CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-795

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

51 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Withheld Track Number: Administrative- 1

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA: 50-795 (This NDA Provides for a new dosage form for Doryx)

p Date: April 7, 2004 Action Date: May 6, 2005 HFD-520

Trade and generic names/dosage form: Doryx ® (doxycycline hyclate) Delayed-Release Tablets, 75 mg and 100 mg

Applicant: F. H. Faulding, Inc, Therapeutic Class: 4010200

Indication(s) previously approved: treatment of a variety of infections as described in the product labeling

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): Multiple

Indication #1: _____

Is there a full waiver for this indication (check one)?

- ☐ Yes: Please proceed to Section A.
- ■ No: Please check all that apply: ___Partial Waiver ___Deferred X___Completed
  NOTE: More than one may apply
  Please proceed to Section B, Section C, and/or Section D and complete as necessary.

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Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Other:_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____	kg_____	mo._____	yr._____	Tanner Stage_____
Max_____	kg_____	mo._____	yr._____	Tanner Stage_____

Reason(s) for partial waiver:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Adult studies ready for approval
- ☐ Formulation needed
- ☐ Other:_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

n C: Deferred Studies

Age/weight range being deferred:

Min ____ kg____ mo.____ yr.____ Tanner Stage____
Max____ kg____ mo.____ yr.____ Tanner Stage____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min ____ <kg 45 mo.____ yr. 8 Tanner Stage____
Max____ kg____ mo.____ yr.____ Tanner Stage____

Comments:

ere are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered o DFS.

This page was completed by:

{See appended electronic signature page}

_____
Regulatory Project Manager, Judit Milstein

cc: NDA 50-795
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

ATTACHMENT

MEMO OF FILING MEETING

DATE: May 14, 2004

BACKGROUND:
Doryx® (coated doxycycline hyclate pellets) Tablets, 75 mg and 100 mg have been developed as a new dosage form for the existing marketed product Dory® (coated doxycycline hyclate pellets), Capsules 75 mg (NDA 50-582/S-015, approved August 31, 2001) and 100 mg (NDA 50-582, approved July 22, 2985).
In support of this new dosage form, the sponsor provided information on the manufacture and controls of the tablets, the results of a single- and multiple dose bioequivalence study, the results of a single-dose food effect study and dissolution testing results.

ATTENDEES: J. Soreth, L. Gavrilovich, J. Alexander, C. Cooper, D. Lin, A. Nostrandt, S. Pagay, J. Vidra, J. Tworzyanski, V. Jarugula, R. Sharwar, A. Sheldon, Judit Milstein

ASSIGNED REVIEWERS:

Discipline	**Reviewer**
Medical:	Charles Cooper, MD
Secondary Medical:	N/A
Statistical:	Sue Bell, PhD
Pharmacology:	Amy Nostrandt, PhD
Statistical Pharmacology:	N/A
Chemistry:	Suresh Pagay, PhD
Environmental Assessment (if needed):	N/A
Biopharmaceutical:	Jeffrey Tworzyanski, PharmD
Microbiology, sterility:	N/A
Microbiology, clinical (for antimicrobial products only):	Ribhi Sharwar, PhD
DSI:	
Regulatory Project Management:	Judit Milstein
Other Consults:	DSI-Bioequivalence

Per reviewers, are all parts in English or English translation? **YES**
If no, explain:

CLINICAL FILE **YES**

- Clinical site inspection needed: **NO**
- Advisory Committee Meeting needed? **NO**
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

  N/A

CLINICAL MICROBIOLOGY	FILE _	**YES**
STATISTICS	FILE _____	**YES**
BIOPHARMACEUTICS	FILE _____	**YES**
• Biopharm. inspection needed:		**YES**
PHARMACOLOGY	FILE _____	**YES**
• GLP inspection needed:		**NO**
CHEMISTRY	FILE _____	**YES**
• Establishment(s) ready for inspection?		**YES**
Microbiology		**N/A**
ELECTRONIC SUBMISSION:		**N/A**

Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:

_____ The application is unsuitable for filing. Explain why:

___X____ The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

____X___ No filing issues have been identified.

_____ Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of the RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3. Document filing issues/no filing issues conveyed to applicant by Day 74.

Judit Milstein, Regulatory Project Manager, HFD-520

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/s/

Judit Milstein
5/6/05 03:19:06 PM
CSO

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 50-795 Supplement # N/A SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8

Trade Name: Doryx ® Tablets
Generic Name: coated doxycycline hyclate pellets
Strengths: 75 mg and 100 mg

Applicant: F. H. Faulding & Co, Ltd. t/a Mayne Pharma Internaltional
c/o Warner Chilcott, Incl

Date of Application: April 5, 2004
Date of Receipt: April 7, 2004
Date clock started after UN:
Date of Filing Meeting: May 14, 2004
Filing Date: June 4, 2004
Action Goal Date (optional): User Fee Goal Date: February 7, 2005

Indication(s) requested: Multiple indications, same as approved for Doryx Capsules

Type of Original NDA: (b)(1) _X_____ (b)(2) _____
OR
Type of Supplement: (b)(1) _____ (b)(2) _____
NOTE: A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2) application, complete the (b)(2) section at the end of this review.

Therapeutic Classification: S X_____ P _____
Resubmission after withdrawal? no_____ Resubmission after refuse to file? no_____
Chemical Classification: (1,2,3 etc.) _3_____
Other (orphan, OTC, etc.) _____

User Fee Status: Paid __X_____ Exempt (orphan, government) _____
Waived (e.g., small business, public health) _____

Form 3397 (User Fee Cover Sheet) submitted: **YES**
User Fee ID # ___4718____
Clinical data? YES _X_____ NO, Referenced to NDA # _____

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?
No, this is an "old antibiotic"

NO

If yes, explain:

Does another drug have orphan drug exclusivity for the same indication? **NO**

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?

NO

Is the application affected by the Application Integrity Policy (AIP)? **NO**
If yes, explain.

If yes, has OC/DMPQ been notified of the submission? **N/A**

- Does the submission contain an accurate comprehensive index? **YES**
- Was form 356h included with an authorized signature? **YES**
- Submission complete as required under 21 CFR 314.50? **YES**
  If no, explain:

- If an electronic NDA, does it follow the Guidance? **N/A**

  If an electronic NDA, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- If in Common Technical Document format, does it follow the guidance? **N/A**

- Is it an electronic CTD? **N/A**

  If an electronic CTD, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- Patent information submitted on form FDA 3542a? This is an "old antibiotic" **NO**
  On submission dated June 10, 2004, the sponsor indicates that Form FDA 3542a will be submitted within 30 days of approval of the pending patent for Composition of drug Product. All other patents do not apply, as this is a new formulation of an "old antibiotic"
- Exclusivity requested? **NO**
  NO exclusivity granted to "old antibiotics"

- Correctly worded Debarment Certification included with authorized signature? **YES**
  Correct wording submitted on June 10, 2004
  NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e.,

"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge . . . ."

- Financial Disclosure forms included with authorized signature? **YES**
  (Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)

- Field Copy Certification (that it is a true copy of the CMC technical section)? **YES**

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? **YES**
  If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name/Applicant name correct in COMIS? **YES**
  If not, have the Document Room make the corrections

- List referenced IND numbers: 66,553

- End-of-Phase 2 Meeting(s)? **NO**
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) August 25, 2003
  If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?
  This NDA is a for a new dosage form of the same DS. No new information added to this PI **NO**

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? **NO**
  This NDA provides for a new dosage form. No changes to the name.

- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? **N/A**

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted?
  N/A

If Rx-to-OTC Switch application: **N/A**

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS?
  N/A YES NO

- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? **N/A**

Chemistry

- Did applicant request categorical exclusion for environmental assessment? **YES**
  If no, did applicant submit a complete environmental assessment? **N/A**
  If EA submitted, consulted to Nancy Sager (HFD-357)? **N/A**

- Establishment Evaluation Request (EER) submitted to DMPQ? **YES**

- If a parenteral product, consulted to Microbiology Team (HFD-805)? **N/A**

If 505(b)(2) application, complete the following section:

- Name of listed drug(s) and NDA/ANDA #:

- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.)

  YES NO

- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9).

  YES NO

- Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9).

  YES NO

- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.

  ____ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA.

  ____ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired.

  ____ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.

  ____ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

  IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder

was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

____ 21 CFR 314.50(i)(1)(ii): No relevant patents.

____ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications.

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____ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)
____ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

- Did the applicant:
  - Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?

    YES NO
  - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

    YES NO
  - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

    N/A YES NO
  - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?

    N/A YES NO
- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):
  - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

    YES NO
  - A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

    YES NO
  - EITHER
    The number of the applicant's IND under which the studies essential to approval were conducted.

    IND # _____ NO

    OR

    A certification that it provided substantial support of the clinical investigation(s) essential to

approval if it was not the sponsor of the IND under which those clinical studies were conducted?

N/A YES NO

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

YES NO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-795

F H Faulding and Co.
c/o Warner Chilcott, Inc.
Attention: David Haenick, PhD
Manager, Regulatory Affairs
Rockaway 80 Corporate Center
100 Enterprise Drive, Suite 280
Rockaway, NJ 07866

Dear Dr. Haenick:

Please refer to your April 5, 2004, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Doryx® (coated doxycycline hyclate pellets), Tablets.

On December 21, 2004, we received your December 20, 2004 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is May 6, 2005.

If you have any questions, call Judit Milstein, Regulatory Health Project Manager, at (301) 827-2207.

Sincerely,

{See appended electronic signature page}

Frances LeSane
Chief, Project Management Staff
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Frances LeSane
1/24/05 04:37:26 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

IND 66,553

F. H. Faulding and Co.
c/o Warner Chilcott, Inc.
Attention: Alvin Howard
Vice President, Regulatory Affairs
80 Rockaway Corporate Center
100 Enterprise Drive, Suite 280
Rockaway, NJ 07866

Dear Mr. Howard:

Please refer to the meeting between representatives of your firm and FDA on August 25, 2003. The purpose of the meeting was to reach consensus on the content and format of a new drug application.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Judit Milstein, Regulatory Project Manager, at (301) 827-2207.

Sincerely,

{See appended electronic signature page}

Frances LeSane
Chief, Project Management Staff
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure: minutes of the meeting

MEETING MINUTES

MEETING DATE: August 25, 2003

TIME: 10 a.m.

LOCATION: Teleconference

APPLICATION: IND 66,553-Doryx (doxycycline hyclate pellets) Tablet, 100 mg

SPONSOR: F H Faulding and Co. Limited (c/o Warner Chilcott Inc.)

TYPE OF MEETING: pre-NDA

FDA ATTENDEES, TITLES, AND OFFICE/DIVISION
Janice Soreth, MD, Director, Division of Anti-Infective Drug Products
Lillian Gavrilovich, MD, Deputy Director
John Alexander, MD, MPH, Medical Team Leader
Sumathi Nambiar, MD, MPH, Medical Reviewer
Paul Buehler, PharmD, PhD, Biopharmaceutics Reviewer
Philip Colangelo, PharmD, PhD, Biopharmaceutics Team Leader
Albert Sheldon Jr., PhD, Microbiology Team Leader
Frederic Marsik, PhD, Microbiology Reviewer (via teleconference)
James Vidra, PhD, Chemistry Team Leader
Amy Nostrandt, DVM, PhD, Pharmacology and Toxicology Reviewer
Judit Milstein, Regulatory Project Manager

EXTERNAL CONSTITUENT ATTENDEES AND TITLES:
Lynn Gold, PhD, Senior Manger, Pharmaceutics
Tina deVries, PhD, Vice President, Pharmaceutics
Herman Ellman, MD, Senior Vice President, Clinical Development
Alvin Howard, Vice President, Regulatory Affairs
Peter Emodi, Director, Project Management

BACKGROUND:

IND 66,553 originally submitted on January 29, 2003, was deemed safe to proceed, and an advice letter containing the Division's comments were sent to the sponsor on May 20, 2003.

The sponsor of this IND is also the holder of NDA 50-582 for Doryx (doxycycline hyclate in pellets), Capsules.

MEETING OBJECTIVES (as per sponsor's briefing package):

1. To reach consensus on the structure and content of the new drug application.

2. To ensure that the studies and information planned to be included in the application are adequate and sufficient to evaluate the safety and efficacy of the product.

SUMMARY OF UNDERSTANDINGS

1. 12 month long-term stability data are necessary at the time of the NDA submission (as per ICH guidelines).

2. An updated labeling will be provided following the innovator's format. This label should included updated Pharmacology and Toxicology information.

QUESTIONS AND ANSWERS

Question 1. Is it acceptable to use the trade name Doryx for this new dosage form?

On its face the Division has no objections for using the trade name Doryx for the tablets; however, a consult will be forwarded to the Office of Drug Safety at the time of the NDA submission.

Question 2. Does the Agency concur that 6 months of accelerated and 6 months long-term stability data on three product batches is sufficient for filing this NDA?

The Agency prefers the submission of 12 months long-term data (per ICH guidelines) at the time of the NDA submission. The Division also noted that dissolution data for delayed release tablets may not always be predictive of release rates when compared to short-term accelerated data.

The content and outline for the CMC section is generally acceptable. Please note the following comments:

Ethanol should meet USP specification. The sponsor indicated that the product is manufactured in Australia, where BP specifications are in place. The Division requested the sponsor submit a side by side comparison of the BP and USP specifications, and indicated that a decision will be made based on this information.

In-process controls: the acceptance criteria for drug release of coated pellets in the acid media should include "Average plus % RSD" or "Average plus no unit greater than x% in 20 minutes"

Acceptance criteria for the related compounds should be based on stability data. Also, provide historical comparative data for the capsules and for setting acceptance criteria for the impurities.

Question 3. Does the Agency concur that doxycycline hyclate is a well-known compound and no pharmacology and toxicology information need be provided beyond a current literature based overview?

The Division concurs.

Question 4. Does the Agency concur that because all of the components of the tablet are compendial no pharmacology and toxicology information need be provided beyond risk-benefit assessment of the proposed use of each excipient?

The Division concurs and recommends the submission of an updated Pharmacology and Toxicology section of the PI.

Question 5. Does the Agency concur with the content and outline proposed for Item 6.

The Division concurs. In addition to the study reports for the two human pharmacokinetic studies (Protocols PR-01402 and PR-08302), it is important that all dissolution information for the FP225 tablet formulation be provided at the time of NDA submission. This information will facilitate the evaluation of the proposed dissolution method and help in the determination of the acceptance criteria. Please, also provide a comparison of the dissolution of the approved Doryx® capsules to that of the FP225 tablets.

Question 6. Does the Agency concur that doxycycline hyclate is a well-known compound and no microbiology information need be provided beyond a current literature based overview.

The Division agrees in principle, but would like to have more recent information on the susceptibility of the microorganisms in the USA, preferably done within the last 5 years. In response to the sponsor's question as to where to find this information, the Division indicated that there are currently several susceptibility profile databases run by private companies, and that the NCCLS (National Committee for Clinical Laboratory Standards, Wayne, PA), and the CDC (Center for Disease Control and Prevention, Atlanta, GA) should be able to provide information on them.

The Division also recommended that the label be updated following the innovator format.

Question 7. Does the Agency concur that the content and outline proposed for Item 6 would be acceptable for inclusion in Item 8?

The Division concurs.

Question 8. Does the Agency concur with the proposal to provide required case report forms as part of the final study reports in Item 6 and not in Item 12?

The Division concurs.

Question 9. Does the Agency concur that draft labeling can be submitted in MS WORD 2000 and pdf files?

The Division concurs. It would also ease the review process if the Final Study Reports could be submitted in electronic format. The sponsor indicated that they would investigate its feasibility.

The Division also requested the submission of a labeling supplement for NDA 50-582 (Doryx, capsules), updating the label according to the information provided in the new NDA.

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/s/

John Alexander
9/24/03 01:09:06 PM

NDA FILABILITY CHECKLIST

NDA Number: 50-795 **Applicant:** Warner-Chilcott **Stamp Date:** 4/9/04
Drug Name: Doryx - Tablet

IS THE CMC SECTION OF THE APPLICATION FILABLE? (Yes or No) Yes

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies.

	Parameter	Yes	No	Comment
1	On its face, is the section organized adequately?	✓		
2	Is the section indexed and paginated adequately?	✓		
3	On its face, is the section legible?	✓		
4	Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	✓		CFN # obtained from OC
5	Is a statement provided that all facilities are ready for GMP inspection?		✓	All are foreign facilities. OC checks the status before the insp
6	Has an environmental assessment report or categorical exclusion been provided?	✓		
7	Does the section contain controls for the drug substance?	✓		
8	Does the section contain controls for the drug product?	✓		
9	Has stability data and analysis been provided to support the requested expiration date?	✓		I will have to analyse the data
10	Has all information requested during the IND phase, and at the pre-NDA meetings been included?	✓		
11	Have draft container labels been provided?	✓		
12	Has the draft package insert been provided?	✓	✓	~~Not a new drug. Prototype information available.~~
13	Has an investigational formulations section been provided?			NA- is Investigational For mulation and formulation.
14	Is there a Methods Validation package?	✓		
15	Is a separate microbiological section included?	✓		

If the NDA is not fileable from a manufacturing and controls perspective state why it is not.

Reviewing Chemist: [signature] **Date:** 5/12/04

Team Leader James D. Vidra **Date:** 5/12/04

cc:
Original NDA ##-###
HFD-###/Division File
HFD-###/Chem/name
HFD-###/PM/name
HFD-830/DivDir/Chen

NDA Number: 50-795 **Applicant:** Warner-Chilcott **Drug Name:** Doryx Tablets

NDA 50-795 filability checklist continue

Have all DMF References been identified?

DMF Number	Holder	Description	LOA Included	Status
			Yes	will review
			Yes	will review
*	see below	container-closure	yes	will check
				and review as
				necessary.
*				

Manufacturing Facilities Inspection Status:

The following 5 facilities were submitted to OC on 5/4/04:

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/s/

Shrikant Pagay
6/25/04 05:37:16 PM
CHEMIST

Jim Vidra
6/28/04 09:07:39 AM
CHEMIST

NDA ACTION PACKAGE CHECKLIST

Application Information			
NDA 50-795	Efficacy Supplement Type N/A	Supplement Number	
Drug: Doryx® (doxycycline hyclate), Tablets, 75 mg and 100 mg		Applicant: F H Faulding & Co, Ltd.c/o Warner Chilcott, Inc.	
RPM: Judit Milstein		HFD-520	Phone # 301-827-2207
Application Type: (X) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates ❖ Major amendment triggered extension of the goal date to	February 7, 2005 May 6, 2005
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver N/A	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception N/A	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted .**This is a new dosage form of an "Old antibiotic". No requirement for patent information**	N/A
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified

Exclusivity (approvals only)	
• Exclusivity summary. **Exclusivity does not apply. This a new dosage form for an "Old antibiotic"**	**N/A**
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!*	( ) Yes, Application #_____ ( ) No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	**May 6, 2005**
General Information	
❖ Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	N/A
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	X
• Reviews	
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	~~N/A~~ Clock Extension
❖ Memoranda and Telecons	N/A
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	
• Pre-NDA meeting (indicate date)	August 25, 2003
• Pre-Approval Safety Conference (indicate date; approvals only)	
• Other	

Advisory Committee Meeting	
• Date of Meeting	**N/A**
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	**N/A**
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	**N/A**
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	May 4, 2005
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	April 20, 2005
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	YES
❖ Statistical review(s) *(indicate date for each review)*	December 3, 2004
❖ Biopharmaceutical review(s) *(indicate date for each review)*	May 2, 2005
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	
• Bioequivalence studies	YES
CMC Information	
CMC review(s) *(indicate date for each review)*	April 25, 2005
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	April 25, 2005
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report) **See CMC review, page 40**	Date completed: **(X)** Acceptable **( )** Withhold recommendation
❖ Methods validation	**(X)** Completed **( )** Requested **( )** Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	September 24, 2004
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A