

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-583

ADMINISTRATIVE
DOCUMENTS/CORRESPONDENCE

PATENT SUBMISSION FORM

Time Sensitive Patent Information Pursuant to 21 C.F.R. 314.53

For

NDA #21-583

The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

- **Trade Name:** (To Be Determined)
- **Active Ingredient(s):** medroxyprogesterone acetate
- **Strength(s):** 104 mg/0.65 mL
- **Dosage Form:** Injectable
- **Approval Date:** Pending

A. Type of Patent: Drug Product (Composition/Formulation)

U.S. Patent Number: 6,495,534

Expiration Date: May 15, 2020

Name of Patent Owner: Pharmacia & Upjohn SpA and Pharmacia & Upjohn Co.

U.S. Agent: N/A

B. Composition/Formulation or Method of Use Claims.

Pharmacia & Upjohn declares that the above stated United States Patent Number 6,495,534 covers the composition, formulation and/or method of use of the medroxyprogesterone acetate product of the present NDA. This product is the subject of this application for which approval is being sought.

Signed: Bruce A. Pokras

Bruce A. Pokras

Date: 11/24/2003

Title: Senior Patent Counsel

The above information should be submitted to the NDA with the original application or as correspondence to an existing NDA. For patents issued after the NDA is filed or approved, the applicant is required to submit the information within 30 days of the date of issuance of the patent.

To expedite publication in the *The Orange Book*,* the above information may be provided to the Orange Book Staff at the address below. You may also contact the Orange Book Staff directly at (301)827-5846 regarding listing of patent information.

Mailing address: (US Mail or FedEx deliveries)
U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs/HFD-610
Orange Book Staff
7500 Standish Place
Metro Park North II
Rockville, MD 20855-2773

OR faxed to: (301)-827-5911

* Please note that patents for unapproved compositions, formulations or uses will NOT be published in *The Orange Book*.

EXCLUSIVITY SUMMARY FOR NDA # 21-583

SUPPL # _____

Trade Name **depo-subQ provera 104(medroxyprogesterone acetate injectable suspension) 104mg/0.65ml** Generic Name _____

Applicant Name **Pfizer, Inc.** HFD # **580**

Approval Date If Known December 17, 2004

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 question 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 / x / NO / /

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

 3 years

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

YES / / NO / x /

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 / x /

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 / x / NO / /

If "yes," identify the approved drug product(s) containing the

active moiety, and, if known, the NDA #(s).

NDA#_20-246 Depo-Provera Injectable 150 mg/ml

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 /_X_/

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 NDA'S 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 /_X_/ 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 /_X_/ 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 /_X_/

(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 /_X_/

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:

_Study #s 267, 269, 267BMD

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 /_X_/

the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
IND # 61,388 YES / x / ! NO / ___ / Explain: _____
Investigation #2 !
IND # 61,388 YES / X / ! NO / ___ / Explain: _____
Investigation #3 !
IND # 61,388 YES / X / ! NO / ___ / Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !
YES / ___ / Explain _____ ! NO / ___ / Explain _____

Investigation #2 !
YES / ___ / Explain _____ ! NO / ___ / 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 / X /

If yes, explain: _____

Signature Charlene Williamson Date: December 16, 2004
Title: _Regulatory Project Manager

Signature of Office/ Date
Division Director

Form OGD-011347 Revised 05/10/2004

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

/s/

Donna Griebel
12/17/04 04:56:36 PM

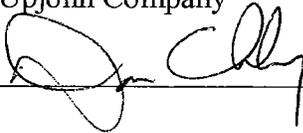
**DEPOT MEDROXYPROGESTERONE ACETATE
SUBCUTANEOUS INJECTION (DMPA-SC)
NDA #21-583
CLAIM FOR EXCLUSIVITY UNDER 21 CFR §314.108(B)(4)**

The following information is provided in accordance with 21 CFR §314.50(j) and 21 CFR §314.108:

1. Pharmacia & Upjohn is claiming three (3) years of exclusivity for DMPA-SC (medroxyprogesterone acetate injectable suspension).
2. 21 CFR §314.108(b)(4) supports the exclusivity claimed by Pharmacia & Upjohn.
3. Pharmacia & Upjohn sponsored and conducted clinical investigations (Protocols 839-FEH-0012-267 and 839-FEH-0012-269) from March 2001 through August 2002. Study 267 was conducted under IND 61,388. Pharmacia & Upjohn Company believes these studies are "essential" for the approval of NDA 21-583 as defined in 21 CFR §314.108(a). Pharmacia & Upjohn Company certifies that to the best of our knowledge, the clinical investigations described in NDA 21-583 meet the definition of "new clinical investigations" defined in 21 CFR §314.108(a).
4. Pharmacia & Upjohn believes there are not sufficient studies published or publicly available to support the approval of this NDA for DMPA-SC. Pharmacia & Upjohn certifies that a scientific literature search has been conducted. The results of the search did not provide any published studies or publicly available reports of clinical investigations that are relevant to the conditions for which Pharmacia & Upjohn is seeking approval.

Pharmacia & Upjohn Company

By: _____



Title: Sr. Regulatory Manager

Date: _____

April 24, 2003

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA/BLA #: 21- 583 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: July 2, 2003 Action Date: December 17, 2004

HFD-580 Trade and generic names/dosage form: depo-subQ Provera 104™ (medroxyprogesterone acetate injectable suspension)

Applicant: Pfizer, Inc Therapeutic Class: S

Indication(s) previously approved:

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

Number of indications for this application(s): 1

Indication #1: Prevention of Pregnancy

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

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Adult studies ready for approval

Formulation needed

Other: _____

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

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

Other: _____

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

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Charlene Williamson
Regulatory Project Manager

cc: NDA – 21-583
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

Attachment A

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

Indication #2: _____

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

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

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.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA – 21-583
HFD-960/ Terrie Crescenzi
(revised 1-18-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

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

/s/

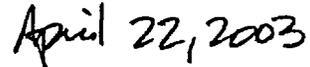
Z. Charlene Williamson
12/20/04 11:31:28 AM

DEBARMENT CERTIFICATION FOR
Depot Medroxyprogesterone Acetate Subcutaneous Injection (DMPA-SC)
NDA 21-583

Pursuant to section 306(k)(1) of the Federal Food, Drug and Cosmetic Act, the applicant certifies that, the applicant did not and will not use in any capacity the services of any person listed pursuant to section 306(e) as debarred under subsections 306(a) or (b) of the Act in connection with this application.



Michael Burdick, Director
Global Regulatory Affairs



Date

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-583	Efficacy Supplement Type SE-	Supplement Number
Drug: depo-subQ provera 104 (medroxyprogesterone acetate subcutaneous injection) 104mg/0.65 ml		Applicant: Pfizer, Inc
RPM: Charlene Williamson		HFD-580 Phone # 301-827-4266
<p>Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed and/or corrected</p>		Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):
❖ Application Classifications:		
• Review priority		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)		3
• Other (e.g., orphan, OTC)		N/A
❖ User Fee Goal Dates		
		December 17, 2004
❖ Special programs (indicate all that apply)		
		<input checked="" type="checkbox"/> None <input type="checkbox"/> Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2
❖ User Fee Information		
• User Fee		<input checked="" type="checkbox"/> Paid UF ID number
• User Fee waiver		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other (specify)
• User Fee exception		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) <input type="checkbox"/> Other (specify)
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.

❖ Exclusivity (approvals only)	
<ul style="list-style-type: none"> Exclusivity summary Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	YES
<ul style="list-style-type: none"> Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	<input type="checkbox"/> Yes, Application # _____ <input type="checkbox"/> No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	

General Information	
❖ Actions	
• Proposed action	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA
• Previous actions (specify type and date for each action taken)	AE – August 2, 2004
• Status of advertising (approvals only)	<input checked="" type="checkbox"/> Materials requested in AP letter <input type="checkbox"/> Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> Not applicable
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> Press Release <input type="checkbox"/> Talk Paper <input type="checkbox"/> Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	X
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (<i>indicate dates of reviews and meetings</i>)	X
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	X
• Applicant proposed	X
• Reviews	X
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	X
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	July 15, 2002
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A

Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	August 2, 2004, December 16, 2004
Clinical Information	
❖ Clinical review(s) (indicate date for each review)	July 29, 2004, December 10, 2004
❖ Microbiology (efficacy) review(s) (indicate date for each review)	February 17, 2004
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	See MO Review Pg. 83 - 7/29/2004
❖ Risk Management Plan review(s) (indicate date/location if incorporated in another rev)	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	December 16, 2004
❖ Demographic Worksheet (NME approvals only)	N/A
❖ Statistical review(s) (indicate date for each review)	July 7, 2004
❖ Biopharmaceutical review(s) (indicate date for each review)	7/26/2004; 12/15/2004
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	3/29/2004
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) (indicate date for each review)	7/29/2004; 12/9/2004
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	7/29/2004
• Review & FONSI (indicate date of review)	N/A
• Review & Environmental Impact Statement (indicate date of each review)	N/A
❖ Microbiology (validation of sterilization & product sterility) review(s) (indicate date for each review)	2/17/2004
❖ Facilities inspection (provide EER report)	Date completed: <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ Methods validation	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	9/11/2003
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	N/A
❖ CAC/ECAC report	N/A

Appendix A to NDA/Efficacy Supplement Action Package Checklist

An application is likely to be a 505(b)(2) application if:

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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/s/

Z. Charlene Williamson
12/20/04 11:17:23 AM

Williamson, Charlene

From: Toyer, Denise P
Sent: Tuesday, December 14, 2004 5:20 PM
To: Williamson, Charlene; Holquist, Carol A; Shames, Daniel A
Cc: Hoppes, Charles V; Mahmud, Alina; Hubbard, Lisa; Beam, Sammie
Subject: NDA 21-583 and NDA 21-584

Dr. Shames,

This e-mail is in response to a request from Charlene Williamson, in your Division regarding the proposed proprietary name Depo-subQ Provera 104. As noted in our proprietary name review (04-0012) and the meeting with the Division on November 5, 2004, DMETS found _____
_____ name unacceptable. _____

_____ A discussion ensued at the aforementioned meeting and the proposal to use a modifier in the middle of the name, Depo subQ Provera, was proposed. Although DMETS did not review this proposed name for any orthographic or phonetic similarities due to time constraints, we felt this proposal was more acceptable than the alternatives previously proposed. A subsequent e-mail which provided two different 'visual' presentations of the proposed name, was received by DMETS on November 17, 2004 and our preference was forwarded by to DRUDP. Several additional label comments were also provided at that time.

This e-mail serves as DMETS response to DRUDP's request for a proprietary name review for Depo-subQ Provera 104.

Please feel free to contact us if you need further assistance.

Thanks

Denise P. Toyer, Pharm.D.
Deputy Director
Division of Medication Errors
and Technical Support
Office of Drug Safety
HFD-420, Room 6-34 Parklawn
301-827-7609
301-443-9664 (Fax)

Williamson, Charlene

From: Chirby, Daniel G [daniel.g.chirby@pfizer.com]
Sent: Thursday, July 15, 2004 3:19 PM
To: Charlene Williamson (E-mail)
Subject: NDA 21-583 post approval commitment

Importance: High



FDA

004 fax tconf m



mmsinfo.txt

(459 B)

Dear Charlene,

Following our discussion today, this message is to confirm that Pfizer commits to undertaking an in-vitro metabolism study in accordance with the timelines laid out in FDA minutes of the meeting (teleconference) conducted between FDA and Pfizer on June 23 (attached below).

<<FDA 25Jun2004 fax tconf min 23June.pdf>>
Unless you advise otherwise, please note that I will also submit general correspondence to NDA 21-583 to officially document the commitment provided in this email message.

Sincerely,
Dan

Dan Chirby
Associate Director
WRAQA-Worldwide Regulatory Strategy
Pfizer, Inc.
Ann Arbor, MI
Tel. 734.622.3750 Fax. 734.622.2856 Cell. 269.806.0268

LEGAL NOTICE

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"MMS <secure.pfizer.com>" made the following annotations on 07/15/2004 03:19:32 PM

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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: October 16, 2003

To: Daniel G. Chirby, M.Sc.	From: Charlene Williamson
Company: Pfizer, Inc.	Division of Division of Reproductive and Urologic Drug Products
Fax number: 269-833-8237	Fax number: 301-827-4267
Phone number: 269-833-9411	Phone number: 301-827-4260
Subject: Please provide the list of variables in the form of SAS data sets	

Total no. of pages including cover: 3

Comments:

Document to be mailed: • YES NO

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NDA 21-583
Depot Medroxyprogesterone Acetate-SC

Please provide the following list of variables in the form of SAS data sets for the three studies: 839-FEH-0012-267, 269 and 267BMD. In addition, please provide the data dictionary for the data.

Subject id
Center id
Investigator id
Protocol id ()
Treatment group
Weight
Age
date on which the first injection is taken
compliant (1=Yes, 0=No)
did the subject become pregnant (1=pregnant/0=not pregnant), if she did then provide:
the cycle in which conception occurred
the date the pregnancy was diagnosed
the date of the lab
the outcome of the pregnancy; and
the days from the first injection taken to the cycle of conception
ectopic pregnancy (1=Yes, 0=No)

did the subject complete the study, if she did, then provide:
on what cycle complete? (6-cycle or 13-cylce)
the date of which the injection was taken
the cycle during which the last injection was taken
the days from the first injection taken to the last injection taken
the total number of cycles competed by the subject

if she did not complete the study, then provide:
the date of discontinuation from the study
the cycle during which the subject discontinued
the reason for discontinuation from the study; and
the days from the first injection to the date of discontinuation

Please provide:

DESCRIPTION OF EACH VARIABLE:

example:

- TRT = Treatment
- INVID =Investigator Id#

DESCRIPTION OF THE VALUES OF EACH VARIABLE:

example:

- SEX (1=male, 2=female)
- Complete (1=Yes, 0=No)

UNIFORMITY OF DATA:

Please name, code and describe all the data in the same manner for all studies throughout the NDA.

THE EFFICACY AND SAFETY DATA FOR EACH OF THE STUDIES SEPARATELY:

Please provide the completed and corrected data (Separate files for separate studies, clearly labeled for each study and variable type (Efficacy or Safety)).

For example:

- File (1): Study 267 Complete Efficacy Data
- File (2): Study 267 Complete Safety Data
- File (3): Study # 269 Complete Efficacy Data
- File (4): Study # 269 Complete Safety Data

THE PROGRAMS USED TO GENERATE THE RESULTS, FOR EACH OF THE STUDIES SEPARATELY:

Please provide separate programs for separate studies, clearly labeled for each study. No need for programs to create tables or pages.

For example:

- File (1): Study # 267 Efficacy Data
- File (2): Study # 267 Safety Data

THE SAS AFORMAT@ PROGRAMS THAT ARE NEEDED TO BE RUN WITH EACH PROGRAM FOR EACH OF THE STUDIES SEPARATELY.

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/s/

Z. Charlene Williamson
6/22/04 06:13:57 PM
CSO

Shahla Farr
7/2/04 11:26:37 AM
BIOMETRICS

Teleconference Meeting Minutes

Date: June 23, 2004 **Time:** 2:00 – 2:30 PM **Location:** PKLN; 17B45

NDA 21-583 **Drug:** Medroxyprogesterone Acetate Injectable Suspension

Indication: Contraception

Sponsor: Pfizer, Inc.

Type of Meeting: Telephone Conference

FDA Attendees:

Ameeta Parekh, Ph.D., Clinical Pharmacology and Biopharmaceutics Team Leader, Office of Clinical Pharmacology and Biopharmaceutics (OCPB), @ Division of Reproductive and Urologic Drug Products DRUDP; HFD-580

Myong-Jin Kim, Pharm.D., Clinical Pharmacology and Biopharmaceutics Reviewer (OCPB), @ DRUDP; HFD-580

Lesley-Anne Furlong, M.D., Medical Officer, DRUDP; HFD-580

Jean Salemme, Ph.D., Chemist, Division of New Drug Chemistry II (DNDC II) @ DRUDP; HFD-580

Charlene Williamson - Project Manager, DRUDP; HFD-580

External Attendees:

Daniel Chirby, M.Sc., US Regulatory

Richard Davison, Senior Research Scientist, CMC

Discussion Points:

The sponsor should characterize the metabolic pathways of medroxyprogesterone acetate and address the drug interaction potential to appropriately address this information in the label. As a Phase IV commitment, the sponsor should conduct an in-vitro metabolism study.

Discussion points not addressed in the telephone conference is this commitment which is listed below:

Protocol Submission:
Study Start:

Final Report Submission:

Additionally, the stability data supports a _____ expiration date period. The expiration dating period can be extended with real-time data.

NDA 21-583

Page 2

Action Items:

- Minutes of the telephone conference due to sponsor within 48 hours.
- Agreement to the post marketing study commitment.

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/s/

Z. Charlene Williamson
6/25/04 03:31:04 PM
CSO

Ameeta Parekh
6/25/04 03:33:21 PM
BIOPHARMACEUTICS
I concur



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: May 26, 2004

To: Daniel Chirby	From: Charlene Williamson
Company: Pfizer, Inc.	Division of Reproductive and Urologic Drug Products
Fax number: 734-622-2856	Fax number: 301-827-4267
Phone number: 734-622-3750	Phone number: 301-827-4260
Subject: T-Con 5.26.04	

Total no. of pages including cover: 3

Comments:

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Teleconference Meeting Minutes

Date: May 26, 2004 **Time:** 9:00 AM – 9:30 AM **Location:** PKLN; 18B45

NDA 21-583 **Drug:** Medroxyprogesterone Acetate Injectable Suspension

Indication: Contraception

Sponsor: Pfizer, Inc.

Type of Meeting: Telephone Conference

FDA Attendees:

Ameeta Parekh, Ph.D., Clinical Pharmacology and Biopharmaceutics Team Leader, Office of Clinical Pharmacology and Biopharmaceutics (OCPB), @ Division of Reproductive and Urologic Drug Products (DRUDP), HFD-580

Myong-Jin Kim, Pharm.D., Clinical Pharmacology and Biopharmaceutics Reviewer (OCPB), @ DRUDP (HFD-580)

Lesley-Ann Furlong, M.D., Medical Officer, DRUDP (HFD-580)

Charlene Williamson - Project Manager, DRUDP (HFD-580)

External Attendees:

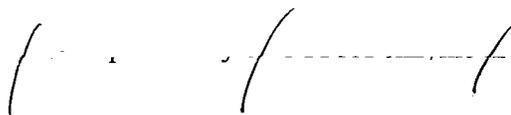
Daniel Chirby, M.Sc., US Regulatory

Lynn Purkins, Ph.D., Clinical Kineticist

Discussion Points:

The sponsor was requested to provide drug-drug interaction potentials for medroxyprogesterone acetate injectable suspension based on published literature data. The sponsor was unable to produce any additional information other than aminoglutethimide. In the absence of prospectively designed drug-drug interaction studies, the following was recommended:

-
-



Action Items:

- FDA will work on current label (physician package insert and patient insert)

Minutes prepared by: Charlene Williamson, Project Manager

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/s/

Z. Charlene Williamson
6/25/04 09:02:43 AM
CSO

Ameeta Parekh
6/25/04 09:35:39 AM
BIOPHARMACEUTICS
I concur



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III**

FACSIMILE TRANSMITTAL SHEET

DATE: May 7, 2004

To: Daniel Chirby Pfizer, Inc.	From: Charlene Williamson Regulatory Project Manager Division of Division of Reproductive and Urologic Drug Products
Fax number: 734-622-2856	Fax number: (301) 827-4267
Phone number: 734-622-3750	Phone number: (301) 827-4260

Subject:

Total no. of pages including cover: 2

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Please populate the following table for Study Z54000261:

Table: Percentage Change from Baseline in BMD

Visit	DMPA-IM		Control		Difference [DMPA-IM – Control] (95% CI)	P-Value
	n	Mean (SD)	n	Mean (SD)		
Femur BMD						
Week 24						
Week 60						
Week 84						
Week 120						
Week 144						
Week 204						
Week 240						
Femoral Neck BMD						
Week 24						
Week 60						
Week 84						
Week 120						
Week 144						
Week 204						
Week 240						
Spine BMD						
Week 24						
Week 60						
Week 84						
Week 120						
Week 144						
Week 204						
Week 240						

The "n" for the control group should consist of subjects who did not receive Depo-Provera up to that week of the study. The "n" for the Depo-Provera group should consist of subjects who had uninterrupted therapy with Depo-Provera up to that week of the study.

We would appreciate receiving a response no later than May 13, 2004.

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/s/

Z. Charlene Williamson
6/22/04 06:39:49 PM
CSO

Leslie Ann Furlong
6/23/04 05:24:21 AM
MEDICAL OFFICER

A

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NDA 21-583

INFORMATION REQUEST LETTER

Pfizer, Inc.
Attention: Daniel Chirby, M.Sc.
Associate Director
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Mr. Chirby:

Please refer to your June 30, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Medroxyprogesterone Acetate Injectable Suspension.

We also refer to your submission dated April 7, 2004, received on April 8, 2004, containing a major clinical amendment.

To facilitate review of the Study Report for Study M5400/0234, please provide the following information no later than April 26, 2004:

- 1) A table similar to the table on page 44 in Study Report M5400/0234 for each of the following subgroups:
 - Women who had 1 to 4 injections of DMPA-IM
 - Women who had 5 to 8 injections of DMPA-IM
 - Women who had 9 to 12 injections of DMPA-IM
 - Women who had 13 to 16 injections of DMPA-IM
 - Women who had 17-20 injections of DMPA-IM
 - Women who had 20 injections of DMPA-IM
 - Women who had 21 injections of DMPA-IM

Please provide 95% confidence intervals for all entries in the column labeled adjusted mean change.

- 2) A dataset in SAS transport format identical to the BMD dataset for Study M5400/0234 contained in your submission of April 7, 2004, except for the addition of a column containing the number of injections of DMPA-IM received by each patient during the study.
- 3) A table similar to the table on page 48 in Study Report M5400/0234 for each of the subgroups:
 - Women who had 1 to 4 injections of DMPA-IM

- Women who had 5 to 8 injections of DMPA-IM
- Women who had 9 to 12 injections of DMPA-IM
- Women who had 13 to 16 injections of DMPA-IM
- Women who had 17-20 injections of DMPA-IM
- Women who had 20 injections of DMPA-IM
- Women who had 21 injections of DMPA-IM

Please also include a row for Week 24 post treatment weights.

If you have any questions, please call Charlene Williamson, Regulatory Project Manager, at 301-827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.
Chief, Project Management Staff
Division of Reproductive and Urologic Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Margaret Kober
4/20/04 12:22:23 PM
Chief, Project Management Staff



NDA 21-583

Pfizer, Inc.
Attention: Daniel Chirby, M.Sc.
Associate Director
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Mr. Chirby:

Please refer to your June 30, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Medroxyprogesterone Acetate Injectable Suspension.

On April 8, 2004, we received your April 7, 2004 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is August 2, 2004.

If you have any questions, please call Charlene Williamson, Regulatory Project Manager, at 301-827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.
Chief, Project Management Staff
Division of Reproductive and Urologic Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Margaret Kober
4/15/04 11:24:05 AM
Chief, Project Management Staff

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Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: April 3, 2004

To: Daniel Chirby Pfizer, Inc.	From: Charlene Williamson Regulatory Project Manager Division of Division of Reproductive and Urologic Drug Products
Fax number: 734-622-2856	Fax number: (301) 827-4267
Phone number: 734-622-3750	Phone number: (301) 827-4260

Subject:

Total no. of pages including cover: 2

Comments:

Document to be mailed: NO

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As discussed during the teleconference between Pfizer and the Division of Reproductive and Urologic Drug Products on March 30, 2004, we are confirming our request for the following information/datasets to facilitate our ongoing review on NDA 21-583. We request that you submit all of the following information to NDA 21-583.

1. Study 267BMD
 - a. Provide treatment assignments (in SAS transport format [.xpt]) for all subjects treated with study drug in Study 267BMD. Alternatively, you can enter the unblinded treatment assignments into data file BMD.xpt that was provided as part of the Safety Update and resubmit the entire data file.
 - b. Provide Data Listing 3.6.1 (listing of BMD data by patient) from the One-Year Interim Report for Study 267BMD with treatment assignments added in PDF format.
2. Study M54000234
 - a. Submit the Final Study Report previously submitted to IND 45,275 to NDA 21-583. This can be accomplished either by cross-reference to the previously submitted report or by submission of the Report, per se.
 - b. Provide the BMD data from Study M54000234 in SAS transport format. A dataset format similar to that used for file BMD.xpt for Study 267BMD is acceptable. The file should include, to the extent possible, all comparable information contained in dataset BMD.xpt from Study 267BMD. In addition, add a variable for [days since last injection plus 91 days] for all posttreatment recovery measurements.
3. Study Z54000261
 - a. Submit the most current Interim Report for Study Z54000261 to NDA 21-583.
 - b. Submit BMD data for each subject in Study Z54000261 in SAS transport format. The dataset should include information comparable to that previously provided for Study 267BMD. For each measurement, provide, where applicable, actual BMD value, change from baseline value (both actual change and percentage change), t-score, and category changes (both for BMD percent changes and t-score changes). Also, provide day of treatment or posttreatment day for each measurement. Provide any additional variables/information (e.g., was treatment continuous or interrupted, age, etc.) that will assist us in our review of the data. Provide a full definition for all column variables.
4. Submit approved product labels for DMPA-IM for Canada, U.K., and Australia.
5. Confirm that (a) no changes in labeling regarding BMD for DMPA IM have been made because of regulatory requests outside of the U.S. and (b) DMPA IM has not been removed from any market because of safety concerns.

Please provide requested information as soon as possible and no later than April 7, 2004. Please notify Charlene Williamson at 301-827-4266, if you will not be able to meet this goal date.



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE III

FACSIMILE TRANSMITTAL SHEET

DATE: March 30, 2004

To: Daniel Chirby	From: Charlene Williamson
Company: Pfizer, Inc.	Division of Reproductive and Urologic Drug Products
Fax number: 734-622-2856	Fax number: 301-827-4267
Phone number: 734-622-3750	Phone number: 301-827-4260
Subject: Requested Info Per 3/20/04 T-Con	

Total no. of pages including cover: 3

Comments:

Document to be mailed: • YES NO

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As discussed during the teleconference between Pfizer and the Division of Reproductive and Urologic Drug Products on March 30, 2004, we are confirming our request for the following information/datasets to facilitate our ongoing review on NDA 21-583. We request that you submit all of the following information to NDA 21-583.

1. Study 267BMD

- a. Provide treatment assignments (in SAS transport format [.xpt]) for all subjects treated with study drug in Study 267BMD. Alternatively, you can enter the unblinded treatment assignments into data file BMD.xpt that was provided as part of the Safety Update and resubmit the entire data file.
- b. Provide Data Listing 3.6.1 (listing of BMD data by patient) from the One-Year Interim Report for Study 267BMD with treatment assignments added in PDF format.

2. Study M54000234

- a. Submit the Final Study Report previously submitted to IND 45,275 to NDA 21-583. This can be accomplished either by cross-reference to the previously submitted report or by submission of the Report, per se.
- b. Provide the BMD data from Study M54000234 in SAS transport format. A dataset format similar to that used for file BMD.xpt for Study 267BMD is acceptable. The file should include, to the extent possible, all comparable information contained in dataset BMD.xpt from Study 267BMD. In addition, add a variable for [days since last injection plus 91 days] for all posttreatment recovery measurements.

3. Study Z54000261

- a. Submit the most current Interim Report for Study Z54000261 to NDA 21-583.
- b. Submit BMD data for each subject in Study Z54000261 in SAS transport format. The dataset should include information comparable to that previously provided for Study 267BMD. For each measurement, provide, where applicable, actual BMD value, change from baseline value (both actual change and percentage change), t-score, and category changes (both for BMD percent changes and t-score changes). Also, provide day of treatment or posttreatment day for each measurement. Provide any additional variables/information (e.g., was treatment continuous or interrupted, age, etc.) that will assist us in our review of the data. Provide a full definition for all column variables.

4. Submit approved product labels for DMPA-IM for Canada, U.K., and Australia.
5. Confirm that (a) no changes in labeling regarding BMD for DMPA IM have been made because of regulatory requests outside of the U.S. and (b) DMPA IM has not been removed from any market because of safety concerns.

Please provide requested information as soon as possible and no later than April 7, 2004. Please notify Charlene Williamson at 301-827-4266, if you will not be able to meet this goal date.

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/s/

Z. Charlene Williamson
3/30/04 05:47:26 PM

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**Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville MD 20857**

CLINICAL INSPECTION SUMMARY

DATE: March 22, 2004

TO: Charlene Williamson, Regulatory Project Manager
Leslie Furlong, M.D.
Division of Reproductive and Urologic Drug Products, HFD-580

THROUGH: Khin Maung U, M.D.
Branch Chief
Good Clinical Practice Branch I, HFD-46
Division of Scientific Investigations

FROM: Roy Blay, Ph.D.
Good Clinical Practice Branch I, HFD-46

SUBJECT: Evaluation of Clinical Inspections

NDA: NDA 21-583

PROTOCOL: Protocol #839-FEH-0012-267 entitled: "Phase III Contraception Study of Depot Medroxyprogesterone Acetate Subcutaneous Injection (DMPA-SC) in Women of Childbearing Potential in the Americas (including a Bone Mineral Density [BMD] Substudy Comparing the Effects of DMPA-SC and DMPA-IM. Also Including a Return of Ovulation Sub-study")

SPONSOR: Pharmacia & Upjohn

DRUG: Depot medroxyprogesterone acetate subcutaneous injection, DMPA-SC

INDICATION: Contraception

CHEMICAL CLASSIFICATION: 3

THERAPEUTIC CLASSIFICATION: S (Standard Review, Substantially Equivalent)

INSPECTION SUMMARY GOAL DATE: April 5, 2004

ACTION GOAL DATE: April 30, 2004

I. BACKGROUND:

Inspection assignments were issued on December 4, 2003 for three domestic sites: Drs. Pogue, Jain, and Heine for Protocol # 839-FEH-0012-267, for the purpose of validating data in support of pending NDA 21-583 for contraception.

Study Objective: To assess the efficacy of DMPA-SC contraceptive injection administered every three months.

Methodology: Phase III open-label multi-center trial with subjects randomized to either the subcutaneous or intramuscular forms of the study drug followed for 1-2 years.

Main Criteria for Inclusion: Female subjects 18 years or older, in general good health desiring long-term contraception.

Primary Efficacy Endpoint: Treatment failure cumulative pregnancy rate at 1 year

Dosage: DMPA-SC at 104 mg or DMPA-IM at 150 mg

Safety: Assessment of systolic and diastolic blood pressure and adverse events throughout the study

II. RESULTS (by site):

NAME	CITY	STATE	ASSIGNED DATE	RECEIVED DATE	CLASSIFICATION/FILE NUMBER
Thomas Purdon, M.D.	Tucson,	AZ	04 Dec 03	4 Feb 04	000138/NAI
John Jain, M.D.	Los Angeles,	CA	04 Dec 03	27 Feb 04	011131/VAI
Bryan C. Pogue, M.D.	Boise	ID	04 Dec 03	27 Feb 04	011128/NAI

Site #1

Thomas Purdon, M.D. (Dr. Heine, retired)
Department of Obstetrics and Gynecology
University of Arizona Health Sciences Center
1501 N. Campbell Avenue
85724

See **Assessment and Recommendations**, below

- a. 34 subjects were enrolled in the study. 20 subjects completed the study. The records for sixteen subjects were reviewed in whole or in part, including, but not limited to PAP tests, pregnancy tests, drug reconciliation, adverse event reporting and adherence to protocol.
- b. There were no limitations to the inspection.

- c. A Form 483 was not issued.

Site #2

John Jain, M.D.

Women's and Children's Hospital

1240 N. Mission Road-L1009

Los Angeles, California 90033

See **Assessment and Recommendations**, below

- a. 45 subjects were randomized to the study at this site. Seven subjects participated in the BMD sub-study. Eleven subjects withdrew from the study due to adverse events, protocol violations or patient request. Fifteen records were reviewed in depth.
- b. There were no limitations to the inspection.
- c. A Form 483 was issued noting inadequate/inaccurate records, that the study was not conducted per the signed investigator agreement, and inadequate records of drug disposition. Dr. Jain responded in writing, providing adequate responses to the observations noted in the Form 483.

Site #3

Bryan C. Pogue, M.D.

Radiant Research-Boise, Inc.

6565 West Emerald Street

Boise, Idaho 83704

See **Assessment and Recommendations**, below

- a. 57 subjects were randomized to the study with 26 subjects completing the study, 31 dropping from the study, and 10 subjects continuing in the study. The records for 30 subjects were reviewed, including diaries consent forms, progress notes, worksheets, bone mineral density tests, pregnancy tests, drug accountability records, etc.
- b. There were no limitations to the inspection.
- c. A Form 483 was not issued.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

The data submitted by Drs. Purdon (Heine), Jain, and Pogue appear satisfactory in support of the relevant submission.

Roy Blay, Ph.D.
Good Clinical Practice Branch I, HFD-46
Division of Scientific Investigations

CONCURRENCE:

Khin Maung U. M.D.
Branch Chief
Good Clinical Practice Branch I, HFD-46
Division of Scientific Investigations

cc:
HFD-540 Doc. Rm. NDA 21-583
HFD-45/Program Management Staff (electronic copy)
HFD-46/RF
HFD-46/c/r/s
HFD-46/Blay

c:\data\royblay\clinicalsummaries\21583.doc
o:\blay\21583.doc

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/s/

Sherry George
3/24/04 10:53:51 AM
TECHNICAL
Signed by Drs. Blay and U on 3/23/04

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Trade Secret / Confidential

Draft Labeling

Deliberative Process



NDA 21-583

INFORMATION REQUEST LETTER

Pfizer, Inc.
Attention: Daniel Chirby, M.Sc.
Associate Director
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Mr. Chirby:

Please refer to your June 30, 2003, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for medroxyprogesterone acetate Injectable Suspension, USP.

We are reviewing the Statistical and Biopharmaceutical sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- 1) Provide us with two datasets for each one of the Studies 267, 267 BMD, and 269 to include:
 - a. Subjects 35 years and younger who did not use any other form of contraception.
 - b. Subjects 35 years and younger who did not use any other method of contraception.

In your response, include the total number of subjects in each of these datasets, total number of injections, total number of months of exposure, and the treatment arm for study 267 BMD only. If a subject had missed an injection or had used any other form of contraception, or did not have intercourse for a specific period, only the observations for those periods should be deleted, **not** all the records for that subject.

- 2) Provide any information on drug-drug interaction potentials with DMPA-SC, this information can be based on literature references.

If you have any questions, call Charlene Williamson, Regulatory Project Manager, at 301-827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.
Chief, Project Management Staff
Division of Reproductive and Urologic Drug
Product; HFD -580
Office of New Drug III
Center for Drug Evaluation and Research

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/s/

Jennifer L. Mercier
3/17/04 05:19:30 PM
for Margaret Kober



NDA 21-583

INFORMATION REQUEST LETTER

Pfizer, Inc.
Attention: Daniel Chirby, M.Sc.
Associate Director
2800 Plymouth Road
Ann Arbor, MI 48105

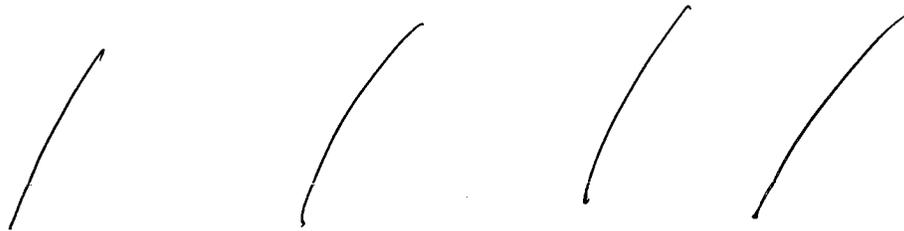
Dear Mr. Chirby:

Please refer to your June 30, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Depot Medroxyprogesterone Acetate Subcutaneous Injection.

We also refer to your submission dated February 23, 2004.

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

- 1.
- 2.
- 3.
- 4.



If you have any questions, call Charlene Williamson, Regulatory Project Manager, at 301-827-4260.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chemistry Team Leader, for
Division of Reproductive and Urologic Drug
Products, HFD-580
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Moo-Jhong Rhee
3/4/04 04:34:59 PM

MEMORANDUM

Date: December 24, 2003

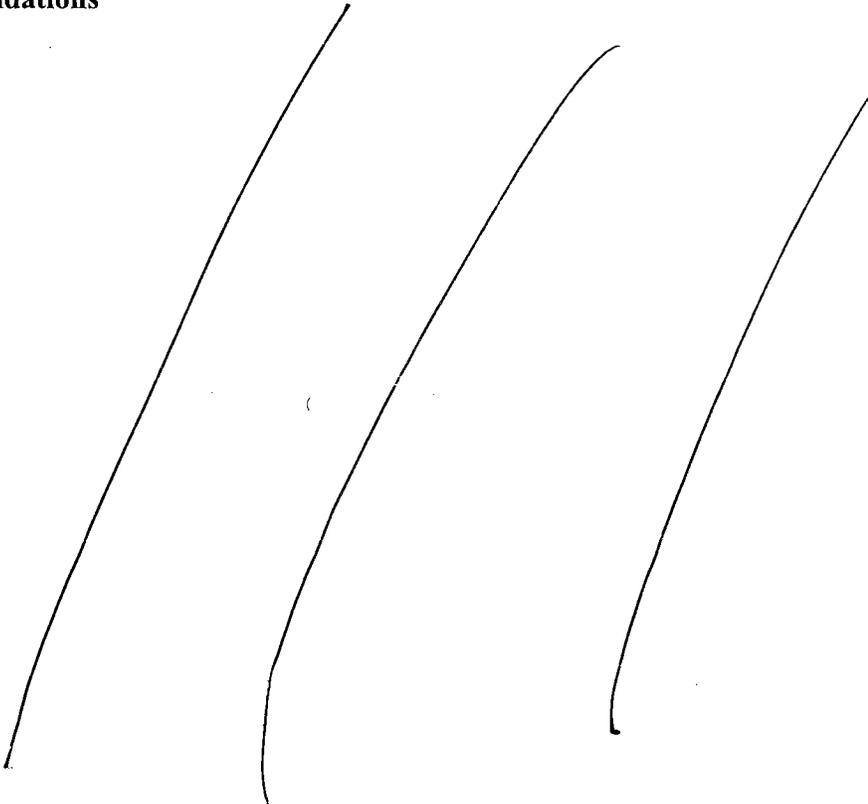
To: Dr. Daniel Shames
Director
Division of Reproductive and Urologic Drug Products
HFD-580

From: Lisa Stockbridge, Ph.D.
Iris Masucci, Pharm. D.
Division of Drug Marketing, Advertising, and Communications
HFD-42

Re: NDA 21-583
Medroxyprogesterone Acetate Subcutaneous Injection PI and PPI

Material Reviewed: June 30, 2003 proposal of Prescribing Information (PI). DDMAC defers to DSRCs for comments on the proposed patient information. We concur that the PPI requires major revision in format and content to ensure comprehension.

Recommendations



E

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/s/

Lisa Stockbridge
12/24/03 02:46:32 PM
DDMAC REVIEWER

MEMORANDUM

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

DATE: December 19, 2003

TO: Daniel Shames, M.D., Director
Division of Reproductive and Urologic Drug Products
HFD-580

VIA: Charlene Williamson, Regulatory Health Project Manager
Division of Reproductive and Urologic Drug Products
HFD-580

FROM: Jeanine Best, M.S.N., R.N., P.N.P.
Patient Product Information Specialist
Division of Surveillance, Research, and Communication Support
HFD-410

THROUGH: Gerald Dal Pan, M.D., M.H.S., Director
Division of Surveillance, Research, and Communication Support
HFD-410

SUBJECT: ODS/DSRCS Review of Patient Labeling for TRADEMARK
(medroxyprogesterone acetate injectable suspension), NDA 21-583

Background

The sponsor submitted Patient Information for TRADEMARK (medroxyprogesterone acetate injectable suspension), NDA 21-583, in the form of a Patient Package Insert (PPI) on June 30, 2003. The submitted PPI has a Flesch-Kincaid Grade Level of 11.0; a Flesch Reading Ease of 47.6%; and average words per sentence of 17.6.

Comments and Recommendations:

We have the following comments and recommendations:

Five handwritten checkmarks are arranged horizontally across the page, indicating that the comments and recommendations have been reviewed or approved.

F

 1 Page(s) Withheld

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 ✓ Draft Labeling

 Deliberative Process

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/s/

Jeanine Best
12/19/03 08:12:21 AM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
12/19/03 03:44:12 PM
DRUG SAFETY OFFICE REVIEWER
for Gerald Dal Pan

NDA REGULATORY FILING REVIEW
(Includes Filing Meeting Minutes)

NDA # 21583 Supplement # _____ SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8

Trade Name: _____

Generic Name: Medroxyprogesterone Acetate Injectable Suspension, USP

Strengths: 104mg/0.65ml

Applicant: Pharmacia and Upjohn

Date of Application: June 30, 2003

Date of Receipt: July 2, 2003

Date of Filing Meeting: August 15, 2003

Filing Date: August 29, 2003

Indication(s) requested: Prevention of Pregnancy in women of child-bearing years (contraceptive)

Type of Application: Original (b)(1) NDA X Original (b)(2) NDA _____
(b)(1) Supplement _____ (b)(2) Supplement _____
[If the Original NDA was a (b)(2), all supplements are (b)(2) s; if the Original NDA was a (b)(1), the supplement can be either a (b)(1) or a (b)(2).]

If the application is a 505(b)(2) application, complete the 505(b)(2) section at the end of this summary.

Therapeutic Classification: S X P _____
Resubmission after a withdrawal _____ or refuse to file _____
Chemical Classification: (1,2,3 etc.) SC
Other (orphan, OTC, etc.) _____

Has orphan drug exclusivity been granted to another drug for the same indication? YES NO

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

Is the application affected by the application integrity policy (AIP)? YES NO
If yes, explain.

If yes, has OC/DMPQ been notified of the submission? YES NO

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

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee ID # 4537
Clinical data? YES _____ NO _____, Referenced to NDA # _____

Date clock started after UN: _____

User Fee Goal Date: May 2, 2004

Action Goal Date (optional): April 30, 2004

Does the submission contain an accurate comprehensive index? YES NO

- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES NO
 If no, explain:

- If an electronic NDA, does it follow the Guidance? N/A YES NO
If an electronic NDA, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

Additional comments:

- If in Common Technical Document format, does it follow the guidance? N/A YES NO

- Is it an electronic CTD? N/A YES NO
If an electronic CTD, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

The entire application was submitted via CTD.

Additional comments:

- Patent information included with authorized signature? YES NO

- Exclusivity requested? YES, 3 years NO
 Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

- Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification must have correct wording, e.g.: "I, the undersigned, hereby certify that _____ Co. 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 the studies listed in Appendix ____." Applicant may not use wording such as "To the best of my knowledge"

- Financial Disclosure information included with authorized signature? YES NO
(Forms 3454 and/or 3455 must be used and must be signed by the APPLICANT.)

- Has the applicant submitted pediatric data and/or deferral request and/or waiver request for all ages and indications? NEED TO REVISE OR DELETE THIS STATEMENT

- | | | |
|-------------------|-----|----|
| | YES | NO |
| • If no, explain. | | |
| Waived | | |

- Field Copy Certification (that it is a true copy of the CMC technical section)? YES NO

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? YES NO
 If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

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

- List referenced IND numbers:

- End-of-Phase 2 Meeting? Date _____ NO
 If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) _____ NO
 If yes, distribute minutes before filing meeting.

Project Management

- Package insert consulted to DDMAC? YES NO

- Trade name (plus PI and all labels and labeling) consulted to ODS/Div. of Medication Errors and Technical Support? YES NO

- MedGuide and/or PPI (plus PI) consulted to ODS/Div. of Surveillance, Research and Communication Support? N/A YES NO

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/ Div. of Surveillance, Research and Communication Support? N/A YES NO

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

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
 If no, did applicant submit a complete environmental assessment? YES NO
 If EA submitted, consulted to Nancy Sager (HFD-357)? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If parenteral product, consulted to Microbiology Team (HFD-805)? YES NO

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

- Name of listed drug(s) and NDA/ANDA #:
- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, “This application provides for a new indication, otitis media” or “This application provides for a change in dosage form, from capsules to solution”).
- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.) YES NO
- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9). YES NO
- Is the rate at which the product’s active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9). YES NO
- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.

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

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

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

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

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

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

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

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

___ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)

___ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

• Did the applicant:

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

YES NO

• Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

YES NO

• Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

N/A YES NO

• Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?

N/A YES NO

• If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

• Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

YES NO

• A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

YES NO

• EITHER

The number of the applicant's IND under which the studies essential to approval were conducted.

YES, IND # _____ NO

OR

A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

N/A YES NO

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

YES NO

BIOPHARMACEUTICS	FILE <input checked="" type="checkbox"/>	REFUSE TO FILE _____		
• Biopharm. inspection needed:			YES	NO
PHARMACOLOGY	FILE <input checked="" type="checkbox"/>	REFUSE TO FILE _____		
• GLP inspection needed:			YES	NO
CHEMISTRY	FILE <input checked="" type="checkbox"/>	REFUSE TO FILE _____		
• Establishment(s) ready for inspection?			YES	NO
• Microbiology			YES	NO

ELECTRONIC SUBMISSION:

Any comments: The entire submission was sent via CTD

REGULATORY CONCLUSIONS/DEFICIENCIES:

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

_____ The application is unsuitable for filing. Explain why:

ACTION ITEMS:

1. Items to be included in the 74-day filing issue letter:
 - a. Is this product approved elsewhere, has it been denied, or removed from the market elsewhere, or are marketing applications pending elsewhere?
 - b. For studies 267, 267 BMD, and 269, please supply the number of women screening for eligibility, the number of women excluded, and a numerical summary of the reasons for exclusion.
 - c. Provide case report form for patient number 425, investigator number 50126, study number 267.
 - d. Provide case report form and follow up information for patient number 350, site number 46120, Study 267.
 - e. Provide 95% confidence intervals for your Pearl indices and life table pregnancy rates, including the rates for subgroups (e.g. weight subgroups).
 - f. MPA accumulation following multi-dose administration

- g. Description of single-dose and multi-dose pharmacokinetics and pharmacodynamics of effect of injection site (anterior thigh vs. abdomen) on drug exposure
- h. Effects of race and body weight on drug exposure
- i. Results of dose-finding studies with Depo-Provera IM formulation given subcutaneously

Charlene Williamson
Regulatory Project Manager, HFD-

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/s/

Z. Charlene Williamson
11/24/03 03:40:48 PM
CSO

Z. Charlene Williamson
11/24/03 03:46:53 PM
CSO

PHARMACIA

Renee Ray
US Regulatory Liaison Office
Global Regulatory Affairs

Pharmacia Corporation
7000 Portage Road (0636-298-112)
Kalamazoo, MI 49001
tel 269.833.0730
fax 269.833.0512
renee.n.ray@pharmacia.com
www.pharmacia.com

June 24, 2003

Food and Drug Administration
P.O. Box 360909
Pittsburgh, PA 15251-6909

RE: User Fee Id 4537
NDA submission
Product: Depot Medroxyprogesterone
Acetate Subcutaneous Injection (DMPA-SC)

Dear Sir or Madam:

Enclosed is a check in the amount of \$533,400 for a NDA submission under User Fee ID number 4537. Submission is currently scheduled for Thursday, June 26, 2003.

Should you have any questions, please feel free to contact me at (269) 833.0730.

Sincerely,



Renee N. Ray
US Regulatory Liaison Office

Enclosure

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

<p>1. APPLICANT'S NAME AND ADDRESS</p> <p>PHARMACIA & UPJOHN COMPANY 7000 Portage Road Kalamazoo, MI 49001</p> <p>Donald H. Hodges Associate Director - Global Regulatory Affairs - Labeling</p>	<p>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER NDA 21-583</p>
<p>2. TELEPHONE NUMBER (Include Area Code)</p> <p>(269) 833-8037</p>	<p>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p>IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.</p> <p>IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:</p> <p><input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: _____ (APPLICATION NO. CONTAINING THE DATA).</p>
<p>3. PRODUCT NAME</p> <p>Depot Medroxyprogesterone Acetate Subcutaneous Injection</p>	<p>6. USER FEE I.D. NUMBER 4537</p>

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)	

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration CDER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	and	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
--	-----	--	--

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Daniel G. Chirby, M.Sc., Senior Regulatory Manager	DATE June 30, 2003
---	--	-----------------------

1. ENVIRONMENTAL ASSESSMENT – CLAIM FOR A CATEGORICAL EXCLUSION

Under the provisions of 21 CFR 25.31(a), action on an NDA are categorically excluded and, therefore, ordinarily do not require the preparation of an Environmental Assessment (EA) or an Environmental Impact Statement (EIS) if the action does not increase the use of the active moiety. Pharmacia is proposing to change the from an IM dosage form to a subcutaneous route of administration for Depo-Provera (medroxyprogesterone acetate). The amount of Depo-Provera to be marketed in the U.S. is not projected to increase as a result of this change in dosage form. To the best knowledge of Pharmacia & Upjohn, the applicant is not aware of the existence of any extraordinary circumstances that would require the preparation of an Environmental Assessment. Also, Pharmacia & Upjohn does not have any information to indicate that medroxyprogesterone acetate may be toxic to organisms in the environment at the expected levels of exposure. Pharmacia & Upjohn claims a categorical exclusion to the EA requirements in accordance with 21 CFR 25.31(a).

1.1. Date

21 February 2003

1.2. Name of Applicant

Pharmacia
7000 Portage Road
Kalamazoo, Michigan 49001-0199

Contact: Daniel E. Sullivan, Ph.D.
Tel. (269) 833-0394

1.3. List of Preparer

Daniel E. Sullivan, Ph.D.
Director of Environmental Affairs

Ph.D. Environmental Engineer with twenty- three years in chemical fate and effect evaluations, WWTP operations, and regulatory compliance.

1.4. Certification

The undersigned certifies that the information presented is true, accurate, and complete to the best knowledge of Pharmacia.



21 FEBRUARY 2003

Daniel E. Sullivan, Ph.D.

Date

NDA 21-583

(Depot Medroxyprogesterone Acetate Subcutaneous Injection)

ADVISORY COMMITTEE MEETING

N/A

NDA 21-583

(Depot Medroxyprogesterone Acetate Subcutaneous Injection)

APPLICATION INTEGRITY

N/A

CW Williams
7/29/04

NDA 21-583

(Depot Medroxyprogesterone Acetate Subcutaneous Injection)

PUBLIC COMMUNICATIONS

N/A

O'Williamson
7/29/04

NDA 21-583
(Depot Medroxyprogesterone Acetate Injectable Suspension)

Safety Update was submitted on October 28, 2003. The primary medical officer's review of the safety update is noted on page 83 of her review.

NDA 21-583
(Depot Medroxyprogesterone Acetate Injectable Suspension)

CONTROLLED SUBSTANCE STAFF REVIEWS

N/A

C. Williamson
7/29/04

NDA 21-583
(Depot Medroxyprogesterone Acetate Injectable Suspension)

METHODS VALIDATION

N/A

C. Williamson
7/29/04

NDA 21-583
(Depot Medroxyprogesterone Acetate Injectable Suspension)

NON-CLINICAL INSPECTION REVIEW
N/A

CW Williamson
7/29/04

NDA 21-583
(Depot Medroxyprogesterone Acetate Injectable Suspension)

STATISTICAL REVIEWS
N/A

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7/29/04