D.
DMEPA	Approval	8/21/13	Dr. MCMILLAN, TERESA
DDMAC			
EA	Categorical exclusion granted (consult not needed)	4/27/10	Elsbeth Chikhale, Ph.D.
Microbiology	N/A		

19. ORDER OF REVIEW: N/A

The Chemistry Review for NDA 22-503

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the CMC point of view the application is recommended for a complete response.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N.A.

II. Summary of Chemistry Assessments

See review #1 by Dr. Elsbeth Chikhale.

C. Basis for Approvability or Not-Approval Recommendation

The application is recommended for a complete response due to the WITHHOLD recommendation from the Office of Compliance.

III. Administrative

A. **Reviewer's Signature:** in DARRTS

B. **Endorsement Block:** in DARRTS

C. **cc Block:** in DARRTS

Chemistry Assessment

The application was recommended for complete response during the first review cycle due to a pending recommendation from the Office of Compliance. The labeling and container labels were not reviewed by ONDQA for the same reason. In this resubmission the applicant claimed that the facilities are ready for inspections, and submitted a revised version of labeling in response to the recommendations from DEMEPA. However, recently the applicant stated that the facilities were not all ready for inspection. The applicant received a WITHHOLD recommendation from the Office of Compliance on 10/24/2013 (see memo by Robert H. Wittorf, Pharm D dated 10/24/2013). The current summary report from EES is duplicated below.

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT**

Application:	NDA 22503/000	Sponsor:	COREPHARMA
Org. Code:	570		215 WOOD AVE
Priority:	3		MIDDLESEX, NJ 08846
Stamp Date:	20-AUG-2009	Brand Name:	(b) (4) 640MG (METAXALONE)
PDUFA Date:	18-DEC-2013	Estab. Name:	
Action Goal:		Generic Name:	
District Goal:	19-OCT-2013	Product Number; Dosage Form; Ingredient; Strengths	001; TABLET; METAXALONE; 640MG

FDA Contacts:	E. JAO	Prod Qual Reviewer	3017961684
	Y. LIU	Product Quality PM	3017961926
	S. NABAVIAN	Regulatory Project Mgr	(HFD-570) 3017962777
	C. BERTHA	Team Leader	3017961646

Overall Recommendation:	PENDING	on 15-JUL-2013	by EES_PROD
	PENDING	on 15-JUL-2013	by EES_PROD
	PENDING	on 02-MAY-2013	by EES_PROD
	WITHHOLD	on 02-MAY-2013	by EES_PROD
	WITHHOLD	on 02-JUN-2010	by EES_PROD

Establishment:	CFN: (b) (4)	FEI: (b) (4)
	(b) (4)	

DMF No:		AADA:	
Responsibilities:	DRUG SUBSTANCE MANUFACTURER		
Profile:	NON-STERILE API BY CHEMICAL SYNTHESIS	OAI Status:	NONE
Last Milestone:	INSPECTION PERFORMED		
Milestone Date:	18-SEP-2013		

No additional CMC deficiencies were cited in the first cycle complete response action letter. No new CMC information is provided in this resubmission. During the first review cycle the following comments pertinent to labeling and container labels were issued by DMEPA on 6/2/2013.

1. The labels and labeling include a proprietary name (b) (4) which we found unacceptable and communicated this decision to you via a letter dated May 27, 2010. The container labels and package insert should be revised to remove all instances of the proposed proprietary name (b) (4).
2. Your logo on the principal display panel of the container labels is large, distracting, and competes for prominence with both the proposed proprietary name and established name of the drug. Delete or reduce the size of your logo and relocate it away from the proposed proprietary name and established name so that it does not compete with prominence with the proposed proprietary name or the established name.
3. The 'Rx Only' statement and the net quantity statement '100 Tablets' and (b) (4) is distracting from more vital information on the PDP of your container labels such as the name of the product and the strength. Decrease the prominence of these statements by un-bolding the font or decreasing the size of the statement.
4. The usual dose is located on the side panel of the container labels. Revise this statement to include the word '(b) (4)' at the beginning of the statement. The revised statement should read "USUAL DOSAGE: The recommended dose for adults and children over 12 years of ages is one tablet (640 mg) three to four times a day".
5. The side panel of the container labels instructs pharmacists to (b) (4) however this product should also be dispensed in a container that is also unless otherwise specified by the patient. Revise the statement to read "Dispense in a well-closed child-resistant container".

Revised labeling and container labels are provided in this resubmission. The followings are the evaluation. Mostly important, the applicant has decided to drop any proprietary name and just use the generic name Metaxalone Tablets.

Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

1. Package Insert

The following evaluation has taken into account the original version of the labeling and comments from the 1st review cycle. See the labeling review by Dr. Jeanne M Delasko dated 6/2/2010.

(a) "Highlights" Section

Evaluations

Item	Comments on the Information Provided in
------	---

NDA	
Drug name (201.57(a)(2))	
Proprietary name and established name	No proprietary name The established name is Metaxalone Tablets Satisfactory <i>Metaxalone is the USAN name</i>
Dosage form, route of administration	tablets Satisfactory.
Controlled drug substance symbol (if applicable)	N/A
<hr/>	
Dosage Forms and Strengths (201.57(a)(8))	(b) (4) tablets, 640 mg. Satisfactory
(b) (4)	

(b) “Full Prescribing Information” Section

#3. Dosage Form and Strength

(b) (4)

 tablets, 640 mg.

Evaluations

Item	Comments on the Information Provided in NDA
Available dosage forms and strengths: in metric system	(b) (4) tablets, 640 mg. Satisfactory
Active moiety expression of strength with equivalence statement (if applicable)	na
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting, when applicable.	(b) (4) tablets, 640 mg Unsatisfactory The description is not complete. See evaluation below

Evaluation:

The 2010 version has the following description:

“Metaxalone (b) (4) is available as a 640 mg oval, (b) (4) peach tablet, debossed on one side with “cor (b) (4) 324” (b) (4) and plain on the other side.”

These wordings are now in section 11 and 16 only. This finding was conveyed to the team during labeling meeting, and whether the same wording should be duplicated in this section is yet decided.

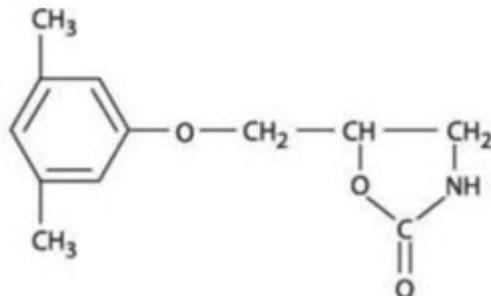
Deficiencies:

Revise the Dosage Form and Strength to read *Metaxalone 640 mg is available as a oval, (b) (4) peach tablet, debossed on one side (b) (4)*

11 DESCRIPTION

Metaxalone is available as a 640 mg oval, (b) (4) peach tablet, debossed on one side with “cor (b) (4) 324” (b) (4) and plain on the other side. The tablets are for oral administration. Each tablet contains 640 mg metaxalone (b) (4) and the following inactive ingredients: alginic acid, FD&C yellow #6, lactose monohydrate, magnesium stearate, propylene glycol alginate and povidone.

Chemically, metaxalone is 5-[(3, 5- dimethylphenoxy) methyl]-2-oxazolidinone. The empirical formula is C₁₂H₁₅NO₃, which corresponds to a molecular weight of 221.25. The structural formula is:



Evaluations

Item	Comments on the Information Provided in NDA
Proprietary name and established name	Metaxalone Satisfactory
Dosage form and route of administration	Oral tablets Satisfactory.
Active moiety expression of strength with equivalence statement (if applicable)	N/A

Inactive ingredient information (quantitative, if injectables 21CFR201.100(b)(5)(iii)).	All inactive ingredients are listed as follows: alginic acid, FD&C yellow # lactose monohydrate, magnesium stearate, propylene glycol alginate and povidone Satisfactory.
Statement of being sterile (if applicable)	N/A
Pharmacological/ therapeutic class	muscle relaxant Satisfactory
Chemical name, structural formula, molecular weight	Chemical name, structural formula and molecular weight are correctly described in this section. Satisfactory.
If radioactive, statement of important nuclear characteristics.	N/A
Other important chemical or physical properties (such as pKa or pH)	None

Evaluation: Satisfactory

The information provided in this section has been revised to incorporate Agency's recommendations for the 2010 version.

16. How Supplied/Storage and Handling

Metaxalone tablets, 640 mg are available as a oval, (b)(4) peach tablet, debossed on one side with "cor (b)(4) 324" (b)(4) and plain on the other side. (b)(4) bottles of 100 (NDC 64720-324-10) (b)(4).

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

Evaluations

Item	Comments on the Information Provided in NDA
Strength of dosage form	Strengths are correctly described as 640 mg Satisfactory.

Available units

Available units are correctly described as 100 (b) (4) tablets bottles, (b) (4)

Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number

Satisfactory
METAXALONE 640 mg (metaxalone) is available as a 640mg oval, (b) (4) peach tablet, debossed on one side with “cor (b) (4) (b) (4) “324” (b) (4) and plain on the other side.

Special handling (e.g., protect from light)
Storage conditions

Satisfactory
n/a
Storage condition is described as Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Manufacturer/distributor name (21 CFR 201.1(h)(5))

Satisfactory
Stated at the end of the labeling.
Satisfactory.

Evaluation: Satisfactory

The information in the current version is the same as that of the 2010 version, which received no comments from the Agency, except that the storage conditions was “Store at Controlled Room Temperature 20°C - 25°C (68°F - 77°F) (b) (4) (b) (4) Both wordings are considered interchangeable found in many labelings of the approved drugs.

2. Immediate container label

(b) (4)



Evaluations: Satisfactory

The current container labels for 100 tablets [REDACTED] (b) (4) have the following revisions

- *The original proprietary name [REDACTED] (b) (4) has been removed, and only the established name Metaxalone is used.*
- *The logo has been relocated to the bottom of the label.*
- *The font for the drug name has been increased.*

- *The dispense instruction has been advised to read “Dispense in a well-closed child-resistant container.”*

The logo is not considered distracting now. The drug name is adequately prominent. The (b) (4) has been replaced by “usual dosage”. All issues listed in the DMEPA review are considered satisfactorily resolved.

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/s/

EDWIN JAO
11/21/2013

PRASAD PERI
11/22/2013
I concur

MEMO TO FILE

To: NDA 22-503 for Tradename (metaxalone) Tablets
From: Elsbeth Chikhale, Ph.D. – CMC reviewer, ONDQA, Div III, Branch VII
Through: Prasad Peri, Ph.D. – Acting Branch Chief, ONDQA, Div III, Branch VIII
Date: June 8, 2010
Subject: NDA 22-503 – CMC recommendation

Per CMC review #1 dated April 27, 2010, from CMC standpoint, the application was recommended APPROVABLE pending an acceptable recommendation from the office of compliance.

On June 2, 2010, the Office of Compliance issued an overall WITHHOLD recommendation for NDA 22-503 (see attached EER summary report).

Labeling review for the PI was conducted in conjunction with the clinical division, and was based on the label of the RLD, Skelaxin (metaxalone) Tablets (NDA 13-217).

The carton and container labels were reviewed by DMEPA and a discipline review letter dated 5/28/2010 was sent to the applicant. A response from the applicant with revised carton and container labels is pending. The revised carton and container label will be reviewed from CMC perspective when it is submitted (second review cycle).

As noted in the CMC review #1 dated April 27, 2010, the stability data provided to date support a shelf life of (b) (4) months for the drug product, instead of the proposed (b) (4) months.

CMC conclusion and recommendation:

From CMC standpoint, the application is NOT recommended for APPROVAL because:

- The Office of Compliance has issued a WITHHOLD overall recommendation for this NDA (see attached EER summary report).
- In order to approve the current application, all manufacturing and testing sites should have an acceptable recommendation from the Office of Compliance.

ATTACHMENT:

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 22503/000
Org. Code: 170
Priority: 3
Stamp Date:
PDUFA Date:
Action Goal:
District Goal: 21-APR-2010

Sponsor: COREPHARMA
215 WOOD AVE
MIDDLESEX, NJ 08846
Brand Name: (b) (4) 640MG (METAXALONE)
Estab. Name:
Generic Name: METAXALONE
Product Number; Dosage Form; Ingredient; Strengths
001; TABLET; METAXALONE; 640MG

Application: NDA 22503/000
Org. Code: 570
Priority: 3
Stamp Date: 20-AUG-2009
PDUFA Date: 20-JUN-2010
Action Goal:
District Goal: 21-APR-2010

Sponsor: COREPHARMA
215 WOOD AVE
MIDDLESEX, NJ 08846
Brand Name: (b) (4) 640MG (METAXALONE)
Estab. Name:
Generic Name: METAXALONE
Product Number; Dosage Form; Ingredient; Strengths
001; TABLET; METAXALONE; 640MG

FDA Contacts:	D. HENRY	Project Manager	301-796-4227
	E. CHIKHALE	Review Chemist	301-796-1659
	D. CHRISTODOULOU	Team Leader	301-796-1342

Overall Recommendation: WITHHOLD on 02-JUN-2010 by A. INYARD ()

Application
Type/Number

Submission
Type/Number

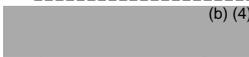
Submitter Name

Product Name

NDA-22503

ORIG-1

COREPHARMA
LLC

 (b) (4)
640MG
(METAXALONE)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ELSBETH G CHIKHALE
06/08/2010

PRASAD PERI
06/09/2010
I concur

Initial Quality Assessment
Division of Pre-Marketing Assessment I, Branch II
Office of New Drug Quality Assessment
Division of Anesthesia, Analgesia and Rheumatology Products

OND Division:	Anesthesia, Analgesia and Rheumatology	
NDA:	22-503	
Chemical Classification:	3S	
Applicant:	CorePharma LLC	
Stamp date:	August 20, 2009	
PDUFA Date:	June 20, 2010	
Trademark:	 (b) (4)	
Established Name:	Metaxalone	
Dosage Form:	Tablet 640 mg	
Route of Administration:	Oral	
Indication:	Treatment of acute painful musculoskeletal conditions	
Pharmaceutical Assessment Lead:	Danae D. Christodoulou, Ph.D.	
	YES	NO
ONDQA Fileability:	<u>√</u>	_____
Comments for 74-Day Letter:	<u>√</u>	_____

Summary, Critical Issues and Comments

A. Summary

The application is filed as a 505(b)(2), non-priority NDA with 10-month review clock. The referenced approved product is Skelaxin® (NDA 13-217, King Pharmaceuticals). Skelaxin® is available as 800 and 400 mg tablets; only the 800 mg is marketed.

The formulation consists of tablets that are (b) (4) metaxalone (b) (4)

The 640 mg tablets are peach colored, oval shaped, debossed (b) (4)

(b) (4) The tablets are packaged in HDPE bottles, size 150, (b) (4) cc, counts 100, (b) (4) with (b) (4) and capped with child resistant closures.

B. Review, Comments and Recommendations

Drug Substance

Molecular Structure, Chemical Name, Molecular Formula and Molecular Weight

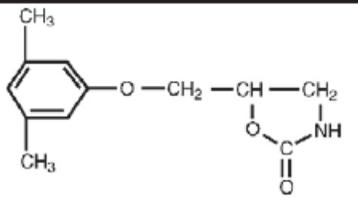
Chemical names:

5-[(3,5-dimethylphenoxy) methyl]-2-oxazolidinone;

5-[(3,5-xilyloxy)methyl]-2-oxazolidinone

CAS: 1665-48-1

Figure 1. Structure of metaxalone

Structure	
Empirical formula	C ₁₂ H ₁₅ NO ₃
Molecular weight	221.2 (b) (4)

The drug substance, metaxalone, is supplied by (b) (4) Description of the manufacturing processes and controls are referenced to the Drug Master File (DMF) (b) (4) Letter of Authorization (LoA) is included in the NDA. DMF (b) (4) has been reviewed previously.

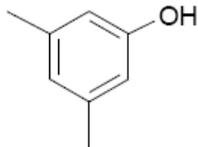
Characterization:

Details of the drug substance characterization are referenced to the DMF. The applicant stated that metaxalone produced by (b) (4) is a (b) (4) The physical properties of (b) (4) metaxalone, e.g., solubility, morphic form, particle size distribution etc., should be assessed by the primary reviewer, for impact on manufacturability, quality and performance (e.g., solubility, bioavailability, stability) of the drug product.

Potential Impurities and degradation products:

One specified impurity, namely, 3,5-xylenol is controlled by (b) (4) and the applicant, at (b) (4)%. Unidentified impurities are controlled a (b) (4)%. 3,5-xylenol was found in batches tested to date by the applicant, at levels not exceeding 0.05%. Maximum proposed daily dose of the drug is 2560 mg.

Figure 2. Process-Related Impurities

Impurity Name	Structure	Type (Source)	Test Method
3,5-Dimethylphenol (3,5-DMP)		(b) (4)	QCM 135

Drug Substance Specifications:

Drug substance specifications are shown below, in Table 1. Methods Validation is provided for the non-compendial method for assay and related substances. This method and its validation should be assessed as per ICH Q2B. The proposed limits for impurities/degradants should be assessed as per ICH Q3A(R2) and Q3B(R) in consultation with the Toxicology Division. Residual solvent limits should be assessed for compliance with ICH Q3C.

Batch analysis:

NDA batches: Metaxalone (b) (4) Core lot #: CR0820, CR0904, CR0905

Metaxalone: Core lot #: RR-8H714, RR-9A011, RR-9A012

Batches met specifications, with 3,5 xylenol <LOD, unspecified impurities <0.05%, total impurities <(b) (4) %.

Reference standard:

(b) (4) tests against qualified working standards referenced to DMF (b) (4) and CorePharma against the reference standards in Table 2 (Certificates of Analysis included).

Table 2. Drug Substance Reference Standards

Compound	Supplier	Corepharma's Lot #	Mfg's Lot #
Metaxalone (b) (4)	(b) (4)	0000000002RS	0000000002
		RR-7F544RS	MH07023054
Metaxalone		RS-07234	MH06083082

Drug substance Stability:

Metaxalone is supported by (b) (4) stability when stored under normal conditions. Stability studies are referenced to DMF (b) (4)

Table 1a. Drug Substance Specifications (Metaxalone (b) (4))

Tests	Method	Acceptance Criteria	
		Executed Specifications	Proposed Specifications
Description	Visual	White to off white crystalline powder	White to off white crystalline powder
Identification	USP/NF <197K> QCM 135	A. Infrared Absorption B. The R. Time of the Metaxalone peak in the assay sample should correspond to that of the standard preparation	A. Infrared Absorption B. The R. Time of the Metaxalone peak in the assay sample should correspond to that of the standard preparation
Melting Range	USP/NF <741>	Between (b) (4) and (b) (4)	Between (b) (4) and (b) (4)
Loss on Drying	USP/NF <731>	NMT (b) (4) (b) (4)	NMT (b) (4) (b) (4)
RESIDUE ON IGNITION	USP/NF <281>	NMT 0.3%	NMT 0.3%
OVI*	USP/NF	Meets the requirements	-
Residual Solvents [§]	QCM 234	(b) (4) NMT (b) (4) ppm (b) (4) NMT (b) (4) ppm	(b) (4) NMT (b) (4) ppm (b) (4) NMT (b) (4) ppm
HEAVY METALS	USP/NF <231>, Method II	NMT (b) (4) %	NMT (b) (4) %
Assay by HPLC	QCM 135	NLT (b) (4) and NMT (b) (4) percent calculated on the (b) (4) basis	NLT (b) (4) % and NMT (b) (4) % calculated on the (b) (4) basis
Impurity Assay by HPLC Specified Identified Impurities 3,5-Dimethylphenol (3,5-xyleneol): Individual Unspecified Unidentified Impurity Total Impurities	QCM 135	NMT 0.05% NMT 0.05% NMT (b) (4) %	NMT 0.05% NMT 0.05% (Report Impurities > 0.03%) NMT 0.5%
Bulk Density	24-010	(b) (4) g/mL	(b) (4) g/mL
Tap Density	24-010	(b) (4) g/mL	(b) (4) g/mL
Particle Size by Malvern	M1208.01	(b) (4) % of the particles: NMT (b) (4) μ (b) (4) % of the particles: NMT (b) (4) μ (b) (4) % of the particles: NMT (b) (4) μ	(b) (4) % of the particles (d ₁₀): NMT (b) (4) μ (b) (4) % of the particles (d ₅₀): NMT (b) (4) μ (b) (4) % of the particles (d ₉₀): NMT (b) (4) μ

Specifications for metaxalone

(b) (4)

Table 1b. Differing Specifications for Metaxalone Drug Substance

Tests	Method	Acceptance Criteria			
		Executed Specifications		Proposed Specifications	
Bulk Density	24-010	(b) (4) g/mL	(b) (4) g/mL	(b) (4) g/mL	(b) (4) g/mL
Tap Density	24-010	(b) (4) g/mL	(b) (4) g/mL	(b) (4) g/mL	(b) (4) g/mL
Particle Size by Sieve	QCM 12	Sieve # (b) (4)	% Retained (b) (4)% NMT (4)% NMT (b) (4)% NMT (b) (4)%	Sieve # (b) (4)	% Retained (b) (4)% NMT (4)% NMT (b) (4)% NMT (b) (4)%

Drug product

The applicant claims that (b) (4) tablets were developed to improve metaxalone bioavailability, (b) (4). This formulation contains (b) (4) drug substance. Metaxalone (b) (4) is claimed to improve on the drug product bioavailability and performance. No novel excipients are used.

Table 2. Quantitative composition of metaxalone tablets 640 mg.

Ingredient	Reference to Quality Standard	Function	Quantity per Tablet (mg)	IIG Limit*
Metaxalone (b) (4)	In-house	Active	(b) (4)	(b) (4)
Metaxalone	In-house	Active	(b) (4)	(b) (4)
Lactose Monohydrate, NF (b) (4)	NF	(b) (4)	(b) (4)	(b) (4)
FD&C Yellow # 6 (b) (4)	In-house	(b) (4)	(b) (4)	(b) (4)
Propylene Glycol Alginate, NF (b) (4)	NF	(b) (4)	(b) (4)	(b) (4)
Alginic Acid, NF (b) (4)	NF	(b) (4)	(b) (4)	(b) (4)
Povidone, USP (b) (4)	USP	(b) (4)	(b) (4)	(b) (4)
Magnesium Stearate, NF	NF	(b) (4)	(b) (4)	(b) (4)

Overages: Not planned.

Manufacturing Process:

Manufacturing, packaging and analytical testing is performed by CorePharma LLC, NJ. (b) (4) performs PSD analysis for metaxalone. The manufacturing process consists of (b) (4)

Manufacturing batch

records (blank and executed) have been included. No re-processing is planned.

NDA Registration batches:
CR0820, CR0904, CR0905

The applicant submitted three primary stability batches, with 3-month long term and 3-month accelerated stability data and amended 12-month data (CR0820) and 6-month data (CR0904, CR0905) upon our request prior to filing. The stability amendment was submitted to the NDA on 10/20/2009. Batch analysis is provided in the NDA. All batches met specifications, listed below, and levels of impurities/degradants were reported at < (b) (4) %.

Table 3. Drug Product Specifications:

TEST	METHOD	SPECIFICATION
DESCRIPTION	QCM 37	Peach Colored, Oval shaped (b) (4) Tablets. Debossed (b) (4) (b) (4) and Plain on the other side and free from any visible defects.
IDENTIFICATION		
A. IR	24-661	The Infrared absorption spectrum of a (b) (4) (b) (4) obtained from the tablet preparation exhibits maxima only at the same wavelength as that of a similar preparation of Metaxalone RS
B. HPLC	QCM 640	The retention time of the Metaxalone peak in the chromatogram obtained from the assay preparation should correspond to that of the Metaxalone peak obtained from standard preparation
WATER	QCM 16	NMT (b) (4) %
DISSOLUTION	QCM 642	NLT (b) (4) % (Q) of the labeled amount dissolved in 90 Minutes.
UNIFORMITY OF DOSAGE BY WEIGHT VARIATION	QCM 640	(b) (4)
ASSAY	QCM 640	(b) (4) %
IMPURITY ASSAY	QCM 640	
Specified Identified Impurities		(b) (4)
(b) (4)		NMT (b) (4) %
Individual Unspecified Unidentified impurities		NMT 0.10%
Total Impurities		NMT 0.5%
(b) (4)		

Batch analysis data:

Certificates of analysis are provided for all batches. No degradation has been observed for the drug product (total impurities \leq (b) (4) %).

The analytical methods for the drug product do not present novel elements. For the HPLC assay and impurities method, validation should be assessed, to confirm the applicant's conclusion that the method resolves impurities of similar structure and chemical properties. Justification of specifications should be assessed as per the ICH Q3B(R) guidelines in consultation with the Toxicology Division.

Container Closure:

Metaxalone tablets are packaged in high-density polyethylene (HDPE) bottle sizes 150 cc/count 100 (b) (4) with child-resistant (CR) closures, (b) (4)

Since the drug product is a solid oral dosage form, review of the packaging DMFs is not required, but the firm's acceptance criteria for their packaging materials should be assessed. Letters of Authorization to the packaging DMFs have been included in the NDA.

Stability:

Stability testing of metaxalone capsules is performed under standard ICH conditions at 25°C/60% RH, and 40°C/75% RH in the proposed commercial packaging. Stability protocols and post-approval stability commitment are provided in the NDA. Long term stability data up to 12 months on one batch and 6-month on two batches have been amended on 10/20/2009. The proposed expiration dating is (b) (4) months. Statistical analysis evaluation has not been performed by the applicant. Note that no significant degradation of the drug product has been observed on stability. Photostability testing has not been reported.

Labeling

Labeling information of the container labels and packaging insert should be assessed with respect to CMC related information. SPL labeling has not been included and should be requested from the applicant.

C. Critical issues for review and recommendation

During assessment of the CMC information provided in this NDA, the primary reviewer should consider addressing issues identified above and other related ones, summarized here, for their impact on drug product quality and performance throughout the shelf-life:

1. Review of the drug substance DMF (b) (4)
2. The physical properties of metaxalone, e.g., solubility, morphic form, particle size distribution etc., should be assessed for impact on manufacturability, quality and performance (e.g., dissolution, bioavailability, stability) of the drug product.
3. Limits of impurities and related substances in the drug substance as per ICH Q3A(R), in consultation with the Toxicology Division (b) (4).
4. The suitability of the compendial specifications of excipients for drug product manufacturability, quality and performance should be assessed.
5. Details of the manufacturing process of the drug product, e.g.: (b) (4)
6. Suitability of the dissolution method and acceptance criteria.
7. Drug product specifications, e.g., impurity/degradant limits as per ICH Q3B(R), in consultation with the Toxicology Division.
8. Proposed metaxalone tablets expiration dating of (b) (4) months. The expiry date was proposed based on 12-month real time data on one batch and 6-month data on two batches.
9. Photostability testing of the drug product has not been reported.
10. Labeling in Structured Product Labeling (SPL) format has not been provided.

D. **Comments for the 74-day Letter:** None

E. **Recommendation for fileability:** The NDA is fileable based on sufficient number of NDA batches, and 12-month long term stability data amended on one batch of the drug product and 6-month on two batches. The NDA is suitable for evaluation and assessment based on FDA and ICH guidelines for submitting CMC information for New Drug Applications.

Recommendation for Team Review: The NDA was not recommended for team review.

Consults:

1. Toxicology; 2. Biopharmaceutics (to be determined and initiated by the primary reviewer). Microbiology consult was not deemed necessary.

Danae D. Christodoulou, Ph.D.
CMC Lead

6/4/2010
Date

Prasad Peri, Ph.D.
Branch II Chief (Acting), ONDQA

6/4/2010
Date

NDA Number: 22503

Supplement Number and Type:

Established/Proper Name:

3S

Metaxalone tablets

Applicant: CorePharma

Letter Date: 08/18/2009

Stamp Date: 08/20/2009

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies. On **initial** overview of the NDA application for filing:

A. GENERAL				
	Parameter	Yes	No	Comment
1.	Is the CMC section organized adequately?	X		
2.	Is the CMC section indexed and paginated (including all PDF files) adequately?	X		
3.	Are all the pages in the CMC section legible?	X		
4.	Has all information requested during the IND phase, and at the pre-NDA meetings been included?		X	

B. FACILITIES*				
	Parameter	Yes	No	Comment
5.	Is a single, comprehensive list of all involved facilities available in one location in the application?	X		(M3)
6.	For a naturally-derived API only, are the facilities responsible for critical intermediate or crude API manufacturing, or performing upstream steps, specified in the application? If not, has a justification been provided for this omission? This question is not applicable for synthesized API.			NA

7.	<p>Are drug substance manufacturing sites identified on FDA Form 356h or associated continuation sheet? For each site, does the application list:</p> <ul style="list-style-type: none"> • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable) 	X		(b) (4) DMF (b) (4)
8.	<p>Are drug product manufacturing sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:</p> <ul style="list-style-type: none"> • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable) 	X		Clarifications and communications with OC.
9.	<p>Are additional manufacturing, packaging and control/testing laboratory sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:</p> <ul style="list-style-type: none"> • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable) 	X		Clarifications and communications with OC.

10.	Is a statement provided that all facilities are ready for GMP inspection at the time of submission?		X	
-----	---	--	---	--

* If any information regarding the facilities is omitted, this should be addressed ASAP with the applicant and can be a *potential* filing issue or a *potential* review issue.

C. ENVIRONMENTAL ASSESMENT				
	Parameter	Yes	No	Comment
11.	Has an environmental assessment report or categorical exclusion been provided?	X		

D. DRUG SUBSTANCE/ACTIVE PHARMACEUTICAL INGREDIENT (DS/API)				
	Parameter	Yes	No	Comment
12.	Does the section contain a description of the DS manufacturing process?	X		Referenced to DMF (b) (4)
13.	Does the section contain identification and controls of critical steps and intermediates of the DS?	X		Referenced to DMF (b) (4)
14.	Does the section contain information regarding the characterization of the DS?	X		Referenced to DMF (b) (4)
15.	Does the section contain controls for the DS?	X		Specifications included in the NDA
16.	Has stability data and analysis been provided for the drug substance?			Referenced to DMF (b) (4)
17.	Does the application contain Quality by Design (QbD) information regarding the DS?		X	
18.	Does the application contain Process Analytical Technology (PAT) information regarding the DS?		X	

E. DRUG PRODUCT (DP)				
	Parameter	Yes	No	Comment
19.	Is there a description of manufacturing process and methods for DP production through finishing, including formulation, filling, labeling and packaging?	X		
20.	Does the section contain identification and controls of critical steps and intermediates of the DP, including analytical procedures and method validation reports for assay and related substances if applicable?	X		
21.	Is there a batch production record and a proposed master batch record?	X		
22.	Has an investigational formulations section been provided? Is there adequate linkage between the investigational product and the proposed marketed product?	X		
23.	Have any biowaivers been requested?		X	
24.	Does the section contain description of to-be-marketed container/closure system and presentations)?	X		
25.	Does the section contain controls of the final drug product?	X		
26.	Has stability data and analysis been provided to support the requested expiration date?	X		
27.	Does the application contain Quality by Design (QbD) information regarding the DP?		X	
28.	Does the application contain Process Analytical Technology (PAT) information regarding the DP?		X	

F. METHODS VALIDATION (MV)				
	Parameter	Yes	No	Comment
29.	Is there a methods validation package?	X		

G. MICROBIOLOGY				
	Parameter	Yes	No	Comment
30.	If appropriate, is a separate microbiological section included assuring sterility of the drug product?		X	NA (Solid Oral Dosage Form)

H. MASTER FILES (DMF/MAF)				
	Parameter	Yes	No	Comment
31.	Is information for critical DMF references (i.e., for drug substance and important packaging components for non-solid-oral drug products) complete?	X		

DMF #	TYPE	HOLDER	ITEM REFERENCED	LOA DATE	COMMENTS
(b) (4)	2	[REDACTED]	(b) (4)	3/19/2009	[REDACTED]
	3		6/24/2008		
	3		6/12/2008		
	3		6/13/2008		
	3		8/8/2005		
	3		1/4/2008		
	3		3/18/2009		
	3		3/19/2008		

I. LABELING				
	Parameter	Yes	No	Comment
32.	Has the draft package insert been provided?	X		
33.	Have the immediate container and carton labels been provided?	X		

J. FILING CONCLUSION				
	Parameter	Yes	No	Comment
34.	IS THE PRODUCT QUALITY SECTION OF THE APPLICATION FILEABLE?	X		Based on sufficient body of data
35.	If the NDA is not fileable from the product quality perspective, state the reasons and provide filing comments to be sent to the Applicant.	X		
36.	Are there any potential review issues to be forwarded to the Applicant for the 74-day letter?		X	

{See appended electronic signature page}

Name of

PAL: Danae Christodoulou 6/4/10
 Division of Pre-Marketing Assessment I
 Office of New Drug Quality Assessment

Date

{See appended electronic signature page}

Name of

Branch Chief (Acting): Prasad Peri
 Division of Pre-Marketing Assessment I
 Office of New Drug Quality Assessment

Date

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22503	ORIG-1	COREPHARMA LLC	(b) (4) 640MG (METAXALONE)

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/s/

DANAE D CHRISTODOULOU
06/04/2010
CMC filing memo

PRASAD PERI
06/04/2010
I concur

Tradename (metaxalone) Tablets

NDA 22-503

Summary of the Basis for the Recommended Action from Chemistry, Manufacturing, and Controls

Applicant: Corepharma LLC
215 Wood Avenue
Middlesex, NJ 08846

Indication: Metaxalone tablets are indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute, painful musculoskeletal conditions. The recommended dose for adults and children over 12 years of age is one 640 mg tablet three to four times a day

Presentation: Metaxalone is available as a 640mg oval, (b) (4) peach colored tablet, debossed on one side (b) (4) and plain on the other side. They are available in bottles of 100 (64720-324-10) (b) (4)

EER Status: Pending a final recommendation.

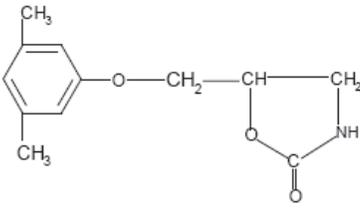
Consults: EA – Categorical exclusion granted under 21 CFR §25.31(c)
Methods Validation – Not likely to pursue since the methods are standard.
Microbiology: N/A
Pharmacology/Toxicology –Acceptable

Original Submission: 18-Aug-2009

Post-Approval CMC Commitments:
None

Drug Substance:

Chemically, metaxalone is 5-[(3,5- dimethylphenoxy) methyl]-2-oxazolidinone. The empirical formula is $C_{12}H_{15}NO_3$, which corresponds to a molecular weight of 221.25.

Structural Formula	
Molecular Formula	$C_{12}H_{15}NO_3$
Molecular Weight	221.2 (b) (4)

Metaxalone is a white to almost white, odorless crystalline powder freely soluble in chloroform, soluble in methanol and in 96% ethanol, but practically insoluble in ether and or water.

Metaxalone is a previously approved drug substance, produced by chemical synthesis. (b) (4)

(b) (4) All information regarding the physicochemical properties, impurities, method of synthesis and purification, process controls, control of raw materials, container closure system, and stability of metaxalone are provided in the Drug Master File (DMF) (b) (4) held by (b) (4). The drug substance is manufactured in (b) (4).

The (b) (4) drug substance specifications include Description, Identification (IR and UV), Melting Range, Loss on Drying, Residue on Ignition, Organic Volatile Impurities, Residual Solvents, Heavy Metals, Assay, Related Substances, Impurities, Bulk Density, Tap Density, and Particle Size Distribution. (b) (4)

Conclusion: The drug substance is satisfactory.

Drug Product:

The proposed drug product is an immediate release tablet, indicated for the relief of discomforts associated with acute, painful musculoskeletal conditions. The tablet is a 640 mg oval, (b) (4)

peach tablet, debossed on one side (b) (4) and plain on the other side.

It is formulated as an uncoated immediate release tablet manufactured by (b) (4). The excipients consist of lactose monohydrate NF, FD&C yellow #6 (b) (4), propylene glycol alginate NF, alginic acid NF, povidone USP, and magnesium stearate NF. This NDA is submitted as a 505(b)2. The reference drug is Skelaxin, NDA 13-217. The applicant has performed bioequivalence studies to support the equivalence to approved listed products. The tablets are packaged in HDPE bottles with child resistant closures for direct sale to the user (150 cc bottles containing 100 tablets) (b) (4)

The specifications for the finished product include testing for Appearance, Identification, Water Content, Dissolution, Uniformity of Dosage Units by Weight Variation, Assay, Impurity, and Residual Solvents.

The proposed commercial drug product is manufactured by Corepharma LLC., in Middlesex, NJ. The proposed commercial batch size is (b) (4) tablets.

The proposed storage condition for the drug product is at controlled room temperature (i.e. store at 20 °C - 25 °C (68 °F - 77 °F) (b) (4) (see USP controlled room temperature). The provided stability data support a shelf life of (b) (4) months when stored at room temperature conditions.

Outstanding issues:

- An acceptable cGMP status for the relevant manufacturing and testing facilities.

Conclusion: The drug product is recommended for approval, pending an acceptable status from the office of compliance on the manufacturing and testing establishments.

Additional Items:

All associated Drug Master Files are acceptable or the pertinent information has been adequately provided in the application.

Method validation will not be requested since all methods are standard.

Overall Conclusion:

From a CMC perspective, the application is recommended for approval **pending** an acceptable recommendation is provided by the Office of Compliance.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22503

ORIG-1

COREPHARMA
LLC

(b) (4)
640MG
(METAXALONE)

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/s/

PRASAD PERI
05/25/2010

NDA 22-503

**Tradename
(metaxalone)
Tablets**

Corepharma LLC

**Elsbeth Chikhale, Ph.D.
ONDQA – DPA I – Branch II
for
Division of Pulmonary, Allergy, and Rheumatology Products**

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III. List Of Information Requests Communicated	N/A

Chemistry Review Data Sheet

1. NDA 22-503
2. REVIEW #: 1
3. REVIEW DATE: 27-APR-2010
4. REVIEWER: Elsbeth Chikhale, Ph.D.
5. PREVIOUS DOCUMENTS: N/A

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	18-AUG-2009
Amendment to original ¹	20-OCT -2009
Amendment to original ²	25-NOV -2009
Amendment to original ³	19-MAR -2010
Amendment to original ⁴	27-APR -2010

- 1) The 10/20/09 amendment provides for additional drug product stability data.
- 2) The 11/25/09 amendment provides for responses to the Agency's information requests.
- 3) The 3/19/10 amendment provides for additional drug product stability data.
- 4) The 4/27/10 amendment provides for a response to a Agency comment.

7. NAME & ADDRESS OF APPLICANT:

Name: Corepharma LLC
Address: 215 Wood Avenue
Middlesex, NJ 08846
Representative: N.A.
Telephone: (732) 805- 5642

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: [REDACTED] (b) (4)
- b) Non-Proprietary Name (USAN): metaxalone
- c) Code Name/#:
- d) Chem. Type/Submission Priority:
- Chem. Type: 5 (new formulation)
 - Submission Priority: Standard

9. **LEGAL BASIS FOR SUBMISSION:** This NDA is submitted as a 505(b)(2) application. The reference listed drug is Tradename (metaxalone) Tablets, 800 mg, NDA 13-217, from King Pharmaceuticals, Inc.

10. PHARMACOL. CATEGORY:

Metaxalone is indicated for the relief of discomforts associated with acute musculoskeletal conditions. Its mechanism of action has not been established.

11. **DOSAGE FORM:** Tablet

12. **STRENGTH/POTENCY:** 640 mg/tablet

13. **ROUTE OF ADMINISTRATION:** Oral

14. **Rx/OTC DISPENSED:** Rx OTC

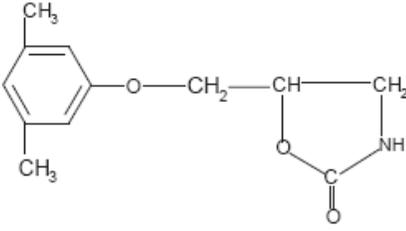
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product Form Completed
 Not a SPOTS product

Chemistry Review Data Sheet

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

Metaxalone:

Structural Formula	
Molecular Formula	C ₁₂ H ₁₅ NO ₃
Molecular Weight	221.2 ^(b) ₍₄₎

Chemical name: 5-(3,5-dimethylphenoxy)methyl]-2-oxazolidone

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	1	Adequate	January 25, 2010	Reviewed by Elsbeth Chikhale, Ph.D.
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no relevant revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other:

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

Chemistry Review Data Sheet

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	13-217	Skelaxin (metaxalone) Tablets, 800 mg, RLD, King Pharmaceuticals Inc
(b) (4)		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biowaiver	N/A		
Biopharmaceutics	Change dissolution acceptance criteria	4/16/10	Sandra Suarez Sharp, Ph.D.
Biometrics	N/A		
EES	pending		
Pharm/Tox	Approval	4/20/10	Jay Chang, Ph.D.
CDRH	N/A		
Clinical Pharmacology	N/A		
Methods Validation	FDA revalidation is not needed	4/27/10	Elsbeth Chikhale, Ph.D.
DMEPA	pending		
DDMAC	pending		
EA	Categorical exclusion granted (consult not needed)	4/27/10	Elsbeth Chikhale, Ph.D.
Microbiology	N/A		

19. ORDER OF REVIEW: N/A

The Chemistry Review for NDA 22-503

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the CMC point of view, the application is APPROVABLE pending an acceptable recommendation from the office of compliance regarding the cGMP status of the manufacturing, testing and packaging facilities. Final labeling will be done in coordination with the clinical division.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N.A.

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

1) Drug Product

The proposed drug product is an immediate release tablet, indicated for the relief of discomforts associated with acute, painful musculoskeletal conditions. The tablet is a 640 mg oval, (b) (4) peach tablet, debossed on one side (b) (4) and plain on the other side. The route of administration is oral. The proposed commercial drug product is manufactured by Corepharma LLC., in Middlesex, NJ. It is formulated as an uncoated immediate release tablet manufactured by (b) (4). The tablets are packaged in HDPE bottles with child resistant closures for direct sale to the user (150 cc bottles containing 100 tablets) (b) (4). The excipients consist of lactose monohydrate NF, FD&C yellow #6 (b) (4), propylene glycol alginate NF, alginic acid NF, povidone USP, and magnesium stearate NF. This NDA is submitted as a 505(b)2. The reference drug is Skelaxin, NDA 13-217. The applicant has performed bioequivalence studies that are reviewed by the clinical pharmacology reviewer (see review by Sayad Al-Habat, Ph.D.). The proposed storage condition for the drug product is at controlled room temperature (i.e. store at 20 °C - 25 °C (68 °F - 77 °F) (b) (4) (see USP controlled room temperature). The provided stability data support a shelf life of (b) (4) months (NOT the proposed (b) (4) months) when stored at room temperature conditions.

2) Drug Substance:

The drug substance, metaxalone, is a previously approved drug substance, produced by chemical synthesis. (b) (4)

(b) (4) All information regarding the physicochemical properties, impurities, method of synthesis and purification, process controls, control of raw materials, container closure system and stability of metaxalone are provided in the Drug Master Files (DMFs) (b) (4) held by (b) (4) DMF (b) (4) was reviewed on 1/25/2010 (review #9 by Elsbeth Chikhale, Ph.D.) and found adequate to support this NDA. The drug substance is manufactured in (b) (4)

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

The drug product is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute, painful musculoskeletal conditions. The recommended dose for adults and children over 12 years of age is one 640 mg tablet three to four times a day.

C. Basis for Approvability or Not-Approval Recommendation

From the CMC point of view, the application is APPROVABLE pending an acceptable recommendation from the office of compliance regarding the cGMP status of the manufacturing, testing and packaging facilities. Final labeling will be done in coordination with the clinical division.

III. Administrative

A. Reviewer's Signature: in DARRTS

B. Endorsement Block: in DARRTS

C. cc Block: in DARRTS

Chemistry Assessment

I. Review of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body of Data

S DRUG SUBSTANCE [Metaxalone, (b) (4)]

(b) (4)

6 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

P DRUG PRODUCT [Tradename, Tablets]

(b) (4)

21 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

A APPENDICES**A.1 Facilities and Equipment (biotech only)**
N/A**A.2 Adventitious Agents Safety Evaluation**
N/A**A.3 Novel Excipients**
N/A**R REGIONAL INFORMATION****R1 Executed Batch Records**

Executed batch record for drug product batch # CR0820, CR0904 and CR0905 are provided in the NDA.

R2 Comparability Protocols

N/A

R3 Methods Validation Package

The NDA contains a method validation data.

Comment: Based on the results from the validation reports, all methods have been validated. Each analytical method is suitable for its intended use. Revalidation by the Agency is not necessary.

II. Review of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

The labeling and labels of this application will be reviewed at a later time in coordination with the clinical division.

B. Environmental Assessment or Claim of Categorical Exclusion

The applicant states that this submission qualifies for a categorical exclusion in accordance with 21 CFR Part 25.31(a) and 25.15. To the applicant's knowledge, no extraordinary circumstances exist that would warrant the preparation of an environmental assessment.

Evaluation: The claim for categorical exclusion is acceptable based on 21 CFR 25.31(a) and 25.15.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22503

ORIG-1

COREPHARMA
LLC

(b) (4)
640MG
(METAXALONE)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ELSBETH G CHIKHALE
04/27/2010

PRASAD PERI
04/27/2010
I concur

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Application: NDA 22503/000
Stamp Date:
Regulatory:

Action Goal:
District Goal: 21-APR-2010

Applicant: COREPHARMA
215 WOOD AVE
MIDDLESEX, NJ 08846

Brand Name: (b) (4) 640MG (METAXALONE)
Estab. Name:
Generic Name: METAXALONE

Priority: 3
Org. Code: 170

Product Number; Dosage Form; Ingredient; Strengths
001; TABLET; METAXALONE; 640MG

Application: NDA 22503/000
Stamp Date: 20-AUG-2009
Regulatory: 20-JUN-2010

Action Goal:
District Goal: 21-APR-2010

Applicant: COREPHARMA
215 WOOD AVE
MIDDLESEX, NJ 08846

Brand Name: (b) (4) 640MG (METAXALONE)
Estab. Name:
Generic Name: METAXALONE

Priority: 3
Org. Code: 570

Product Number; Dosage Form; Ingredient; Strengths
001; TABLET; METAXALONE; 640MG

Application Comment: THE CONTACT PERSON FOR THE APPLICATION IS PRAKASH KULKARNI 732-805-5642, FAX NO 732-805-5643 (on 24-SEP-2009 by D. HENRY () 301-796-4227)

THIS IS A 505(B)(2) APPLICATION AND THE REFERENCE LISTED DRUG IS SKELAXIN 800MG TABLETS (APPLICANT: KING PHARMACEUTICALS) (on 24-SEP-2009 by D. HENRY () 301-796-4227)

FD Contacts:	D. HENRY	Project Manager	301-796-4227
	E. CHIKHALE	Review Chemist	301-796-1659
	D. CHRISTODOULOU	Team Leader	301-796-1342

Overall Recommendation: WITHHOLD on 02-JUN-2010 by A. INYARD ()

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)

(b) (4)
DMF No: (b) (4)

AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Estab. Comment: (b) (4)

Profile: NON-STERILE BULK BY CHEMICAL SYNTHESIS OAT Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	01-OCT-2009				CHRISTODOULO
OC RECOMMENDATION	02-OCT-2009			ACCEPTABLE BASED ON PROFILE	STOCKM

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)

(b) (4)

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE RELEASE TESTER
FINISHED DOSAGE RELEASE TESTER

Estab. Comment:

Profile: CONTROL TESTING LABORATORY OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	29-DEC-2009				CHIKHALEE
OC RECOMMENDATION	30-DEC-2009			ACCEPTABLE BASED ON PROFILE	INYARDA

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: 2249375 FEI: 3002535019
COREPHARMA LLC
215 WOOD AVE
MIDDLESEX, NJ 08846

DMF No: **AADA:**
Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER

Estab. Comment: THE PACKAGING FACILITY IS PART OF THE SAME CAMPUS, BUT HAS A DIFFERENT ADDRESS WHICH IS (b)(4)
(b)(4) (on 30-SEP-2009 by D. HENRY () 301-796-4227)
MANUFACTURING, PACKAGING, STORAGE, RELEASE AND STABILITY TESTING, AND DISTRIBUTION OF THE DRUG
PRODUCT. ALSO RAW MATERIAL TESTING AND RECEIVING (on 24-SEP-2009 by D. HENRY () 301-796-4227)

Profile: TABLETS, PROMPT RELEASE **OAI Status:** OAI ALERT

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	01-OCT-2009				CHRISTODOULO
SUBMITTED TO DO	02-OCT-2009	10-Day Letter			KIEL
INSPECTION SCHEDULED	16-DEC-2009		30-DEC-2009		KDOBILAS
ASSIGNED INSPECTION TO IB	16-DEC-2009	Product Specific			KDOBILAS
INSPECTION PERFORMED 509446	20-JAN-2010		20-JAN-2010		ERIN.MCCAFFERY
OC RECOMMENDATION PENDING REGULATORY REVIEW/ACTION	02-JUN-2010			WITHHOLD BASED ON FILE REVIEW	INYARDA

**FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT**

Establishment: CFN: (b) (4) FEI: (b) (4)

(b) (4)

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE RELEASE TESTER
FINISHED DOSAGE RELEASE TESTER

Estab. Comment:

Profile: CONTROL TESTING LABORATORY OAI Status: NONE

<u>Milestone Name</u>	<u>Milestone Date</u>	<u>Request Type</u>	<u>Planned Completion</u>	<u>Decision</u>	<u>Creator</u>
<u>Comment</u>				<u>Reason</u>	
SUBMITTED TO OC	29-DEC-2009				CHIKHALEE
OC RECOMMENDATION	30-DEC-2009			ACCEPTABLE BASED ON PROFILE	INYARDA