

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-201

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

FIRMAGON® (degarelix for injectable) _____ NDA 22-201

Date: 28 Jan 2008

R-InfMEx-1; Ver: 1.0

Supersedes: None

Page 1 of 1

1.3.5.3 Statement of Claimed Exclusivity

b(4)

1.3.5.3. Statement of Claimed Exclusivity

This NDA is a 505(b)(1) application since it relies on clinical efficacy studies and non-clinical studies sponsored expressly by Ferring for approval. In addition, the active pharmaceutical ingredient in FIRMAGON®, degarelix, is a new chemical entity which has not previously been the subject of an NDA. Therefore, a 5-year period of exclusivity is claimed for FIRMAGON®, on approval, in accordance with 505(c) (3)(D)(m) and (j)(5)(D)(m) of the FD and C Act and under the provisions of 21 CFR 314.108(b)(2).

Signature:

Ronald T. Hargreaves.

Name of Responsible Person:

Ronald T. Hargreaves, Ph.D.
Vice President, Regulatory Affairs
Ferring Pharmaceuticals Inc.

EXCLUSIVITY SUMMARY

NDA # 22-201

SUPPL #

HFD # 150

Trade Name None approved

Generic Name degarelix

Applicant Name Ferring Pharmaceuticals

Approval Date, If Known Week of December 15, 2008; PDUFA date is December 28, 2008

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a

Explain:

! Explain:

Investigation #2

!

YES

!

! NO

Explain:

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

Name of person completing form: Carl Huntley

Title: Senior Regulatory Project Manager

Date: December 15, 2008

Name of Office/Division Director signing form: Robert Justice, MD

Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

Robert Justice
12/24/2008 04:00:10 PM

FIRMAGON[®] (degarelix for injectable) NDA number: 22-201;

Date: 28 Jan 2008
R-ReWaiPe-1; Ver. 2.0
Supersedes: None
Page 1 of 1

1.9.1 Request for Waiver of Pediatric Studies

b(4)

1.9.1 Request for Waiver of Pediatric Studies

Ferring Pharmaceuticals Inc. requests a full waiver of the requirements for pediatric studies under 21 CFR 314.55(c)(2). The justification for this request is provided below.

This 505(b)(1) application is for approval of FIRMAGON[®] (degarelix for injectable suspension) for the following indication:

FIRMAGON is a GnRH receptor blocker indicated for treatment of patients with prostate cancer

b(4)

At this time, FIRMAGON does not have a therapeutic use for pediatric patients.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-201

Supplement Number: _____

NDA Supplement Type (e.g. SE5): _____

Division Name: DDOP

PDUFA Goal Date: 12/28/08

Stamp Date: 2/28/2008

Proprietary Name: None

Established/Generic Name: (degarelix for injection) for subcutaneous administration

Dosage Form: Injectable

Applicant/Sponsor: Ferring Pharmaceuticals, Inc.

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

- (1) _____
- (2) _____
- (3) _____
- (4) _____

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1

(Attach a completed Pediatric Page for each indication in current application.)

Indication: 1

Q1: Is this application in response to a PREA PMR?

Yes Continue

No Please proceed to Question 2.

If Yes, NDA/BLA#: _____

Supplement #: _____

PMR #: _____

Does the division agree that this is a complete response to the PMR?

Yes. Please proceed to Section D.

No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW active ingredient(s) (includes new combination); indication(s); dosage form; dosing regimen; or route of administration?*

(b) No. PREA does not apply. Skip to signature block.

* Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.

Q3: Does this indication have orphan designation?

Yes. PREA does not apply. Skip to signature block.

No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

Deferred for some or all pediatric subpopulations (Complete Sections C)

Completed for some or all pediatric subpopulations (Complete Sections D)

Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^A
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

Not feasible:

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____

* Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of

pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received	
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Date studies are due (mm/dd/yy): _____							

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpms@fda.hhs.gov) OR AT 301-796-0700.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?.	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

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Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpms@fda.hhs.gov) OR AT 301-796-0700.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

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Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Q1: Does this indication have orphan designation?

- Yes. PREA does not apply. **Skip to signature block.**
- No. Please proceed to the next question.

Q2: Is there a full waiver for all pediatric age groups for this indication (check one)?

- Yes: (Complete Section A.)
 - No: Please check all that apply:
 - Partial Waiver for selected pediatric subpopulations (Complete Sections B)
 - Deferred for some or all pediatric subpopulations (Complete Sections C)
 - Completed for some or all pediatric subpopulations (Complete Sections D)
 - Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
 - Extrapolation in One or More Pediatric Age Groups (Complete Section F)
- (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

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On Original**

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^Δ
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and **attach a brief justification**):

Not feasible:

- Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____

* Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Section C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so,

proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for some or all pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Date studies are due (mm/dd/yy): _____							

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Appears This Way
On Original

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):

Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

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On Original

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)? No; Yes.

Are the indicated age ranges (above) based on Tanner Stage? No; Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 6/2008)

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/s/

Frank Cross
12/22/2008 06:10:56 PM
Frank Cross, CPMS, for Carl Huntley, RPM

FIRMAGON® (degarelix for injectable

NDA 22-201

Date: 25 Jan 2008
R-DebaCer-2; Ver. 1.0
Supersedes: None
Page 1 of 1

1.3.3 Debarment Certification

b(4)

1.3.3 Debarment Certification

Ferring Pharmaceuticals Inc. 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.

Ronald T. Hargreaves.

Ronald T. Hargreaves, Ph.D.
Vice President, Regulatory Affairs
Ferring Pharmaceuticals Inc.

Cross Jr, Frank H

From: ron.hargreaves@ferring.com
Sent: Wednesday, December 24, 2008 4:57 PM
To: Cross Jr, Frank H
Subject: RE: NDA 22-201

Frank,

Received your email. Thanks for all the work on this.

Best regards,

Ron

From: Cross Jr, Frank H [mailto:frank.crossjr@fda.hhs.gov]
Sent: Wednesday, December 24, 2008 4:50 PM
To: Hargreaves, Ron
Subject: FW: NDA 22-201

From: Cross Jr, Frank H
Sent: Wednesday, December 24, 2008 4:45 PM
To: 'ron.hargreaves@ferring.com'
Subject: NDA 22-201

Dear Dr. Hargreaves,

Attached is an electronic copy of our letter which will be mailed to you as well.

Please let me know when you receive this e-mail.

Sincerely,
Frank Cross (for Carl Huntley)

Frank Cross, M.A., MT (ASCP)
CAPT, USPHS Commissioned Corps
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
White Oak Building 22, Rm. 2110
10903 New Hampshire Blvd.
Silver Spring, MD 20993

12/29/2008

Ph: 301-796-0876
Fax: 301-796-9845
e-mail: frank.crossjr@fda.hhs.gov

<<09001469802ce081.pdf - Adobe Acrobat Professional.pdf>>

Proprietary or confidential information belonging to Ferring Holding SA or to one of its affiliated companies may be contained in the message.
If you are not the addressee indicated in this message (or responsible for the delivery of the message to such person), please do not copy or deliver this message to anyone.
In such case, please destroy this message and notify the sender by reply e-mail. Please advise the sender immediately if you or your employer do not consent to e-mail for messages of this kind.
Opinions, conclusions and other information in this message represent the opinion of the sender and do not necessarily represent or reflect the views and opinions of Ferring.

Cross Jr, Frank H

From: Cross Jr, Frank H
Sent: Monday, December 22, 2008 9:27 AM
To: 'ron.hargreaves@ferring.com'
Cc: Huntley, Carl
Subject: FW: degarelix NDA 22-201 labeling - carton-container labeling

Ron,

Please respond right away to the below comments

Thanks,

Frank (for Carl)

b(4)

Cross Jr, Frank H

From: Cross Jr, Frank H
Sent: Monday, December 22, 2008 9:13 AM
To: 'ron.hargreaves@ferring.com'
Cc: Huntley, Carl
Subject: NDA 22-201 Labeling comments
Attachments: NDA 22-201 DRISK.pdf

Dear Dr. Hargreaves,

Attached is our revised PPI for this NDA (highlight/strike-out and clean).

Please provide your response right away.

Sincerely,

CAPT Frank Cross

Frank Cross, M.A., MT (ASCP)
CAPT, USPHS Commissioned Corps
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
White Oak Building 22, Rm. 2110
10903 New Hampshire Blvd.
Silver Spring, MD 20993
Ph: 301-796-0876
Fax: 301-796-9845
e-mail: frank.crossjr@fda.hhs.gov



NDA 22-201
ISK.pdf (1381)

1 INTRODUCTION

Ferring Pharmaceuticals submitted an original NDA 22-201 on February 14, 2008. In October, 2008 the sponsor responded to the Chemistry Manufacturing and Controls (CMC) reviewers' inquiries concerning sterility and other issues. In November 2008, FDA requested from the sponsor changes to the drug [REDACTED]. The sponsor agreed with changes to [REDACTED] and submitted a revised PI. After further revisions, DDOP provided a substantially complete PI to DRISK on December 11, 2008. The revisions included the addition of detailed "Instructions for Proper Use" for the healthcare provider who will reconstitute and inject the product. Since then, the CMC has added minor changes to the Highlights Section under "Dosage and Administration." The originally proposed trade name, Firmagon, was not approved and the new name, [REDACTED] was submitted for approval on November 25, 2008. The new trade name has not been approved as of this date so the term "[TRADENAME]" will be used for this review. The review materials for this Package Insert (PI) and Patient Package Insert (PPI) were received in DRISK on December 11, 2008. The PDUFA date is December 31, 2008. b(4)

The Division of Drug Oncology Products requested that the Patient Labeling and Education Team review the Patient Package Insert for this product. This review was written in response to that request.

2 MATERIAL REVIEWED

- Draft [TRADENAME] (degarelix for injectable [REDACTED]) PI submitted by the Sponsor on December 4, 2008, revised substantially by the Review Division and sent to DRISK on December 18, 2008. b(4)
- Draft [TRADENAME] (degarelix for injectable [REDACTED]) PPI submitted by the Sponsor on December 4, revised by the Review Division and sent to DRISK on December 18, 2008.

3 DISCUSSION

The purpose of patient directed labeling is to facilitate and enhance appropriate use and provide important risk information about medications. Our recommended changes are consistent with current research to improve risk communication to a broad audience, including those with lower literacy.

The draft PPI submitted by the sponsor has a Flesch Kinkaid grade level of [REDACTED] and a Flesch Reading Ease score of [REDACTED]. To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60% (60% corresponds to an 8th grade reading level). Our revised PPI has a Flesch Kinkaid grade level of 8.7 and a Flesch Reading Ease score of 54.9%.

In our review of the PPI we have:

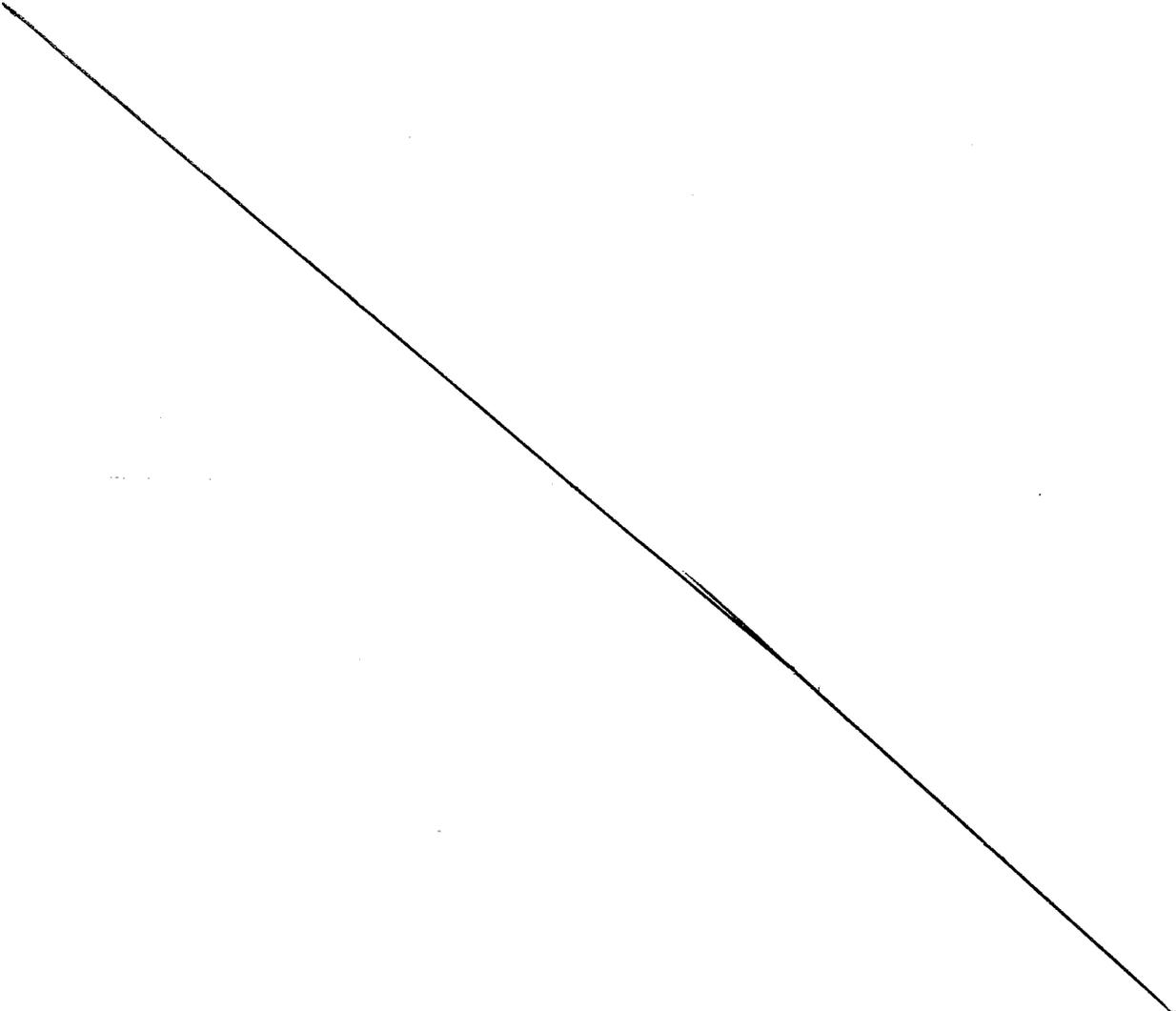
- simplified wording and clarified concepts where possible, b(4)
- made the PPI consistent with the PI,
- removed unnecessary or redundant information
- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

In 2008, The American Society of Consultant Pharmacists Foundation in collaboration with The American Foundation for the Blind published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. They recommend using fonts such as Arial, Verdana, or APHont to make medical information more accessible for patients with low vision. We have reformatted the PPI document using the font APHont, which was developed by the American Printing House for the Blind specifically for low vision readers.

See the attached document for our recommended revisions to the PPI. Comments to the review division are **bolded, underlined and italicized**.

We are providing the review division a marked-up and clean copy of the revised PPI.
We recommend using the clean copy as the working document.

4 CONCLUSIONS AND RECOMMENDATIONS



b(4)

Please let us know if you have any questions.

7 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

Withheld Track Number: Administrative-1

MEMORANDUM OF TELECON

DATE: DATE OF TELEPHONE CONVERSATION

APPLICATION NUMBER: NDA 22-201

BETWEEN:

Name: Marianne Kock, Senior VP of Global Regulatory Affairs for Ferring in
Copenhagen
Per Cantor, Head, Clinical Research
Ron Hargreaves, VP, Regulatory Affairs

Phone: 1-800-910-3597

Representing: Ferring Pharmaceuticals Inc.

AND

Name: Amna Ibrahim, Janet Jamison, Robert Justice
DDOP, HFD-150

SUBJECT: To discuss the Post Marketing Request for study CS21A. The sponsor agreed to provide the protocol submission date, the trial start date and the final report submission date.

Carl Huntley, R.Ph. MBA
Senior Regulatory Project Manager

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/s/

Carl Huntley
12/19/2008 09:11:10 PM

MEMORANDUM OF TELECON

TELECONFERENCE DATE: September 29, 2008, 15:00 ET

APPLICATION NUMBER: NDA 22-201

DRUG NAME: Firmagon

BETWEEN:

NAME: Ferring Pharmaceuticals
Ronald Hargreaves, VP Regulatory Affairs
Michael Cimino, Senior Manager, Manufacturing
Thomas McMullen, Regulatory Affairs

AND

NAME: ONDQA/DPAMS
Terrance Ocheltree, Ph.D., R.Ph. Pharmaceutical Assessment Lead
(Acting)
Deborah Mesmer, M.S., Regulatory Health Project Manager

SUBJECT: Prototype Samples of Firmagon Including Commercial Packaging Material

THE CALL:

FDA referenced a call to Dr. Hargreaves placed on September 10, 2008, by Deborah Mesmer and requesting that Ferring submit for Firmagon samples representing the commercial product including all packaging materials.

In the call of September 29, 2008, FDA clarified that we want to see the actual product and packaging. It should include a mock-up of the carton and drug container closure system and any special packaging. It is acceptable to submit containers containing placebo. FDA stated that Ferring should submit the cover letter for the shipment of their samples to their NDA. Further, the samples should be shipped to the attention of Deborah Mesmer.

Ferring agreed to send the prototype samples as requested.

{See appended electronic signature page}

Deborah M. Mesmer
Regulatory Health Project Manager for Quality
Division of Pre-Marketing Assessment III and Manufacturing Science
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Deborah M Mesmer
12/19/2008 05:20:31 PM
PROJECT MANAGER FOR QUALITY

MEMORANDUM OF TELECON

TELECONFERENCE DATE: November 12, 2008

APPLICATION NUMBER: NDA 22-201

DRUG NAME: Firmagon

BETWEEN:

NAME: Ferring Pharmaceuticals (Ronald Hargreaves, Ph.D., Lead)

AND

NAME: ONDQA/DPAMS, Richard T. Lostritto, Ph.D., Meeting Chair

SUBJECT: Drug Product — Composition and Drug Product Labeling

MEETING ATTENDEES:

b(4)

FDA

Debasis Ghosh, Ph.D., Review Chemist, ONDQA
Terrance Ocheltree, Ph.D., R.Ph. Pharmaceutical Assessment Lead (Acting), ONDQA
Richard T. Lostritto, Ph.D., Division Director, ONDQA
Deborah Mesmer, M.S., Regulatory Health Project Manager, ONDQA
Carl Huntley, R.Ph. MBA, Regulatory Health Project Manager, DDOP

FERRING

Called from Parsippany, NJ:

Ronald Hargreaves, VP Regulatory Affairs
Henri Boodee, Medical Director, Medical Affairs
Jeff Sherman, Executive Director, Marketing
Paul Stapel, Senior Manager, Quality Services
Michaël Cimino, Senior Manager, Manufacturing

Called from Copenhagen, Denmark:

Katja Gustafsson, Associate Director, Global Regulatory Affairs
Thomas Bock, Associate Director, Product Technology Support
Thomas Kratz, Regulatory Manager, Global Regulatory Affairs
John Kim, Director, Regulatory Affairs
Jørgen Wittendorff, Vice President, Pharmaceutical Drug Development
Grégoire Schwach, Director, Early Stage Development

THE MEETING:

The following comments were conveyed to the Applicant prior to the meeting by email:

From: Lostritto, Richard T
Sent: Wednesday, November 12, 2008 1:06 PM
To: 'ron.hargreaves@ferring.com'
Cc: Mesmer, Deborah
Subject: RE: Firmagon telecon: NDA 22-201_IR request_111208.doc

Dear Dr. Hargreaves,

As previously agreed, the following items are provided to you in advance of our 3:00 p.m. (EST) teleconference so that you may assemble the appropriate personnel for discussion at this meeting. I am sending these comments on behalf of Ms. Deborah Mesmer who is involved with other PDUFA business until 3:00 p.m.

3. The reconstituted drug product is a solution which turns cloudy after the in-use shelf life. It is _____

b(4)

b(4)

Thank you.

Rik Lostritto for Deborah Mesmer.

POST MEETING COMMENT:

After the meeting discussion, Ferring submitted a written response via email on November 13, 2008, and an amended response by email on November 17, 2008. Ferring submitted the email response to their NDA in a letter dated December 5, 2008, with a submission date of December 9, 2008.

{See appended electronic signature page}

Deborah M. Mesmer
Regulatory Health Project Manager for Quality
Division of Pre-Marketing Assessment III and Manufacturing Science
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Deborah M Mesmer
12/19/2008 03:25:58 PM
PROJECT MANAGER FOR QUALITY

Huntley, Carl

From: Huntley, Carl
Sent: Thursday, December 11, 2008 3:12 PM
To: 'ron.hargreaves@ferring.com'
Cc: Huntley, Carl
Subject: degarelix label NDA 22-201

Attachments: Degarilix Label from FDA 1500 12 11 08.doc

b(4)

Dear Ron,
CMC had some minor changes to the description/name of degarelix:
In Highlights:

3 **DOSAGE FORMS AND STRENGTHS**

Starting dose

Powder for injection 120 mg:

One vial of TRADENAME 120 mg contains _____ 120 mg degarelix). Each vial is to be reconstituted with 3 mL of Sterile Water for Injection. 3 mL is withdrawn to deliver 120 mg degarelix at a concentration of 40 mg/mL.

b(4)

One starting dose comprises 240 mg given as two 3 mL injection of 120 mg each.

Maintenance dose

Powder for injection 80 mg:

One vial of TRADENAME 80 mg contains _____ 80 mg degarelix). Each vial is to be reconstituted with 4.2 mL of Sterile Water for Injection. 4 mL is withdrawn to deliver 80 mg degarelix at a concentration of 20 mg/mL.

b(4)

One maintenance dose comprises 80 mg given as one 4 mL injection.

This was cut and pasted from an e-mail - I can't adjust the last sentence.
It is fixed in the label:



Degarilix
from FDA 1

If you are curious, I named it 1500 to reflect the time (to preserve what sanity I have left).

Regards,
-carl

Carl Huntley, R. Ph., MBA
Senior Regulatory Project Manager
FDA/CDER/OND/OODP/DDOP
pH. (301) 796-1372
FAX (301) 796-9845

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Carl Huntley
12/17/2008 11:04:35 AM
CSO

MEMO OF Pre-APPROVAL SAFETY CONFERENCE

DATE: December 2, 2008

NDA #: 22-201

DRUG NAMES: degarelix, 80 mg and 120 mg

APPLICANT: Ferring Pharmaceuticals

BACKGROUND:

Ferring Pharmaceuticals is applying for a marketing authorization for degarelix powder _____ for injection, in a one-month dosing regimen (degarelix).

Degarelix is a third generation gonadotropin releasing hormone (GnRH) antagonist (blocker). FIRMAGON is indicated for treatment of patients with prostate cancer ←

b(4)

_____ Degarelix is a synthetic decapeptide, which forms a depot following subcutaneous injection; this depot formation results in a sustained release of degarelix. A starting dose of 240 mg, followed by a monthly maintenance dose of 80 mg has been demonstrated to be clinically effective.

The proposed indication: degarelix is a GnRH receptor blocker indicated for treatment of patients with prostate cancer _____

b(4)

Dr. Max Ning provided background information and reviewed the adverse events reported in the study CS21, the registration trial.

Drs. Terry Ocheltree, Debasis Ghosh and Rik Lostritto briefly outlined their CMC concerns. The concerns included the formulation issues and carton and container issues with regard to medication errors.

Carl Huntley, R.Ph., MBA
Senior Regulatory Project Manager



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Ronald T. Hargreaves, Ph.D.
Vice President, Regulatory Affairs
Ferring Pharmaceuticals, Inc.
4 Gatehall Drive, Third Floor
Parsippany, NJ 07054-4518

Dear Dr. Hargreaves:

Between September 16, 2008 and October 3, 2008, Ms. Deborah B. Nixon, representing the Food and Drug Administration (FDA), conducted an investigation and met with you and other Ferring Pharmaceuticals staff to review your conduct as the sponsor of the clinical investigation of the investigational drug Firmagon[®] (degarelix), protocol FE200486 CS21 entitled "An Open-label, Multi-Centre, Randomized, Parallel-group Study, Investigating the Efficacy and Safety of Degarelix One Month Dosing Regimens: 160 mg (40 mg/ml) and 80 mg (20 mg/ml), in Comparison to LUPRON DEPOT[®] 7.5 mg in Subjects with Prostate Cancer Requiring Androgen Ablation Therapy". We are aware that at the conclusion of the inspection, Ms. Nixon presented and discussed with you Form FDA 483, Inspectional Observations.

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of those studies have been protected.

From our evaluation of the establishment inspection report, the documents submitted with that report, your October 13, 2008 letter and your follow-up November 14, 2008 letter written in response to the Form FDA 483, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations and the protection of human subjects.

We wish to emphasize the following:

You did not maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug [21 CFR 312.57(a)].

Specifically, review of the overall accountability data revealed that the final disposition of the unused investigational medicinal product for 13 out of 13 countries is not all complete. In the European Union approximately 219 vials are missing and in the US, Canada, and Mexico, approximately 615 vials are missing. There were no Notes to File and/or Investigational reports regarding the unaccounted unused investigational medicinal product.

Page 2– *Ferring Pharmaceuticals*

We acknowledge that you appear to have taken appropriate corrective actions to prevent the recurrence of the finding above. Any response and all correspondence will be included as a permanent part of your file.

We appreciate the cooperation shown Investigators Nixon and Chacko during the inspection. Should you have any questions or concerns regarding this letter or the inspection, please contact me by letter at the address given below.

Sincerely,

{See appended electronic signature page}

Tejashri Purohit-Sheth, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg. 51, Rm. 5358
10903 New Hampshire Avenue
Silver Spring, MD 20993

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/s/

Tejashri Purohit-Sheth
11/28/2008 06:32:34 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Ronald T. Hargreaves, Ph.D.
Vice President, Regulatory Affairs
Ferring Pharmaceuticals, Inc.
4 Gatehall Drive, Third Floor
Parsippany, NJ 07054-4518

Dear Dr. Hargreaves:

Between September 16, 2008 and October 3, 2008, Ms. Deborah B. Nixon, representing the Food and Drug Administration (FDA), conducted an investigation and met with you and other Ferring Pharmaceuticals staff to review your conduct as the sponsor of the clinical investigation of the investigational drug Firmagon® (degarelix), protocol FE200486 CS21 entitled "An Open-label, Multi-Centre, Randomized, Parallel-group Study, Investigating the Efficacy and Safety of Degarelix One Month Dosing Regimens: 160 mg (40 mg/ml) and 80 mg (20 mg/ml), in Comparison to LUPRON DEPOT® 7.5 mg in Subjects with Prostate Cancer Requiring Androgen Ablation Therapy". We are aware that at the conclusion of the inspection, Ms. Nixon presented and discussed with you Form FDA 483, Inspectional Observations.

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/s/

Cynthia Kleppinger
11/14/2008 01:56:06 PM
MEDICAL OFFICER

Tejashri Purohit-Sheth
11/14/2008 04:27:50 PM
MEDICAL OFFICER

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

CLINICAL INSPECTION SUMMARY

DATE: November 12, 2008

TO: Carl Huntley, R.Ph., MBA, Regulatory Project Manager
Max Ning, M.D., Medical Officer
Division of Drug Oncology Products

FROM: Cynthia F. Kleppinger, M.D.
Good Clinical Practice Branch II
Division of Scientific Investigations

THROUGH: Tejashri Purohit-Sheth, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA#: 22-201

APPLICANT: Ferring Pharmaceuticals, Inc.

DRUG: FIRMAGON[®] (degarelix) for injectable _____

NME: Yes b(4)

THERAPEUTIC CLASSIFICATION: Priority Review

INDICATIONS: Treatment of patients with prostate cancer _____

CONSULTATION REQUEST DATE: July 23, 2008 b(4)

DIVISION ACTION GOAL DATE: November 1, 2008; *revised to* November 10, 2008

PDUFA DATE: December 28, 2008

I. BACKGROUND:

Ferring Pharmaceuticals, Inc. submitted an NDA for Firmagon[®] (degarelix), for an 80 mg and 120 mg _____ powder for injection. The sponsor is seeking an indication for the treatment of prostate cancer patients _____

b(4)

Degarelix is a third generation gonadotropin releasing hormone (GnRH) antagonist (blocker). Degarelix is reported to selectively bind to GnRH receptors resulting in the suppression of pituitary gonadotropins which subsequently affects the gonadal tissues.

The sponsor submitted efficacy data from a pivotal Phase III Study (Protocol FE 200486 CS21) in support of the indication. The sponsor claims that data from this study and other submitted data from Phase II/III trials demonstrate that degarelix is an effective GnRH blocker with a favorable safety profile and that the treatment appears to be effective in achieving sustained suppression of testosterone plasma level below 0.5 ng/ml.

The following protocol was audited:

Protocol: FE 200486 CS21 entitled "An Open-label, Multi-Centre, Randomized, Parallel-group Study, Investigating the Efficacy and Safety of Degarelix One Month Dosing Regimens: 160 mg (40 mg/ml) and 80 mg (20 mg/ml), in Comparison to LUPRON DEPOT[®] 7.5 mg in Subjects with Prostate Cancer Requiring Androgen Ablation Therapy"

Study Protocol FE 200486 CS21 is an open-label, three-arm, multi-center, stratified, randomized, controlled, parallel group study designed to compare the efficacy and safety of degarelix with LUPRON DEPOT[®] (leuprolide) 7.5 mg in patients with prostate cancer requiring androgen ablation therapy. Subjects were randomized 1:1:1 to one of the three treatment groups described below:

- Degarelix 240 mg initially then 160 mg maintenance Q28 days
- Degarelix 240 mg initially then 80 mg maintenance Q28 days
- Leuprolide 7.5 mg Q28 days

A total of 620 subjects were randomized to the three treatment groups. A total of 504 subjects completed the study. The study was conducted in 11 countries (82 sites) which included US (21), Canada (13), Mexico (10), Europe (7), Czech Republic (6), Hungary (7), Romania (8), Russia (6), and Ukraine (4).

The study was initiated on February 7, 2006 and concluded on October 8, 2007.

At the end of the study, subjects who completed the study and met appropriate criteria were offered the opportunity to received long-term treatment and support in an extension study, CS21A.

Basis for Sites Selection:

Three clinical sites were selected for inspection: one domestic and two foreign sites.

DDOP selected one domestic site _____ with relatively high subject numbers and considered essential for the approval of the application. This site has had two past inspections done 3/05/96 (VAI) and 5/23/2000 (NAI). DDOP considers the efficacy results from this site pertinent to their approval decision; no single site drove the study results. *DDOP did not identify any specific problems with the study data or specific areas to emphasize during the inspection.*

b7

DDOP selected two foreign sites _____ with relatively high subject numbers and considered essential for the approval of the application. There have been no past inspections at these two sites. Since there are insufficient domestic data, DDOP considers the efficacy results from these two sites pertinent to decision making; no single site drove the study results. *DDOP did not identify any specific problems with the study data or specific areas to emphasize during the inspection except as noted:*

b7

- Two of the _____ center enrollments for the study (Romania) are located in the same city.
- Subjects recruited from Romania (with 7 study centers) account for 21% of patients (a total of 408) who were randomized to the study agent, equal to the total number of patients in USA (18 centers) assigned to the study agent.
- The ratios of patients with documented medical castration (Day 28 – Day 364) to patients enrolled per center appear to be generally higher in Romania as compared in USA. This may be ascribed to socioeconomic differences but DDOP would like other possibilities to be considered and investigated.

b7

In addition, a sponsor inspection was also conducted. These inspections were conducted as part of the routine pre-NDA clinical investigation data validation in support of NDA 22-201:

- High Priority CDER User Fee NDA Pre-Approval, Clinical Investigator Data Validation Domestic Inspection using the Bioresearch Monitoring Compliance Program (CP 7348.811)
- High Priority CDER User Fee NDA Pre-Approval, Clinical Investigator Data Validation Foreign Inspection using the Bioresearch Monitoring Compliance Program (CP 7348.811)
- High Priority CDER Sponsor/Monitor/CRO Inspection using the Bioresearch Monitoring Compliance Program (CP 7348.810) linked to Clinical Investigator Inspection. The focus of this inspection was the pivotal study Protocol FE 200486 CS21.

II. RESULTS (by Site):

Name of CI/Sponsor City and State/Country	Protocol Subjects	Inspection Date	Classification	
			Interim	Final

b7

4	Ferring Pharmaceuticals Parsippany, NJ 07054	Study: FE 200486 CS21	September 16, 2008- October 3, 2008	VAI	Pending
---	--	-----------------------	--	-----	---------

Key to Classifications

NAI = No deviation from regulations.

VAI = Deviation(s) from regulations.

OAI = Significant deviations from regulations. Data unreliable.

Pending = Preliminary classification based on information in 483 or preliminary communication with the field;
EIR has not been received from the field and/or EIR has been received, however, complete review of
EIR is pending.

b7

a. What was inspected:

The clinical records of 15 subjects enrolled/consented were audited. Of these 15 subjects, 10 completed the study. One subject dropped out, 3 were lost to follow-up and 1 discontinued. The charts reviewed were:

b7

The above files were audited for inclusion/exclusion criteria, adverse events, consistency between source data and case report forms, primary endpoint verification, informed consent, and drug accountability. It was verified that all protocol deviation reports were submitted to the IRB. There was one drug accountability protocol deviation for study subject _____ (The site dispensed IP from FE200486 CS21A to the subject at Visit 18 in error.)

b7

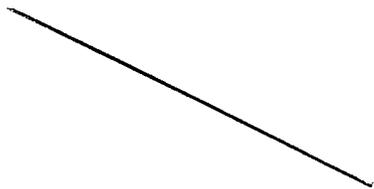
b. General observations/commentary:

The inspectional findings indicate adequate adherence to good clinical practice regulations and the study protocol. No Form FDA-483, Inspectional Observations, was issued.

c. Assessment of data integrity:

Data from this site are acceptable. The audit did not indicate serious deviations/findings that would impact the validity or reliability of the submitted data.

Note: The preliminary communications and the EIR report were generated by the field inspector's supervisor.



b7

a. What was inspected:

Ten (10) subject records underwent in-depth audit. Files were audited for inclusion/exclusion criteria, adverse events, consistency between source data and case report forms, primary endpoint verification, informed consent, and drug accountability. A Romanian Food and Drug Administration Inspector, who was also a physician, was present to assist with translation of the files. The files of the withdrawn subjects were also reviewed.

b7

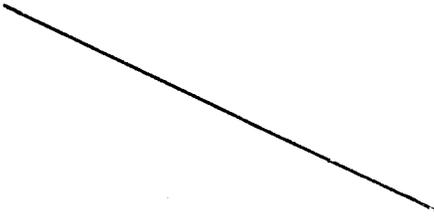
b. General observations/commentary:

The inspectional findings indicate adequate adherence to good clinical practice regulations and the study protocol. No Form FDA-483, Inspectional Observations, was issued.

c. Assessment of data integrity:

Data from this site are acceptable. Preliminary review does not indicate serious deviations/findings that would impact the validity or reliability of the submitted data.

The observations noted above are based on communication from the field inspector. Further review and evaluation of the observations will be made when the EIR and exhibits are submitted. An inspection summary addendum will be generated after the inspection has been completed and the results have been evaluated by DSI.



b7

a. What was inspected:

Eight (8) subject records underwent in-depth audit. Files were audited for inclusion/exclusion criteria, adverse events, consistency between source data and case report forms, primary endpoint verification, informed consent, and drug accountability. A Romanian Food and Drug Administration Inspector, who was also a physician, was present to assist with translation of the files. The files of the withdrawn subjects were also reviewed.

b7

b. General observations/commentary:

The inspectional findings indicate adequate adherence to good clinical practice regulations and the study protocol. No FDA 483 was issued.

c. Assessment of data integrity:

Data from this site are acceptable. Preliminary review does not indicate serious deviations/findings that would impact the validity or reliability of the submitted data.

The observations noted above are based on communication from the field inspector. Further review and evaluation of the observations will be made when the EIR and exhibits are submitted. An inspection summary addendum will be generated after the inspection has been completed and the results have been evaluated by DSI.

D. Sponsor/Monitor Inspection:

Ferring Pharmaceuticals Inc.
4 Gatehall Drive, Third Floor
Parsippany, NJ 07054

a. What was inspected

No original documents for the FE200486 CS21 clinical trial were available at the inspection site, only scanned documents of the originals as filed in Copenhagen. The original records were at Ferring Copenhagen, the Sponsor location. Ferring Pharmaceuticals, Inc., Parsippany, NJ is the location for the IND holder. A copy of the document entitled "Trial Master File-Index" was provided to the field inspector which identified the original documentation filed at the investigator sites.

Documents reviewed were:

Sponsor study records for Protocol FE 200486 CS21, including organizational charts, copies of the contracts for the CRO/Vendors documenting the Sponsors delegated or transferred responsibilities, CVs for the four lead — monitors, CRO Management Manual, SOPs used in FE 200486 CS21, the Data Handling Manual for FE 200486 CS21, the monitoring plan used during the conduct of the study, listing of all audited clinical sites for the audited protocol and review of the overall drug accountability for the protocol.

b7

Site records for US site — Romania sites — including

- All IRB/EC approvals/correspondences
- All site monitoring reports
- Training documents for the CIs and monitors
- FDA 1572s (US and Non-US study centers), C.V.s, and financial disclosures for all of the clinical investigators (CIs) and Sub-CIs

b7

Site enrollment data:

- ~~_____~~
- ~~_____~~

b7

The following study subjects were selected for detailed review:

- ~~_____~~
- ~~_____~~
- ~~_____~~

b7

The review consisted of the following:

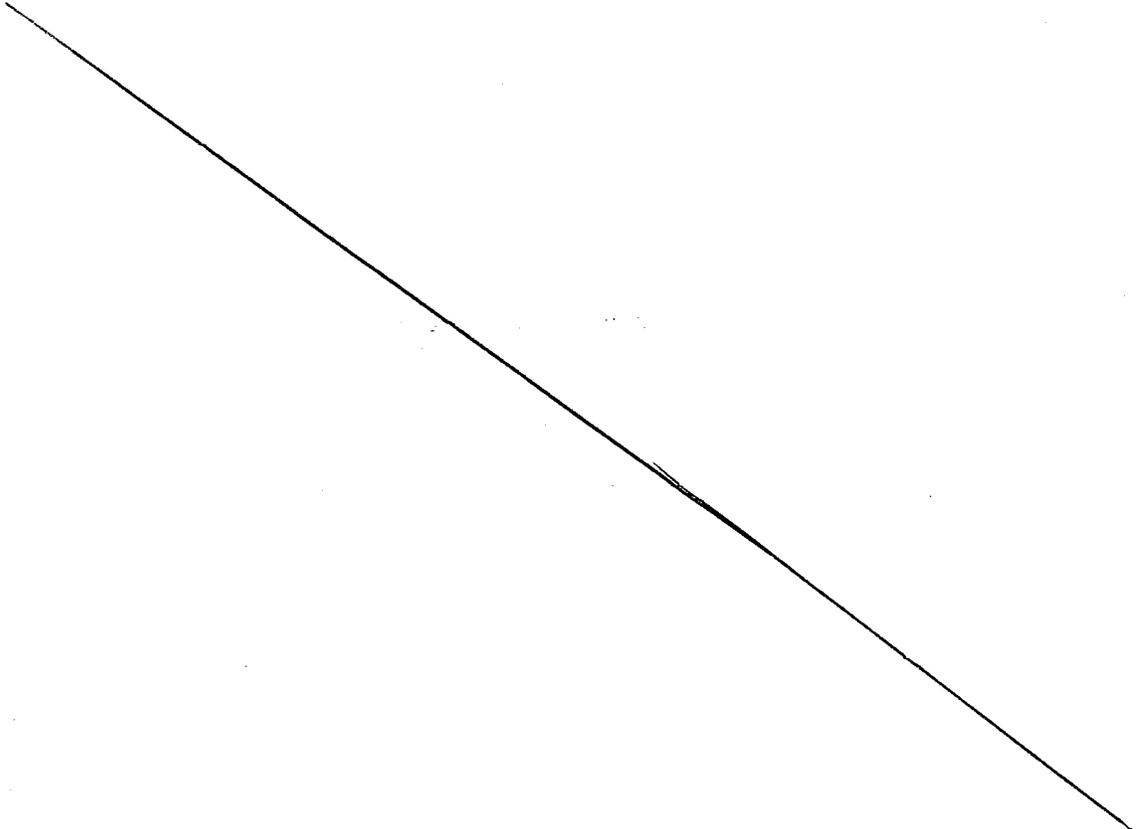
- eCRFs data for the protocol specified study visits/assessments and data to support the primary/secondary endpoints
- eDiaries/QOL Questionnaires

- Laboratory data (specifically testosterone, luteinizing hormone, follicle stimulating hormone, and prostate-specific antigen)
- Review of protocol violations, adverse events, serious adverse events (from both the Sponsor database with the data listings in the clinical study report and with the monitoring reports and subject's eCRF).
- Select subjects not meeting the inclusion criteria
- Randomization
- Review of data queries to confirm resolution
- MRI sub study

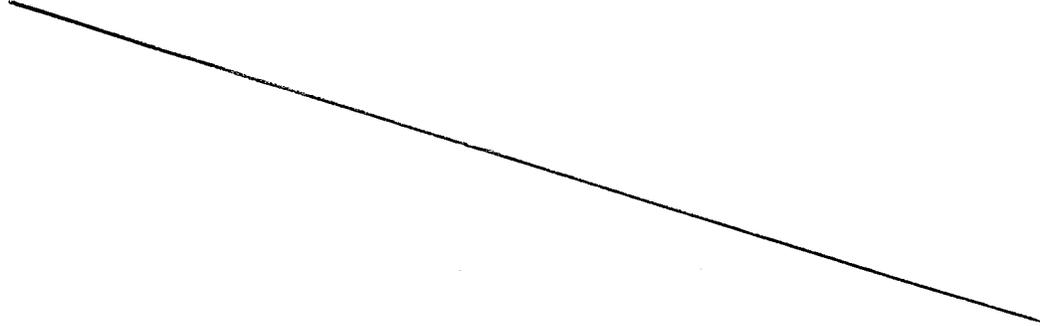
b. General observations/commentary

The inspectional findings indicate adequate adherence to good clinical practice regulations and the study protocol. The firm's safety database is Clintrace version 2.10.3. There was no evidence of late reporting of adverse events.

The major finding was the overall drug accountability with lack of adequate records covering disposition of an investigational drug (Form FDA-483). Specifically, for protocol FE 200486 CS21, documentation for the final disposition of the investigational product for 13 out of 13 countries is not all complete.



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b7

Other observations noted during the inspection were:

- There was one site where the CI was not entering the source data into the eCRFs in a timely manner and the CI requested to no longer participate in the study due to other priorities. This CI site (5204-Mexico) was closed 6/19/2007 and the one enrolled patient and the associated source and eCRF/eDiary data were transferred to another site (5215-Mexico) starting on Visit 15. This event was not reported to the agency until at the time of the Clinical Study Report submission dated 1/7/2008.
- No deficiencies were noted with regards to the monitor report availability, overall monitoring, follow-up of identified issues, and monitor frequency except upon reviewing the monitoring reports signatures for US site — The monitoring report was created and sent electronically to the reviewing manager, who then signed for both individuals. This was noted for all but one monitoring report. This was not consistent with the CRO's SOPs.
- No apparent deficiencies were observed during review of the study subjects except one patient — received drug product for the extension study; however; this patient had not yet rolled over into the extension study. The Sponsor captured this as a protocol deviation. The site was reportedly reeducated by the monitor to avoid reoccurrences.

b7

c. Assessment of data integrity

Although the lack of drug accountability is important, it does not suggest compromised data integrity and should not impact study outcome, as site audits have verified adequate disposition of drug to randomized subjects.

IV. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The inspection for this NDA consisted of one US and 2 foreign (Romania) clinical sites, as well as the Sponsor. Observations noted above are based on the Form FDA 483, preliminary results, EIRs and communications from field investigators. The final inspection

reports for Sites _____ are pending. In general, based on the inspection of the 3 clinical study sites combined with the sponsor/monitor audit for this NDA, the inspectional findings with the isolated deficiencies noted with the sponsor/monitor audit, support validity of data as reported by the sponsor under this NDA.

b(4)

Upon receipt and review of the final inspection reports, an inspection summary addendum will be generated if additional observations of clinical or regulatory significance are discovered.

{See appended electronic signature page}

Cynthia F. Kleppinger, M.D.
Good Clinical Practice Branch II
Division of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Tejashri Purohit-Sheth, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

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/s/

Cynthia Kleppinger
11/14/2008 01:56:06 PM
MEDICAL OFFICER

Tejashri Purohit-Sheth
11/14/2008 04:27:50 PM
MEDICAL OFFICER

Huntley, Carl

From: Huntley, Carl
Sent: Tuesday, October 07, 2008 2:43 PM
To: 'ron.hargreaves@ferring.com'
Cc: Huntley, Carl
Subject: NDA 22-201, Firmagon

Importance: High

Dear Ron,

The CMC review team has an information request as the microbiology review is on-going.

Please provide the following information or reference to its location in the subject NDA:

1. The test method used for demonstration of container closure integrity for the sterile powder.

b(4)

Thanks

Regards,

-carl

Carl Huntley, R. Ph., MBA
Senior Regulatory Project Manager
FDA/CDER/OND/OODP/DDOP
pH. (301) 796-1372
FAX (301) 796-9845



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-201

Ferring Pharmaceuticals
Attention: Ronald T. Hargreaves, Ph.D.
Vice President, Regulatory Affairs
4 Gatehall Drive, Third Floor
Parsippany, NJ 07054

Dear Dr. Hargreaves:

Please refer to your new drug application (NDA) dated February 14, 2008, received February 28, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Firmagon (degarelix for injectable _____ 80 mg and 120 mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following request for information. We request a prompt written response in order to continue our evaluation of your NDA.

Drug Substance

b(4)

b(4)

b(4)

Drug Product

7. Provide a detailed description of the lyophilization process utilized to manufacture the drug product.
8. Tighten the acceptance criterion _____ based on history of clinical batches.
9. Tighten the specification of _____ total impurities in the drug product based on manufacturing history of the clinical batches and clinical exposure.

b(4)

b(4)

b(4)

Other

11. Provide the complete name, address and contact information for the manufacturing facility _____ used to manufacture the two drug substance batches used in the clinical and stability studies.
12. Clarify the nomenclature of the intermediates. It is noted that _____

13. Please check if the abbreviated chemical name of the starting material _____
_____ on page 11, Sec 3.2.S.2.2.5 is correct.

b(4)

b(4)

b(4)

If you have any questions, call Deborah Mesmer, Regulatory Health Project Manager, at 301-796-4023.

Sincerely,

{See appended electronic signature page}

Richard T. Lostritto, Ph.D.
Division Director
Division of Pre-Marketing Assessment III and
Manufacturing Science
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Richard Lostritto
9/12/2008 03:41:12 PM

**FOOD AND DRUG ADMINISTRATION
OFFICE OF ONCOLOGY DRUG PRODUCTS**



DIVISION OF DRUG ONCOLOGY PRODUCTS

**5901-B Ammendale Road
Beltsville, Maryland 20705-1266**

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PHONE: (301) 796-1365 FAX: (301) 796-9845

TO: Ronald Hargreaves, Ph.D.
 Vice president, Regulatory Affair
 FAX (973) 796-1694
 e-mail: ron.hargreaves@ferring.com

FROM: Carl Huntley, R.Ph. MBA

DATE: July 22, 2008

Total number of pages, including cover sheet 1

COMMENTS: Regarding NDA 22-201 and your submission dated February 14, 2008 for FIRMAGON®, we have the following request for information.

In order to verify the information your label section 12.3 - Pharmacokinetics/Excretion, please identify which study(s) were used to support this statement, and where the data and report is located in the electronic submission.

Regards,
-carl

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/s/

Diane Hanner

7/22/2008 04:10:48 PM

CSO

Entering for CH his DFS is not working

**FOOD AND DRUG ADMINISTRATION
OFFICE OF ONCOLOGY DRUG PRODUCTS**



DIVISION OF DRUG ONCOLOGY PRODUCTS

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PHONE: (301) 796-1365 FAX: (301) 796-9845

TO: Ronald Hargreaves, Ph.D.
 Vice president, Regulatory Affairs
 FAX (973) 796-1694
 e-mail: ron.hargreaves@ferring.com

FROM: Carl Huntley, R.Ph. MBA

DATE: July 8, 2008

Total number of pages, including cover sheet 2

COMMENTS: Regarding NDA 22-201 and your submission dated February 14, 2008 for FIRMAGON®, we have the following request for information.

Please submit the following datasets to support your population PK analyses:

- All datasets used for model development and validation should be submitted as a SAS transport files (*.xpt). A description of each data item should be provided in a Define.pdf file. Any concentrations and/or subjects that have been excluded from the analysis should be flagged and maintained in the datasets.
- Model codes or control streams and output listings should be provided for all major model building steps, e.g., base structural model, covariates models, final model, and validation model. These files should be submitted as ASCII text files with *.txt extension (e.g.: myfile_ctl.txt, myfile_out.txt).
- A model development decision tree and/or table which gives an overview of modeling steps. For the population analysis reports we request that you submit, in addition to the

Page 2

standard model diagnostic plots, individual plots for a representative number of subjects. Each individual plot should include observed concentrations, the individual predication line and the population prediction line. In the report, tables should include model parameter names and units. For example, oral clearance should be presented as CL/F (L/h) and not as THETA(1). Also provide in the summary of the report a description of the clinical application of modeling results.

If any of the above were included with the original submission, please provide detailed instructions on where they can be located in your electronic submission.

Regards,
-carl



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD. 20857

FILING COMMUNICATION

NDA 22-201

Ferring Pharmaceuticals Inc.
Attention: Ronald Hargreaves, Ph.D.
4 Gatehall Drive, Third Floor
Parsippany, NJ 07054

Dear Dr. Hargreaves:

Please refer to your new drug application (NDA) dated February 14, 2008, received February 28, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Firmagon (degarelix for injectable _____, 80 mg and 120 mg. b(4)

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is Standard. Therefore, the user fee goal date is December 28, 2008.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a full waiver of pediatric studies for this application for pediatric patients.

If you have any questions, call Carl Huntley, Regulatory Project Manager, at (301) 796-1372.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D.

Division Director

Division of Drug Oncology Products

Office of Oncology Drug Products

Center for Drug Evaluation and Research

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/s/

Robert Justice
5/14/2008 07:46:24 PM

REQUEST FOR CONSULTATION

TO (Office/Division): David Hussong/Jim McVey/Sylvia Gantt
NEW DRUG MICROBIOLOGY STAFF
OC/OO/CDER/OPS/NDMS - HFD-805

FROM (Name, Office/Division, and Phone Number of Requestor): Debasis Ghosh through Debbie Mesmer, Office of New Drug Quality Assessment, 301 796-4023

DATE
September 3, 2008

IND NO.

NDA NO.
22-201

TYPE OF DOCUMENT
Original NDA

DATE OF DOCUMENT
28 February, 2008

NAME OF DRUG
FIRMAGON® (degarelix
for injectable _____
80 mg and 120 mg

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG
Oncology

DESIRED COMPLETION DATE
First part of November,
2008. Potential early
decision (PDUFA date 28
December, 2008.)

NAME OF FIRM: Ferring Pharmaceuticals Inc.

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|---|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input checked="" type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: Microbiology review requested of the original NDA. Please direct questions to Debasis Ghosh at 64093. Electronic submission is in the-EDR.

SIGNATURE OF REQUESTOR
{See appended electronic signature page}

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

b(4)

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/s/

Carl Huntley
10/21/2008 03:31:55 PM

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/s/

Terrance Ocheltree
9/3/2008 12:03:15 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD-110, Denise Hinton/Devi Kozeli (IRT)			FROM: HFD-150/Carl Huntley	
DATE July 8, 2008	IND NO.	NDA NO. 22-201	TYPE OF DOCUMENT NDA submission	DATE OF DOCUMENT February 28, 2008
NAME OF DRUG Degarelix for inj, _____ (Firmagon)		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG 3 rd generation gonadotropin releasing hormone antagonist.	DESIRED COMPLETION DATE
NAME OF FIRM: Ferring Pharmaceuticals				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY				
<input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT				
<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS:				
<p>Submission for IRT/QT review (consult). The electronic submission is in the edr. <u>\\CDSESUB1\EVSPROD\NDA022201\0000.</u></p> <p>Please let me know if you need more data. MO = Max Ning. PDUFA date - 12/28/08</p> <p>This was thought to have been sent out previously for review/consult.</p>				
SIGNATURE OF REQUESTER Thanks!, Carl Huntley			METHOD OF DELIVERY (Check one)	
			<input type="checkbox"/> MAIL <input type="checkbox"/> HAND <input checked="" type="checkbox"/> ELECTRONIC	
SIGNATURE OF RECEIVER			SIGNATURE OF DELIVERER	

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Milinda Vialpando

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- carl

From: Cross Jr, Frank H
Sent: Thursday, October 25, 2007 10:25 AM
To: 'ron.hargreaves@ferring.com'
Subject: IND 51,222; Pre-NDA meeting - October 17, 2007

Attachments: 090014698016b5fd.pdf
Good Morning, Dr. Hargreaves,

Our minutes of our 10/17/07, meeting are attached.

Sincerely,

Frank Cross



0900146980
5fd.pdf (128

Frank H. Cross, Jr., M.A., MT (ASCP), CAPT, USEPHS
Co-Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Ph: 301-796-0876
Fax: 301-796-9845
e-mail: frank.crossjr@fda.hhs.gov

MEETING MINUTES

MEETING/TELECON DATE: October 17, 2007

TIME: 10:00 a.m.

LOCATION: WO Bldg 22, Room 1315

IND/NDA: 51,222

Meeting Request Submission Date:

July 19, 2007

FDA Response Date:

August 21, 2007

Briefing Document Submission Date:

September 12, 2007

DRUG: FE 200486 (degarelix)

SPONSOR/APPLICANT: Ferring Pharmaceuticals, Inc.

TYPE of MEETING/TELECON:

1. Pre-NDA Meeting
2. Advanced prostate cancer

FDA PARTICIPANTS:

Ann Farrell, M.D., Deputy Division Director, DDOP (Chair)
Ming-Yang Ning (Max), M.D., Medical Officer, DDOP
Sarah Pope, Ph.D., Pre-Marketing Assessment Lead, ONDQA (Pre-Mtg)
Xiao Chen, Ph.D., CMC Reviewer, DPAMS, ONDQA (Pre-mtg)
William McGuinn, Ph.D., Acting Pharmacology/Toxicology Supervisor, DDOP
Leigh Verbois, Ph.D., Pharmacology/Toxicology Reviewer, DDOP
Gene Williams, Ph.D., Clinical Pharmacology Reviewer, DCP5 (Pre-Mtg)
Rajeshwari Sridhara, Ph.D., Biostatistics Team Leader, DBV (Pre-Mtg)
Shenghui Tang, Ph.D., Biostatistics Reviewer, DBV
Frank Cross, PM, DDOP

INDUSTRY PARTICIPANTS:

Ronald T. Hargreaves, Ph.D., Vice President, Regulatory Affairs
Marianne Kock, M.Sc.Pharm., M.B.A., Senior Vice President, Global Regulatory Affairs,
Pharmacovigilance
Per Cantor M.D, Ph.D.. Senior Vice President, Clinical & Non-Clinical R&D
Ilona Rybicka, M.D., M.B.A., Global Project Director
Inger-Marie Ravn, M.Sc.Pharm. – Senior Director, Global Regulatory Affairs
Katja Gustafsson, M.Sc., Pharmacology, Senior Regulatory Affairs Manager, Global Regulatory
Affairs
Tine Kold Olesen, M.Sc., Pharmacology, Director, Global Clinical R&D
Egbert van der Meulen, Ph.D - Director, Statistical Services
Grégoire Schwach, Ph.D - Associate Director, Pharmaceutical Formulation

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Background:

The purpose of this meeting, according to the sponsor, is "to identify issues and receive guidance from the Division before submission of an NDA for degarelix."

Questions:

Ferring would like to get FDA's response to the below questions:

Timing of NDA:

Question#1: Ferring is considering the possibility of submitting the CTD Module 3 and/or Module 4 in December 2007 and the Clinical and Administrative parts in February 2008. Does the Agency concur that a rolling submission is possible?

FDA: Rolling submissions are possible if a product has received a Fast Track Designation.

Question#2: The data from the pivotal Phase 3 study CS21 are scheduled to be available in mid-November 2007. Ferring plans to discuss the results and the draft label with FDA at a mid-December 2007 pre-filing meeting. Does the Agency concur with the timing and purpose of this consultation?

FDA: A meeting to discuss results and draft labeling is not necessary prior to filing the NDA. In addition, any discussion on draft labeling would be general as any discussion regarding product specific labeling is an NDA review issue.

NDA format (background presented in section 7 of this document)

Question#3: Please confirm it is acceptable that CRF data for coded variables will contain both a variable holding the coded, and a variable holding the decoded values (the text). Both variables will be listed in the define.pdf file and next to the coded variable all codes and decodes will be listed.

FDA: This is acceptable.

Question#4: Please confirm it is acceptable that the CRF datasets that are in non-CDISC structure are assigned the Study Tagging File tag "tabulations".

FDA: CDISC is preferred.

Discussion: The FDA clarified that CDISC is preferred not required. The sponsor plans to submit using non-CDISC format in the the section entitled tabulations.

NDA content (background presented in section 8 of this document):

Module 1:

No questions.

Module 2: Questions included under Module 3-5

No questions.

Module 3:

Question#5 on Definition of Starting Materials:

Does the Agency agree on the definition of starting materials?

FDA: No. We do not agree with the proposed definition of starting materials. The degarelix drug substance is a linear decapeptide, and the starting materials for such a peptide should be the

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Module 4:

Question#6 on female reproduction studies:

Ferring plans not to include the female reproduction toxicity studies with this submission for prostate cancer indication. Does the FDA concur?

FDA: Given the indication and that only men will be included in the treatment population, reproductive toxicology studies in treated female rodents are not necessary for NDA submission of degarelix for the treatment of prostate cancer.

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Module 5:

Question#7 on presentation of the ISS and 2.7.4:

Does the FDA concur with having identical text portion (including key tables as described in Attachment 5) for the ISS and CTD Section 2.7.4 cross referencing supporting listings and datasets for the ISS in Section 5.3.5.3?

FDA: Yes.

Question#8 on content of the ISS and 2.7.4:

Does the FDA concur with the suggested content including the suggested integrated analyses as described in Attachment 5?

In particular advice is asked for but not limited to:

- the selected study-groups (male volunteers studies, uncontrolled studies in prostate cancer patients, controlled prostate cancer patient study, all Phase 2/3 studies in prostate cancer patients)
- the explorative analyses proposed to identify drug-related adverse events (see Sections 2.7.4.2.1.1.3-5), next to tabulating adverse events related according to the investigator

FDA: The three-month dosing trials (CS15/15A : ——— may have different profiles of adverse reactions. They should not be integrated with the other studies as you mentioned for safety evaluation. However, separate safety analyses for these trials should be submitted with your NDA for the safety overview of your agent.

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It is acceptable to incorporate your exploratory analyses.

Discussion: The sponsor shared a revised plan (attached) and asked for FDA feedback. The FDA emphasized that pooling of the safety data from different formulations is not needed. For your own internal purposes, you may pool the 3 month depot data with the data from the one month depot data. Contingent upon the NDA submission, the FDA may request additional analyses.

Question#9 on presentation of the ISE and 2.7.3:

Does the FDA concur with having identical text portion (including key tables as described in attachment 6) for the ISE and CTD section 2.7.3 and to presenting the text in Section 2.7.3, cross referencing supporting listings and datasets for the ISE in Section 5.3.5.3?

FDA: In general, the proposed formatting is acceptable. Please also see additional comments below.

Question#10 on content of the ISE and 2.7.3:

Does the FDA concur with the suggested content including the suggested integrated analysis as described in Attachment 6?

In particular advice is asked for but not limited to:

- the selected study-groups (controlled study, and studies pertinent to the evaluation of the starting dose)

FDA: Yes. It is necessary to focus on the controlled one-month dosing study and the studies supporting the starting doses used for the controlled studies.

Question#11 on data from ongoing studies in prostate cancer indication:

Does the FDA concur to integrate the safety data from the ongoing studies in the Summary of Clinical Safety and not to analyze and report each on-going study individually?

FDA: No. Please see above

Discussion: In the NDA submission, the sponsor will present its safety data in an integrated format listing study numbers, dosing, formulation, etc. The sponsor will pool the ongoing studies. This is acceptable to the FDA. The 120 day safety update will also be provided in the same format along with status of all studies.

Question#12 on data from Japanese study:

Does the FDA concur that the Japanese data will be reported separately in the Summary of Clinical Safety and not be a part of the integrated statistical analysis of the data, and the SAEs will be presented as a part of the clinical study report?

FDA: No, we do not concur. Please provide your Japanese data as part of the ISS of the NDA.

Discussion: The sponsor will integrate data from CS11 in the Phase 2/3 study uncontrolled pooled analysis.

Question#13 on data from female study:

Does the FDA concur that the female data will be reported separately in the Summary of Clinical Safety and not be a part of the integrated statistical analysis of the data and the SAEs will be presented as a part of the clinical study report?

FDA: Yes.

Question#14 on CRFs for male Phase 1 and 2 studies:

Does FDA concur that for male Phase 1 and 2 studies including long-term extension studies for the Phase 2 program, and the dose finding studies for the three month dosing regimen the following CRFs will be included?

- Patients with an SAE.
- Patients that died
- Patients withdrawn due to an AE

FDA: Yes.

Question#15 on CRFs for Phase 3 study in prostate cancer indication:

Does FDA concur that for the controlled confirmatory study the following CRFs will be included?

- Patients with an SAE
- Patients that died
- Patients withdrawn due to an AE
- Patients that experienced lack of efficacy (testosterone > 0.5 ng/mL)

FDA: Yes. Please also include patients with dosing interruption due to an adverse reaction and patients with overt protocol violations.

Discussion: The sponsor will include patients with dosing interruptions as FDA requested above. The criteria for overt protocol violations as proposed by the sponsor in the handout and as pre-specified in CS21 are acceptable to the FDA.

Additional FDA Comments:

1. Please note the non-inferiority analyses will be considered as exploratory. The study has to demonstrate a response rate with the lower bound of the 95% CI no lower than 90% in the degarelix arm.
2. Revise the acceptance criteria for the ID test by mass spectrometry to include the _____
3. Propose specifications for the _____
4. The proposed specifications limits for the specified degradation products _____ need to be justified by acceptable safety and toxicology data.

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6. Please apply for a USAN for degarelix drug substance, if you have not already done so.
7. Ensure that all manufacturing, testing, packaging, and labeling sites for drug substance and drug product are ready for inspection at the time of NDA submission.
8. Provide a concise pharmaceutical development report in the NDA highlighting your product development and process understanding, as well as the delineation of critical quality attributes and critical process parameters. Also, you are encouraged to apply the quality-by-design (QbD) approach to pharmaceutical development as outlined in ICH Q8 Guidance on Pharmaceutical Development. If appropriate, please include QbD-related information and questions in a CMC-specific meeting or request a CMC guidance meeting to discuss your QbD approach.

The sponsor will take these comments into consideration.

Frank Cross
Project Manager

Concurrence Chair: _____
Ann Farrell, M.D.
Deputy Division Director

Attachments: Sponsor October 17, 2007, Pre-NDA Meeting Handout

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Deliberative Process (b5)

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Ann Farrell

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Frank Cross
10/25/2007 01:25:10 PM

INDUSTRY MEETING MINUTES

MEETING DATE: September 30, 2005 **TIME:** 9:30am **LOCATION:** G

IND/NDA IND 51,222

Meeting Request Submission Date: 7-7-05
Briefing Document Submission Date: 9-7-05
Additional Submission Dates:

DRUG: FE200486

SPONSOR/APPLICANT: Ferring Pharmaceuticals

TYPE OF MEETING: End-of-Phase 2 (EOP2)

Proposed Indication: — treatment of prostate cancer.

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FDA PARTICIPANTS:

Robert Justice, M.D., Acting Director, DDOP
Ramzi Dagher, M.D., Clinical Team Leader, DDOP
Edwin Rock, MD, Clinical Reviewer, DDOP
Mark Hirsch, M.D., Clinical Reviewer, DRUP
David Morse, PhD, Supv. Pharmacologist, DDOP (pre-only)
Lilliam Rosario, Ph.D., Pharmacology Reviewer, DDOP
Rajeshwari Sridhara, Ph.D., Statistical Team Leader, OB
Brian Booth, Ph.D., Acting Biopharm Team Leader, OCPB
Angela Men, Ph.D., Biopharm Reviewer, OCPB
Amy Baird, Consumer Safety Officer, DDOP

Ferring Pharmaceuticals:

Hendrik de Koning Gans, MD, VP Global Clin Research & Dev
Ronald T. Hargreaves, PhD, Exec. Dir., Global Regulatory Affairs
Marianne Kock, MSc Pharm, MBA, Sr. VP, Global Reg. Affairs
Inger-Marie Ravn, MSc Pharm, Sr. Dir., Global Reg. Affairs
Pascal Danglas, MD, Exec. VP, Clinical & Product Development
Patrick O'Connor, MB, FRCP (Edin), PhD, Sr. VP, Global Clin R&D
Thomas Senderovitz, MD, VP Experimental Medicine
Ketil Bjarnason, MD, PhD, Global Project Director
Tine Kold Olesen, MSc Pharm, Dir., Clinical R&D, Urology
Jens-Kristian Jensen, MSc, Project Statistician, Biometrics
Thomas Bock, PhD, Assoc. Dir., Pharmaceutical Formulation
Richard White, PhD, Principal Scientist, Fertility

b(4)

MEETING OBJECTIVES:

Discuss sponsor's questions in briefing document dated September 7, 2005.

QUESTIONS for DISCUSSION with FDA RESPONSE and DECISIONS REACHED:

Preclinical documentation:

1. Does the Agency concur that the preclinical package fulfils the requirements for an NDA? If further studies are requested please advise.

FDA Response:

We agree that the non-clinical package appears adequate for inclusion in your NDA.

Clinical Pharmacology:

2. Does the agency concur with the decision to use degarelix derived _____
_____ in all future clinical trials?

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FDA Response:

Yes.

Clinical phase III program (one month dosing regime):

3. Does the Agency concur with the choice of degarelix doses for the phase III study?

FDA Response:

Initial and maintenance degarelix doses for Phase 3 Study CS21 appear to be reasonable.

4. Does the Agency concur with the proposed comparator (Lupron® 7.5 mg) and in Europe the Investigator's discretionary use of an antiandrogen (Casodex®), in the first month of treatment in the phase III one month dosing regimen study?

FDA Response:

Lupron is an acceptable comparator. Discretionary use of bicalutamide (Casodex) in the first month of treatment is acceptable. We point out that the use of Casodex could effect the interpretation of clinical data within the first month, such as clinical flare symptoms.

We strongly suggest stratification by country at randomization.

5. **Considering the proposed indication, does the agency concur with the choice of study population for the planned phase III pivotal study?**

FDA Response:

Your proposed CS21 study population appears to be appropriate. We note that licensed GNRH agonists are approved for *palliative* treatment of advanced prostate cancer.

See also FDA response to question 6.

6. **Does the Agency agree with the proposed non-inferiority margins?**

FDA Response:

No. A fixed margin approach is not acceptable. For a non-inferiority design, the active control effect size should be estimated by meta-analysis of randomized studies and a percentage of active control effect size should be retained. You have not provided this sort of information to justify your non-inferiority margin.

In studies comparing proportions, we suggest use of odds ratio rather than difference in proportions.

Discussion: Ferring provided some data in support of using difference in proportion instead of odds ratio. Ferring also provided additional data to support active control effect size. The Division will discuss internally and follow-up with Ferring ASAP.

7. **Does the agency concur with Ferring's proposal to perform an open label pivotal study?**

FDA Response:

An open label study with blinded laboratory analysis may support registration.

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[Redacted]

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[Redacted]

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Clinical phase III study (three month dosing regimen):

10. Does FDA concur that study CS15 _____

[Redacted]

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Testosterone Analysis

- 11. Does the agency concur that the procedure and reporting of results for testosterone, as described above, is acceptable for the ongoing study CS15 and the planned study CS21?**

FDA Response:

This will depend on the amount of variability among samples within a patient. This will be a review issue.

Safety:

- 12. Does the Agency concur that the predicted size of the safety database at the end of the proposed one-month and three-month dosing regimen is adequate to define the safety profile for degarelix?**

FDA Response:

Your proposed safety database population to support the 1 month dosing regimen is likely to be adequate. Your total safety database population must be adequate to enable calculation of the incidence of serious hypersensitivity reactions. Completeness of data collected will be a review issue.

Discussion: The Division clarified that serious is intended to mean clinically serious hyper sensitivity reactions vs. the regulatory definition of serious. Ferring has provided preliminary information regarding this issue.

- 13. Does the FDA concur that the degarelix safety profile supports the indication of "treatment of advance prostate cancer?"**

FDA Response:

The specific indication on approval will be a review issue that is determined by study population(s) and results obtained. We note again that licensed GNRH agonists are approved for *palliative treatment of advanced prostate cancer*.

- 14. Does FDA concur with the suggested study synopsis for _____**

FDA Response:

This appears acceptable. However, we are awaiting a consultation from the Division of Pulmonary and Allergy Products and therefore, comments may be forthcoming.

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QT/QTc Intervals:

15. Does the FDA concur with the study design?

FDA Response:

Please provide the full protocol for the QTc study for review.

Please provide justification for conducting your acute QTc safety study in healthy volunteers versus the intended clinical population.

Please justify the dose and IV infusion duration time of degarelix: 30-35 µg/kg given at constant rate over 60 minutes, in your proposed QT study. It is unclear how the proposed dose relates to the subcutaneous dose used in the phase 3 clinical trial.

16. Does FDA concur with the proposed procedure for ECG safety monitoring in study CS21?

FDA Response:

We recommend the initial EKG is obtained at Cmax/Tmax after the first dose.

Discussion: Ferring intends to do this around day 3 which is close to Cmax. This is acceptable to the Division.

Additional Comment:

Pharmacokinetics/Pharmacodynamics (PK/PD): The sponsor should correlate the PK of degarelix with changes of testosterone, LH, FSH, and PSA and safety endpoints.

Action Items:

1. Oncology Division to follow-up with the Division of Pulmonary and Allergy Products regarding the _____

b(4)

The meeting concluded at 10:30am.

Amy Baird
Consumer Safety Officer

Concurrence Chair: _____
Ramzi Dagher, M.D.
Clinical Team Leader

Attachment: Ferring's slides presented at meeting.

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Ramzi Dagher
2/7/2006 04:28:28 PM

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Amy Baird
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