

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-998**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

**PATENT INFORMATION SUBMITTED UPON AND  
AFTER APPROVAL OF AN NDA OR SUPPLEMENT**

**For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation or  
Composition) and/or Method of Use**

NDA NUMBER

21-998

NAME OF APPLICANT / NDA HOLDER

Gedeon Richter, Ltd.

**The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.**

TRADE NAME

Levonorgestrel 1.5 mg Tablet

ACTIVE INGREDIENT(S)

Levonorgestrel [18,19-Dinorepregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17  $\alpha$ )-(-)-]

STRENGTH(S)

1.5 mg

DOSAGE FORM

Tablet

APPROVAL DATE OF NDA OR SUPPLEMENT

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) within thirty (30) days after approval of an NDA or supplement or within thirty (30) days of issuance of a patent as required by 21 CFR 314.53(c)(2)(ii) at the address provided in 21 CFR 314.53(d)(4). To expedite review of this patent declaration form, you may submit an additional copy of this declaration form to the Center for Drug Evaluation and Research "Orange Book" staff.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

**FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.**

**For each patent submitted for the approved NDA or supplement referenced above, you must submit all the information scribed below. If you are not submitting any patents for this NDA or supplement, complete above section and sections 5 d 6.**

a. United States Patent Number

b. Issue Date of Patent

c. Expiration Date of Patent

d. Name of Patent Owner

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

☐ Yes

☐ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

☐ Yes

☐ No

**For the patent referenced above, provide the following information on each patent that claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing. FDA will consider an incomplete patent declaration to be a declaration that does not include a response to all the questions contained within each section below applicable to the patent referenced above.**

|                                                                                                                                                                                                                                                                                                                                                                                                                                |                              |                             |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------------------|
| 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the approved NDA or supplement?                                                                                                                                                                                                                                                                                    | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the NDA?                                                                                                                                                                                                                                                                                                        | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).                                                                                                            | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.                                                                                                                                                                                                                                                                                                                |                              |                             |
| 2.5 Does the patent claim only a metabolite of the approved active ingredient? (Complete the information in section 4 below if the patent claims an approved method of using the approved drug product to administer the metabolite.)                                                                                                                                                                                          | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2.6 Does the patent claim only an intermediate?                                                                                                                                                                                                                                                                                                                                                                                | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)                                                                                                                                                                                                                                     | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| <b>FDA will not list the patent in the Orange Book as claiming the drug substance if:</b> <ul style="list-style-type: none"> <li>• the answers to 2.1 and 2.2 are "No," or,</li> <li>• the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,</li> <li>• the answer to 2.3 is "Yes" and there is no response to 2.4, or,</li> <li>• the answer to 2.5 or 2.6 is "Yes,"</li> <li>• the answer to 2.7 is "No."</li> </ul> |                              |                             |

|                                                                                                                                                                                                                                                                                        |                              |                             |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------------------|
| 3.1 Does the patent claim the approved drug product as defined in 21 CFR 314.3?                                                                                                                                                                                                        | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 3.2 Does the patent claim only an intermediate?                                                                                                                                                                                                                                        | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)                                                                                             | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| <b>FDA will not list the patent in the Orange Book as claiming the drug product if:</b> <ul style="list-style-type: none"> <li>• the answer to question 3.1 is "No," or,</li> <li>• the answer to question 3.2 is "Yes," or,</li> <li>• the answer to question 3.3 is "No."</li> </ul> |                              |                             |

**Sponsors must submit the information in section 4 separately for each patent claim claiming an approved method of using the approved drug product. For each method of use claim referenced, provide the following information:**

|                                                                                                                             |                                                                                                            |                             |
|-----------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|-----------------------------|
| 4.1 Does the patent claim one or more approved methods of using the approved drug product?                                  | <input type="checkbox"/> Yes                                                                               | <input type="checkbox"/> No |
| 4.2 Patent Claim Number (as listed in the patent)                                                                           | Does the patent claim referenced in 4.2 claim an approved method of use of the approved drug product?      |                             |
|                                                                                                                             | <input type="checkbox"/> Yes                                                                               | <input type="checkbox"/> No |
| 4.2a If the answer to 4.2 is "Yes," identify the use with specific reference to the approved labeling for the drug product. | Use: (Submit indication or method of use information as identified specifically in the approved labeling.) |                             |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>4.2b</b> If the answer to 4.2 is "Yes," also provide the information on the indication or method of use for the Orange Book "Use Code" description.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Use: (Submit the description of the approved indication or method of use that you propose FDA include as the "Use Code" in the Orange Book, using no more than 240 total characters including spaces.) |
| I will not list the patent in the Orange Book as claiming the method of use if: <ul style="list-style-type: none"> <li>the answer to question 4.1 or 4.2 is "No," or</li> <li>if the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                        |
| <b>Patent Information</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                        |
| For this NDA or supplement, there are no relevant patents that claim the approved drug substance (active ingredient) or the approved drug product (formulation or composition) or approved method(s) of use with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. <span style="float: right;"><input checked="" type="checkbox"/> Yes</span>                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                        |
| <b>Patent Certification</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                        |
| <b>6.1</b> The undersigned declares that this is an accurate and complete submission of patent information for the NDA or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.<br><br><b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b>                                                                                                                                                                                                                                              |                                                                                                                                                                                                        |
| <b>6.2</b> Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Date Signed                                                                                                                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                        |
| <b>NOTE:</b> Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                        |
| Check applicable box and provide information below.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                        |
| <input type="checkbox"/> NDA Applicant/Holder                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official                                                                             |
| <input type="checkbox"/> Patent Owner                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official                                                                                                  |
| <b>Name</b><br>Joseph A. Carrado, M.Sc., R.Ph.<br>Vice-President<br>Clinical Regulatory Affairs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                        |
| <b>Address</b><br>Duramed Research, Inc.<br>One Belmont Ave.<br>11 <sup>th</sup> Floor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>City/State</b><br>Bala Cynwyd, PA                                                                                                                                                                   |
| <b>ZIP Code</b><br>19004                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <b>Telephone Number</b><br>610-747-2600                                                                                                                                                                |
| <b>FAX Number (if available)</b><br>610-747-2979                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>E-Mail Address (if available)</b><br>Jcarrado@barriabs.com                                                                                                                                          |
| <p>The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Food and Drug Administration<br/>         CDER (HFD-007)<br/>         5600 Fishers Lane<br/>         Rockville, MD 20857</p> <p style="text-align: center;"><i>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.</i></p> |                                                                                                                                                                                                        |

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**LEVONORGESTREL 1.5 mg**  
tablet

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**Patent Certification**

In accordance with Section 505 (b) of the Federal Food, Drug and Cosmetic Act and as specified by 21 CFR 314.50 (h) and 21 CFR 314.53 (c) (3), Gedeon Richter, Ltd. (Duramed Research, Inc. regulatory agent) hereby declares that there are no patents which claims a single 1.5 mg Levonorgestrel Tablet for emergency contraception (to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse) with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of a single 1.5 mg tablet of Levonorgestrel Tablet for emergency contraception.

Therefore, a patent certification is not applicable.

Date

1/19/2006

  
\_\_\_\_\_  
Joseph A. Carrado, M.Sc., R.Ph.  
Vice-President  
Clinical Regulatory Affairs  
Duramed Research Inc.  
Regulatory Agent for Gedeon Richter, Ltd.

## EXCLUSIVITY SUMMARY

NDA # NDA 21-998

SUPPL #

HFD # 580

Trade Name Plan B One-Step

Generic Name levonorgestrel tablet, 1.5 mg

Applicant Name Duramed Pharmaceuticals, Inc.

Approval Date, If Known July 10, 2009

### 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?

3 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# 21-045

Plan B (levonorgestrel tablets, 0.75 mg)

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:

WHO 97902

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 similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

WHO 97902

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !  
!  
IND # YES ☐ ! NO ☐  
! Explain:

Investigation #2 !  
!  
IND # YES ☐ ! 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 ☒ ! NO ☐  
Explain: ! Explain:  
Gedeon Richter, Ltd., the

manufacturer of Plan B One-Step tablets, provided the levonorgestrel tablets for the WHO 97902 new clinical investigation essential to the approval of NDA 21-998. Please see attached documentation.

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 ☒

If yes, explain:

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Name of person completing form: Pamela Lucarelli  
Title: Regulatory Health Project Manager  
Date: June 30, 2009

Name of Office/Division Director signing form: Scott Monroe, M.D.  
Title: Director, Division of Reproductive and Urologic Products

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



Duramed Research Inc.  
One Belmont Avenue  
11<sup>th</sup> Floor  
Bala Cynwyd, PA 19004

July 8, 2009

Scott Monroe, MD  
Director, Division of Reproductive and Urologic Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document and Records Section  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

**NDA 21-998  
Plan B<sup>®</sup> One-Step  
(levonorgestrel) tablets, 1.5 mg**

**Response to Information Request – Exclusivity**

Dear Dr. Monroe:

Reference is made to NDA 21-998 Plan B<sup>®</sup> One-Step (Levonorgestrel Tablet 1.5 mg) filed to the Division of Reproductive and Urologic Drug Products on January 24, 2006 by Duramed Research, regulatory agent for Gedeon Richter, Ltd.; to the June 26, 2009 letter indicating transfer of ownership of the NDA from Gedeon Richter, Ltd. to Duramed Pharmaceuticals, Inc.; and to the request on July 8, 2009 from Pamela Lucarelli, FDA Project Manager to provide additional information to support the exclusivity determination for Plan B<sup>®</sup> One-Step according to 21 CFR §314.108.

The purpose of this submission is to certify that Gedeon Richter, Ltd., the manufacturer of the Plan B One-Step tablets, provided the levonorgestrel tablets for WHO/HRP study 97902, the new clinical investigation essential to the approval of this NDA. This information is documented in the clinical study report for the study submitted in the original NDA, Section 6 Investigators and Study Administrative Structure (page 16 of 116).

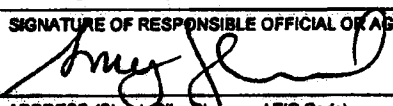
Please contact the undersigned at (610) 747-2731 if you have any questions or comments.

Sincerely,

**Duramed Research, Inc.**

Amy C. Hummel, MS  
Manager, Clinical Regulatory Affairs

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                       |                                                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| <b>DEPARTMENT OF HEALTH AND HUMAN SERVICES</b><br><b>FOOD AND DRUG ADMINISTRATION</b><br><br><b>APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,</b><br><b>OR AN ANTIBIOTIC DRUG FOR HUMAN USE</b><br><i>(Title 21, Code of Federal Regulations, Parts 314 &amp; 601)</i>                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                       | Form Approved: OMB No. 0910-0430<br>Expiration Date: April 30, 2009<br>See OMB Statement on page 2. |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                       | FOR FDA USE ONLY                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                       | APPLICATION NUMBER                                                                                  |
| <b>APPLICANT INFORMATION</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                       |                                                                                                     |
| <b>NAME OF APPLICANT</b><br>Duramed Pharmaceuticals, Inc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <b>DATE OF SUBMISSION</b><br>07/08/2009                                                                                                                                                                               |                                                                                                     |
| <b>TELEPHONE NO. (Include Area Code)</b><br>610-747-2600                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>FACSIMILE (FAX) Number (Include Area Code)</b><br>610-747-2979                                                                                                                                                     |                                                                                                     |
| <b>APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):</b><br>One Belmont Avenue, 11 <sup>th</sup> Floor<br>Bala Cynwyd, PA 19004                                                                                                                                                                                                                                                                                                                                                                           | <b>AUTHORIZED U.S. AGENT NAME &amp; ADDRESS (Number, Street, City, State, ZIP Code, telephone &amp; FAX number) IF APPLICABLE</b><br>Duramed Research Inc.<br>One Belmont Avenue, 11th Floor<br>Bala Cynwyd, PA 19004 |                                                                                                     |
| <b>PRODUCT DESCRIPTION</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                       |                                                                                                     |
| NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) <b>21-998</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                       |                                                                                                     |
| <b>ESTABLISHED NAME (e.g., Proper name, USP/USAN name)</b><br>Levonorgestrel 1.5 mg Tablets                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <b>PROPRIETARY NAME (trade name) IF ANY</b><br>Plan B One-Step                                                                                                                                                        |                                                                                                     |
| <b>CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                       | <b>CODE NAME (if any)</b>                                                                           |
| <b>DOSAGE FORM:</b><br>Tablet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <b>STRENGTHS:</b><br>1.5 mg                                                                                                                                                                                           | <b>ROUTE OF ADMINISTRATION:</b><br>Oral                                                             |
| <b>(PROPOSED) INDICATION(S) FOR USE:</b><br>Emergency Contraceptive                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                       |                                                                                                     |
| <b>APPLICATION DESCRIPTION</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                       |                                                                                                     |
| <b>APPLICATION TYPE (check one)</b> <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                       |                                                                                                     |
| <b>IF AN NDA, IDENTIFY THE APPROPRIATE TYPE</b> <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 505 (b)(2)                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                       |                                                                                                     |
| <b>IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION</b><br>Name of Drug _____ Holder of Approved Application _____                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                       |                                                                                                     |
| <b>TYPE OF SUBMISSION (check one)</b> <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION<br><input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT<br><input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER                                     |                                                                                                                                                                                                                       |                                                                                                     |
| <b>IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION:</b> _____                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                       |                                                                                                     |
| <b>IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY</b> <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                       |                                                                                                     |
| <b>REASON FOR SUBMISSION</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                       |                                                                                                     |
| Response to Request for Information                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                       |                                                                                                     |
| <b>PROPOSED MARKETING STATUS (check one)</b> <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                       |                                                                                                     |
| <b>NUMBER OF VOLUMES SUBMITTED</b> 1 <b>THIS APPLICATION IS</b> <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                       |                                                                                                     |
| <b>ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)</b><br>Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready. |                                                                                                                                                                                                                       |                                                                                                     |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                       |                                                                                                     |
| <b>Cross References (List related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)</b><br>NDA 21-045; DMF 8806                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                       |                                                                                                     |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                          |                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|------------------|
| <b>This application contains the following items: (Check all that apply)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                          |                  |
| <input checked="" type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1. Index                                                                                                                 |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 2. Labeling ( <i>check one</i> ) <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 3. Summary (21 CFR 314.50 (c))                                                                                           |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 4. Chemistry section                                                                                                     |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)                          |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)                                     |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)                                               |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)                             |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)                          |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))                                                                     |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)                                                       |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)                                                 |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)                                                        |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)                                                    |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)                                                         |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))                                     |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))          |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 15. Establishment description (21 CFR Part 600, if applicable)                                                           |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 16. Debarment certification (FD&C Act 306 (k)(1))                                                                        |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 17. Field copy certification (21 CFR 314.50 (l)(3))                                                                      |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 18. User Fee Cover Sheet (Form FDA 3397)                                                                                 |                  |
| <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 19. Financial Information (21 CFR Part 54)                                                                               |                  |
| <input checked="" type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 20. OTHER ( <i>Specify</i> ) Information for exclusivity determination                                                   |                  |
| <b>CERTIFICATION</b><br><p>I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:</p> <ol style="list-style-type: none"> <li>1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.</li> <li>2. Biological establishment standards in 21 CFR Part 600.</li> <li>3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.</li> <li>4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.</li> <li>5. Regulations on making changes in application in FD&amp;C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.</li> <li>6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.</li> <li>7. Local, state and Federal environmental impact laws.</li> </ol> <p>If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.</p> <p>The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.</p> <p>Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.</p> |                                                                                                                          |                  |
| SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                          | DATE:            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                          | 07/08/2009       |
| TYPED NAME AND TITLE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                          | Telephone Number |
| Amy C. Hummel, MS<br>Manager, Clinical Regulatory Affairs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                          | ( 610 ) 747-2600 |
| ADDRESS (Street, City, State, and ZIP Code)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                          |                  |
| One Belmont Ave, 11th Floor, Bala Cynwyd, PA 19004                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                          |                  |
| <p>Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>Department of Health and Human Services<br/>Food and Drug Administration<br/>Center for Drug Evaluation and Research<br/>Central Document Room<br/>5901-B Amundson Road<br/>Belleville, MD 20705-1266</p> </div> <div style="width: 45%;"> <p>Department of Health and Human Services<br/>Food and Drug Administration<br/>Center for Biologics Evaluation and Research (HFM-99)<br/>1401 Rockville Pike<br/>Rockville, MD 20852-1448</p> </div> </div> <p style="text-align: right;">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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                          |                  |



**DEPARTMENT OF HEALTH AND HUMAN SERVICES**  
Food and Drug Administration

**Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with  
Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))**

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

**SPONSOR/APPLICANT/SUBMITTER INFORMATION**

|                                                                                                               |                                                                                                 |
|---------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| 1. NAME OF SPONSOR/APPLICANT/SUBMITTER<br><br>Duramed Pharmaceuticals, Inc.                                   | 2. DATE OF THE APPLICATION/SUBMISSION<br>WHICH THIS CERTIFICATION ACCOMPANIES<br>07/08/2009     |
| 3. ADDRESS (Number, Street, State, and ZIP Code)<br>One Belmont Avenue<br>11th Floor<br>Bala Cynwyd, PA 19004 | 4. TELEPHONE AND FAX NUMBER<br>(Include Area Code)<br>(Tel.) 610-747-2600<br>(Fax) 610-747-2979 |

**PRODUCT INFORMATION**

5. FOR DRUGS/BIOLOGICS: Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s)  
FOR DEVICES: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)  
(Attach extra pages as necessary)

Plan B One-Step

levonorgestrel tablets, 1.5 mg

**APPLICATION/SUBMISSION INFORMATION**

|                                                                                                                                                                                                                                                                                                                                                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 6. TYPE OF APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES<br><br><input type="checkbox"/> IND <input checked="" type="checkbox"/> NDA <input type="checkbox"/> ANDA <input type="checkbox"/> BLA <input type="checkbox"/> PMA <input type="checkbox"/> HDE <input type="checkbox"/> 510(k) <input type="checkbox"/> PDP <input type="checkbox"/> Other |
| 7. INCLUDE IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/OTHER NUMBER (If number previously assigned)<br>21-998                                                                                                                                                                                                                                                               |
| 8. SERIAL NUMBER ASSIGNED TO APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES                                                                                                                                                                                                                                                                            |

**CERTIFICATION STATEMENT/INFORMATION**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 9. CHECK ONLY ONE OF THE FOLLOWING BOXES (See instructions for additional information and explanation)<br><input type="checkbox"/> A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply because the application/submission which this certification accompanies does not reference any clinical trial.<br><input checked="" type="checkbox"/> B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply to any clinical trial referenced in the application/submission which this certification accompanies.<br><input type="checkbox"/> C. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that those requirements have been met. |
| 10. IF YOU CHECKED BOX C, IN NUMBER 9, PROVIDE THE NATIONAL CLINICAL TRIAL (NCT) NUMBER(S) FOR ANY "APPLICABLE CLINICAL TRIAL(S)" UNDER 42 U.S.C. § 282(j)(1)(A)(i), SECTION 402(j)(1)(A)(i) OF THE PUBLIC HEALTH SERVICE ACT, REFERENCED IN THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES (Attach extra pages as necessary)<br><br>NCT Number(s):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |

The undersigned declares, to the best of his/her knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 333, section 301 of the Federal Food, Drug, and Cosmetic Act. WARNING: A willful and knowing false statement is a criminal offense, U.S. Code, title 18, section 1001.

|                                                                                                                                                        |                                                                                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|
| 11. SIGNATURE OF SPONSOR/APPLICANT/SUBMITTER OR AN AUTHORIZED REPRESENTATIVE (Sign)<br><br>                                                            | 12. NAME AND TITLE OF THE PERSON WHO SIGNED IN NO. 11<br><br>(Name) Amy C. Hummel, MS<br><br>(Title) Manager, Clinical Regulatory Affairs |
| 13. ADDRESS (Number, Street, State, and ZIP Code) (of person identified in No. 11 and 12)<br>One Belmont Avenue<br>11th Floor<br>Bala Cynwyd, PA 19004 | 14. TELEPHONE AND FAX NUMBER<br>(Include Area Code)<br>(Tel.) 610-747-2731<br>(Fax) 610-747-2979                                          |
| 15. DATE OF CERTIFICATION<br>07/08/2009                                                                                                                |                                                                                                                                           |

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

/s/

-----  
Scott Monroe  
7/10/2009 03:51:38 PM

**PEDIATRIC PAGE**

**(Complete for all filed original applications and efficacy supplements)**

NDA/BLA#: 21-998

Supplement Number: N/A

NDA Supplement Type (e.g. SE5): N/A

Division Name: Division of  
Reproductive and Urologic Drug  
Products (HFD-580)

PDUFA Goal Date: July 12,  
2009

Stamp Date: January 12, 2009

Proprietary Name: Plan B One-Step

Established/Generic Name: Levonorgestrel 1.5 mg

Dosage Form: Tablets

Applicant/Sponsor: Duramed 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:** Emergency oral contraception

**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)

**IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cdernmhs@fda.hhs.gov](mailto:cdernmhs@fda.hhs.gov)) OR AT 301-796-0700.**

(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 <sup>#</sup>           | Not meaningful therapeutic benefit <sup>*</sup> | Ineffective or unsafe <sup>†</sup> | Formulation failed <sup>Δ</sup> |
| <input type="checkbox"/>            | Neonate | __ wk. __ mo. | __ wk. __ mo.                          | <input type="checkbox"/>            | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input checked="" type="checkbox"/> | Other   | 0 yr. 0 mo.   | 12 yr. 0 mo.                           | <input checked="" 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):

<sup>#</sup> 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): \_\_\_\_\_

<sup>\*</sup> 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

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

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<br>† |
|----------------------------------------------------|---------------|---------------|------------------------------|-----------------------------------------------|-------------------------------------------|--------------------------|------------------------------|
| 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 ([cderpmhs@fda.hhs.gov](mailto:cderpmhs@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.

**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 checked="" type="checkbox"/> | Other                        | 12 yr. 0 mo.  | 16 yr. 11 mo. | <input checked="" 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 ([cderpmts@fda.hhs.gov](mailto:cderpmts@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 attachment sheet for signature page)*

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Regulatory Health Project Manager

(Revised: 6/2008)

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

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

/s/

-----  
Pamela Lucarelli

7/9/2009 01:41:23 PM

## PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-998 Supplement Type (e.g. SE5): \_\_\_\_\_ Supplement Number: \_\_\_\_\_

Stamp Date: January 24, 2006 PDUFA Goal Date: November 24, 2006

HFD 580 Trade and generic names/dosage form: levonorgestrel 1.5 mg tablet

Applicant: Gedeon Richter, Ltd. Therapeutic Class: 5S

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? \*

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

\* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): emergency contraception (Prescription & behind-the-counter)

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: Emergency Contraception

Is this an orphan indication?

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

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: Use of this product before menarche is not indicated.

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 (fill in applicable criteria below):

|     |    |     |     |              |
|-----|----|-----|-----|--------------|
| 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 (fill in applicable criteria below):

|     |    |     |     |              |
|-----|----|-----|-----|--------------|
| 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 (fill in applicable criteria below):

|     |    |     |     |              |
|-----|----|-----|-----|--------------|
| 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.*

NDA 21-998

Page 3

**This page was completed by:**

*{See appended electronic signature page}*

**Nenita Crisostomo, R.N.**  
**Regulatory Health Project Manager**

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

**(Revised: 10/10/2006)**

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

/s/

-----  
Nenita Crisostomo  
11/22/2006 12:21:49 PM

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**LEVONORGESTREL 1.5 mg**  
tablet

---

**Debarment Certification**

Duramed Research, Inc., the regulatory agent representing Gedeon Richter Plc. for the submission of a New Drug Application for Levonorgestrel 1.5 mg Tablets for emergency contraception NDA 21-998, and Gedeon Richter Plc. the manufacturer of the product hereby certifies that the following studies did 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.

\_\_\_\_\_ conducted study #02162 entitled:

*Pilot, Randomized 2-way Cross-Over Comparative Bioavailability Study of Levonorgestrel (Gedeon Richter LTD) 1.5 mg Tablets and Levonorgestrel 0.75 mg (Gedeon Richter LTD) Tablets Administered as 1x 1.5 mg single dose and 1 x 0.75 mg given Twice Daily in Healthy Subjects Under Fasting Conditions.*

b(4)

\_\_\_\_\_ Study #2990 entitled:

*A two-way crossover, open-label, single-dose fasting, Bioequivalence study of levonorgestrel 1 x 1.5 mg Tablet versus Plan B® 2 x 0.75 mg tablets in normal healthy non-smoking female subjects.*

b(4)

\_\_\_\_\_ Study #AA24017-01(sub study c) \_\_\_\_\_ Study #2990  
entitled:

*A two-way crossover, open-label, single-dose fasting, Bioequivalence study of levonorgestrel 1 x 1.5 mg Tablet versus Plan B® 2 x 0.75 mg tablets in normal healthy non-smoking female subjects.*

b(4)

*WHO Study 97902, entitled:*

*A Randomized, Double-Blind, Multi-National Study to compare mifepristone and two regimens of levonorgestrel for emergency contraception.*

  
\_\_\_\_\_  
Joseph A. Carrado, M.Sc., R.Ph.  
Vice-President  
Clinical Regulatory Affairs  
Duramed Research Inc.  
Regulatory Agent for Gedeon Richter Plc.

  
\_\_\_\_\_  
Dr. György Thaler  
Director, Development  
Gedeon Richter Plc.

  
\_\_\_\_\_  
Dr. László Sümeghy  
Manager of Department  
Regulatory Affairs, API Department  
Gedeon Richter Plc.

## ACTION PACKAGE CHECKLIST

| APPLICATION INFORMATION <sup>1</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                               |                                                                                                                                                           |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| NDA # 21-998<br>BLA #                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | NDA Supplement #<br>BLA STN # | If NDA, Efficacy Supplement Type:                                                                                                                         |
| Proprietary Name: Plan B One-Step<br>Established/Proper Name: Levonorgestrel<br>Dosage Form: 1.5 mg Tablet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                               | Applicant: Duramed Pharmaceuticals, Inc.<br>Agent for Applicant (if applicable): Duramed Research, Inc.                                                   |
| RPM: Pamela Lucarelli                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                               | Division: Division of Reproductive and Urologic Products                                                                                                  |
| <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b>NDAs:</b><br/> NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)<br/> Efficacy Supplement:    <input type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> </div> <div style="width: 50%;"> <p><b>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</b><br/> Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p><b>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</b></p> <p><input type="checkbox"/> No changes    <input type="checkbox"/> Updated<br/> Date of check:</p> <p><b>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</b></p> <p><b>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</b></p> </div> </div> |                               |                                                                                                                                                           |
| ❖ User Fee Goal Date<br>Action Goal Date (if different)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                               | July 12, 2009<br>July 10, 2009                                                                                                                            |
| ❖ Actions                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                               |                                                                                                                                                           |
| • Proposed action                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | <input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE<br><input type="checkbox"/> NA <input type="checkbox"/> CR |
| • Previous actions (specify type and date for each action taken)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                               | <input type="checkbox"/> None Approvable –<br>November 22, 2006                                                                                           |
| ❖ Promotional Materials (accelerated approvals only)<br>Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance <a href="http://www.fda.gov/cder/guidance/2197dft.pdf">www.fda.gov/cder/guidance/2197dft.pdf</a> ). If not submitted, explain _____                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                               | <input type="checkbox"/> Received                                                                                                                         |

<sup>1</sup> The Application Information section is (only) a checklist. The Contents of Action Package section (beginning on page 5) lists the documents to be included in the Action Package.

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ❖ Application <sup>2</sup> Characteristics                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                      |
| Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority<br>Chemical classification (new NDAs only):<br><br><div style="display: flex; justify-content: space-between;"> <div> <input type="checkbox"/> Fast Track<br/> <input type="checkbox"/> Rolling Review<br/> <input type="checkbox"/> Orphan drug designation         </div> <div> <input type="checkbox"/> Rx-to-OTC full switch<br/> <input type="checkbox"/> Rx-to-OTC partial switch<br/> <input type="checkbox"/> Direct-to-OTC         </div> </div><br><div style="display: flex; justify-content: space-between;"> <div>           NDAs: Subpart H<br/> <input type="checkbox"/> Accelerated approval (21 CFR 314.510)<br/> <input type="checkbox"/> Restricted distribution (21 CFR 314.520)<br/>           Subpart I<br/> <input type="checkbox"/> Approval based on animal studies<br/> <br/> <input type="checkbox"/> Submitted in response to a PMR<br/> <input type="checkbox"/> Submitted in response to a PMC<br/> <br/>           Comments: _____         </div> <div>           BLAs: Subpart E<br/> <input type="checkbox"/> Accelerated approval (21 CFR 601.41)<br/> <input type="checkbox"/> Restricted distribution (21 CFR 601.42)<br/>           Subpart H<br/> <input type="checkbox"/> Approval based on animal studies         </div> </div> |                                                                                                                                                                                                                      |
| ❖ Date reviewed by PeRC ( <i>required for approvals only</i> )<br>If PeRC review not necessary, explain: _____                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | April 8, 2009                                                                                                                                                                                                        |
| ❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM ( <i>approvals only</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <input type="checkbox"/> Yes, date                                                                                                                                                                                   |
| ❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 ( <i>approvals only</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                             |
| ❖ Public communications ( <i>approvals only</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                      |
| • Office of Executive Programs (OEP) liaison has been notified of action                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                  |
| • Press Office notified of action (by OEP)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                                  |
| • Indicate what types (if any) of information dissemination are anticipated                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <input type="checkbox"/> None<br><input checked="" type="checkbox"/> HHS Press Release<br><input type="checkbox"/> FDA Talk Paper<br><input checked="" type="checkbox"/> CDER Q&As<br><input type="checkbox"/> Other |

All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

| Exclusivity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                              | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes                                                                                       |
| <ul style="list-style-type: none"> <li>NDA and BLA: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? <i>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.</i></li> </ul>                                                                                                                                                                                             | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes<br>If, yes, NDA/BLA # _____ and date exclusivity expires: _____                       |
| <ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>                                                                                                                                                                                                                                                        | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date exclusivity expires: _____                                       |
| <ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>                                                                                                                                                                                                                                                        | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date exclusivity expires: _____                                       |
| <ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>                                                                                                                                                                                                                                             | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date exclusivity expires: _____                                       |
| <ul style="list-style-type: none"> <li>NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>                                                                                                                                                                                                                                        | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date 10-year limitation expires: _____                                |
| ❖ Patent Information (NDAs only)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                           |
| <ul style="list-style-type: none"> <li>Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.</li> </ul>                                                                                                                                                                                                                                                                                                            | <input checked="" type="checkbox"/> Verified<br><input type="checkbox"/> Not applicable because drug is an old antibiotic.                                |
| <ul style="list-style-type: none"> <li>Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.</li> </ul>                                                                                                                                                                                                                                                                                             | 21 CFR 314.50(i)(1)(i)(A)<br><input type="checkbox"/> Verified<br><br>21 CFR 314.50(i)(1)<br><input type="checkbox"/> (ii) <input type="checkbox"/> (iii) |
| <ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).</li> </ul>                                                                                                                                                                                                                                             | <input type="checkbox"/> No paragraph III certification<br>Date patent will expire _____                                                                  |
| <ul style="list-style-type: none"> <li>[505(b)(2) applications] For each <b>paragraph IV</b> certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (Summary Reviews)).</i></li> </ul> | <input type="checkbox"/> N/A (no paragraph IV certification)<br><input type="checkbox"/> Verified                                                         |

- [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for each paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

☐ Yes ☐ No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

*If "Yes," skip to question (4) below. If "No," continue with question (2).*

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, 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 the rest of the patent questions.*

*If "No," continue with question (3).*

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

☐ Yes ☐ No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) 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 section below (Summary Reviews).*

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

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) 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).</p> <p><i>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 section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p> | <input type="checkbox"/> Yes <input type="checkbox"/> No                                                                                                                                  |
| <b>CONTENTS OF ACTION PACKAGE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                           |
| Copy of this Action Package Checklist <sup>3</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Included                                                                                                                                                                                  |
| <b>Officer/Employee List</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                           |
| ❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list ( <i>approvals only</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <input checked="" type="checkbox"/> Included                                                                                                                                              |
| Documentation of consent/non-consent by officers/employees                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <input checked="" type="checkbox"/> Included                                                                                                                                              |
| <b>Action Letters</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                           |
| ❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Action(s) and date(s)<br>Approvable – November 22, 2006<br>Approved – July 10, 2009                                                                                                       |
| <b>Labeling</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                           |
| ❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                           |
| • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Included                                                                                                                                                                                  |
| • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Included                                                                                                                                                                                  |
| • Original applicant-proposed labeling                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Included                                                                                                                                                                                  |
| • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | N/A                                                                                                                                                                                       |
| ❖ Medication Guide/Patient Package Insert/Instructions for Use ( <i>write submission/communication date at upper right of first page of each piece</i> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <input type="checkbox"/> Medication Guide<br><input type="checkbox"/> Patient Package Insert<br><input type="checkbox"/> Instructions for Use<br><input checked="" type="checkbox"/> None |

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.  
Version: 9/5/08

|                                                                                                                                                   |                                                                                                                                                                                                                                                           |
|---------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)                                        |                                                                                                                                                                                                                                                           |
| • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)                              |                                                                                                                                                                                                                                                           |
| • Original applicant-proposed labeling                                                                                                            |                                                                                                                                                                                                                                                           |
| • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable                                                           |                                                                                                                                                                                                                                                           |
| ❖ Labels (full color carton and immediate-container labels) (write submission/communication date at upper right of first page of each submission) |                                                                                                                                                                                                                                                           |
| • Most-recent division proposal for (only if generated after latest applicant submission)                                                         | Included                                                                                                                                                                                                                                                  |
| • Most recent applicant-proposed labeling                                                                                                         | Included                                                                                                                                                                                                                                                  |
| ❖ Labeling reviews (indicate dates of reviews and meetings)                                                                                       | <input type="checkbox"/> RPM<br><input checked="" type="checkbox"/> DMEDP<br><input type="checkbox"/> DRISK<br><input checked="" type="checkbox"/> DDMAC<br><input type="checkbox"/> CSS<br><input checked="" type="checkbox"/> Other reviews OTC Reviews |
| ❖ Proprietary Name                                                                                                                                |                                                                                                                                                                                                                                                           |
| • Review(s) (indicate date(s))                                                                                                                    | Included – May 1, 2009 and June 24, 2009                                                                                                                                                                                                                  |
| • Acceptability/non-acceptability letter(s) (indicate date(s))                                                                                    | Included – May 13, 2009                                                                                                                                                                                                                                   |

### Administrative / Regulatory Documents

|                                                                                                                                                                                                                            |                                                                       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| ❖ Administrative Reviews (e.g., RPM Filing Review <sup>4</sup> /Memo of Filing Meeting) (indicate date of each review)                                                                                                     | RPM Filing Review Included – November 22, 2006                        |
| ❖ NDAs only: Exclusivity Summary (signed by Division Director)                                                                                                                                                             | <input checked="" type="checkbox"/> Included                          |
| ❖ Application Integrity Policy (AIP) Status and Related Documents<br><a href="http://www.fda.gov/ora/compliance_ref/aip_page.html">www.fda.gov/ora/compliance_ref/aip_page.html</a>                                        |                                                                       |
| • Applicant in on the AIP                                                                                                                                                                                                  | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| • This application is on the AIP                                                                                                                                                                                           | <input type="checkbox"/> Yes <input type="checkbox"/> No              |
| • If yes, Center Director's Exception for Review memo (indicate date)                                                                                                                                                      |                                                                       |
| • If yes, OC clearance for approval (indicate date of clearance communication)                                                                                                                                             | <input type="checkbox"/> Not an AP action                             |
| ❖ Pediatric Page (approvals only, must be reviewed by PERC before finalized)                                                                                                                                               | <input checked="" type="checkbox"/> Included                          |
| ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (include certification) | <input checked="" type="checkbox"/> Verified, statement is acceptable |
| ❖ Postmarketing Requirement (PMR) Studies                                                                                                                                                                                  | <input checked="" type="checkbox"/> None                              |
| • Outgoing communications (if located elsewhere in package, state where located)                                                                                                                                           |                                                                       |
| • Incoming submissions/communications                                                                                                                                                                                      |                                                                       |
| ❖ Postmarketing Commitment (PMC) Studies                                                                                                                                                                                   | <input checked="" type="checkbox"/> None                              |
| • Outgoing Agency request for postmarketing commitments (if located elsewhere in package, state where located)                                                                                                             |                                                                       |

<sup>4</sup> Filing reviews for other disciplines should be filed behind the discipline tab.

|                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| • Incoming submission documenting commitment                                                                                                                                                                                                                                                                                                                                       |                                                       |
| ❖ Outgoing communications ( <i>letters (except previous action letters), emails, faxes, telecons</i> )                                                                                                                                                                                                                                                                             | Included                                              |
| ❖ Internal memoranda, telecons, etc.                                                                                                                                                                                                                                                                                                                                               |                                                       |
| ❖ Minutes of Meetings                                                                                                                                                                                                                                                                                                                                                              |                                                       |
| • PeRC ( <i>indicate date; approvals only</i> )                                                                                                                                                                                                                                                                                                                                    | <input type="checkbox"/> Not applicable April 8, 2009 |
| • Pre-Approval Safety Conference ( <i>indicate date; approvals only</i> )                                                                                                                                                                                                                                                                                                          | <input checked="" type="checkbox"/> Not applicable    |
| • Regulatory Briefing ( <i>indicate date</i> )                                                                                                                                                                                                                                                                                                                                     | <input checked="" type="checkbox"/> No mtg            |
| • Pre-NDA/BLA meeting ( <i>indicate date</i> )                                                                                                                                                                                                                                                                                                                                     | <input type="checkbox"/> No mtg January 13, 2006      |
| • EOP2 meeting ( <i>indicate date</i> )                                                                                                                                                                                                                                                                                                                                            | <input checked="" type="checkbox"/> No mtg            |
| • Other (e.g., EOP2a, CMC pilot programs)                                                                                                                                                                                                                                                                                                                                          |                                                       |
| ❖ Advisory Committee Meeting(s)                                                                                                                                                                                                                                                                                                                                                    | <input checked="" type="checkbox"/> No AC meeting     |
| • Date(s) of Meeting(s)                                                                                                                                                                                                                                                                                                                                                            |                                                       |
| • 48-hour alert or minutes, if available                                                                                                                                                                                                                                                                                                                                           |                                                       |
| <b>Decisional and Summary Memos</b>                                                                                                                                                                                                                                                                                                                                                |                                                       |
| ❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                                         | <input checked="" type="checkbox"/> None              |
| Division Director Summary Review ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                                          | <input type="checkbox"/> None July 10, 2009           |
| Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                                       | <input type="checkbox"/> None July 8, 2009            |
| <b>Clinical Information<sup>5</sup></b>                                                                                                                                                                                                                                                                                                                                            |                                                       |
| ❖ Clinical Reviews                                                                                                                                                                                                                                                                                                                                                                 |                                                       |
| • Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                                          | July 8, 2009                                          |
| • Clinical review(s) ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                                                      | July 9, 2009                                          |
| • Social scientist review(s) (if OTC drug) ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                                | <input checked="" type="checkbox"/> None              |
| ❖ Safety update review(s) ( <i>indicate location/date if incorporated into another review</i> )                                                                                                                                                                                                                                                                                    | Included                                              |
| ❖ Financial Disclosure reviews(s) or location/date if addressed in another review<br>OR<br>If no financial disclosure information was required, review/memo explaining why not                                                                                                                                                                                                     | Included in Clinical Review                           |
| ❖ Clinical reviews from other clinical areas/divisions/Centers ( <i>indicate date of each review</i> )                                                                                                                                                                                                                                                                             | <input checked="" type="checkbox"/> None              |
| ❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )                                                                                                                                                                                                                                                                       | <input checked="" type="checkbox"/> Not needed        |
| ❖ Risk Management <ul style="list-style-type: none"> <li>• Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)</li> <li>• REMS Memo (<i>indicate date</i>)</li> <li>• REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>)</li> </ul> | <input checked="" type="checkbox"/> None              |
| ❖ DSI Clinical Inspection Review Summary(ies) ( <i>include copies of DSI letters to investigators</i> )                                                                                                                                                                                                                                                                            | <input checked="" type="checkbox"/> None requested    |
| <b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None                                                                                                                                                                                                                                                                                                              |                                                       |
| Clinical Microbiology Team Leader Review(s) ( <i>indicate date for each review</i> )                                                                                                                                                                                                                                                                                               | <input type="checkbox"/> None                         |

<sup>5</sup> Filing reviews should be filed with the discipline reviews.

|                                                                                                                                                                          |                                                                                       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| Clinical Microbiology Review(s) (indicate date for each review)                                                                                                          | <input type="checkbox"/> None                                                         |
| <b>Biostatistics</b> <input type="checkbox"/> None                                                                                                                       |                                                                                       |
| ❖ Statistical Division Director Review(s) (indicate date for each review)                                                                                                | <input checked="" type="checkbox"/> None                                              |
| Statistical Team Leader Review(s) (indicate date for each review)                                                                                                        | <input checked="" type="checkbox"/> None                                              |
| Statistical Review(s) (indicate date for each review)                                                                                                                    | <input type="checkbox"/> None September 26, 2006, November 21, 2006 and June 16, 2009 |
| <b>Clinical Pharmacology</b> <input type="checkbox"/> None                                                                                                               |                                                                                       |
| ❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)                                                                                      | <input checked="" type="checkbox"/> None                                              |
| Clinical Pharmacology Team Leader Review(s) (indicate date for each review)                                                                                              | <input checked="" type="checkbox"/> None                                              |
| Clinical Pharmacology review(s) (indicate date for each review)                                                                                                          | <input type="checkbox"/> None October 23, 2006 and June 22, 2009                      |
| ❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)                                                                                    | <input checked="" type="checkbox"/> None                                              |
| <b>Nonclinical</b> <input type="checkbox"/> None                                                                                                                         |                                                                                       |
| ❖ Pharmacology/Toxicology Discipline Reviews                                                                                                                             |                                                                                       |
| • ADP/T Review(s) (indicate date for each review)                                                                                                                        | <input checked="" type="checkbox"/> None                                              |
| • Supervisory Review(s) (indicate date for each review)                                                                                                                  | <input checked="" type="checkbox"/> None                                              |
| • Pharm/tox review(s), including referenced IND reviews (indicate date for each review)                                                                                  | <input type="checkbox"/> None September 21, 2006 and April 22, 2009                   |
| Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)                                                               | <input checked="" type="checkbox"/> None                                              |
| ❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)                                                                                       | <input checked="" type="checkbox"/> No carc                                           |
| ❖ ECAC/CAC report/memo of meeting                                                                                                                                        | <input checked="" type="checkbox"/> None<br>Included in P/T review, page              |
| ❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)                                                                                              | <input checked="" type="checkbox"/> None requested                                    |
| <b>CMC/Quality</b> <input type="checkbox"/> None                                                                                                                         |                                                                                       |
| ❖ CMC/Quality Discipline Reviews                                                                                                                                         |                                                                                       |
| • ONDQA/OBP Division Director Review(s) (indicate date for each review)                                                                                                  | <input checked="" type="checkbox"/> None                                              |
| • Branch Chief/Team Leader Review(s) (indicate date for each review)                                                                                                     | <input checked="" type="checkbox"/> None                                              |
| • CMC/product quality review(s) (indicate date for each review)                                                                                                          | <input type="checkbox"/> None November 14, 2006 and June 16, 2009                     |
| • BLAs only: Facility information review(s) (indicate dates)                                                                                                             | <input type="checkbox"/> None                                                         |
| ❖ Microbiology Reviews                                                                                                                                                   |                                                                                       |
| • NDAs: Microbiology reviews (sterility & pyrogenicity) (indicate date of each review)                                                                                   | <input checked="" type="checkbox"/> Not needed                                        |
| • BLAs: Sterility assurance, product quality microbiology (indicate date of each review)                                                                                 |                                                                                       |
| ❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)                                                        | <input checked="" type="checkbox"/> None                                              |
| ❖ Environmental Assessment (check one) (original and supplemental applications)                                                                                          | Included in Clinical Review                                                           |
| <input type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population) |                                                                                       |

|                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                        |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input type="checkbox"/> Review & FONSI ( <i>indicate date of review</i> )                                                                                                                                                                                                                         |                                                                                                                                                                                                                                        |
| <input type="checkbox"/> Review & Environmental Impact Statement ( <i>indicate date of each review</i> )                                                                                                                                                                                           |                                                                                                                                                                                                                                        |
| ❖ NDAs: Methods Validation                                                                                                                                                                                                                                                                         | <input type="checkbox"/> Completed<br><input type="checkbox"/> Requested<br><input type="checkbox"/> Not yet requested<br><input checked="" type="checkbox"/> Not needed                                                               |
| ❖ Facilities Review/Inspection                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                        |
| <ul style="list-style-type: none"> <li>• NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>)</li> </ul>                                                                                                                              | Date completed:<br>February 10, 2009<br><input checked="" type="checkbox"/> Acceptable<br><input type="checkbox"/> Withhold recommendation                                                                                             |
| <ul style="list-style-type: none"> <li>• BLAs: <ul style="list-style-type: none"> <li>○ TBP-EER</li> <li>○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (<i>date completed must be within 60 days prior to AP</i>)</li> </ul> </li> </ul> | Date completed:<br><input type="checkbox"/> Acceptable<br><input type="checkbox"/> Withhold recommendation<br>Date completed:<br><input type="checkbox"/> Requested<br><input type="checkbox"/> Accepted <input type="checkbox"/> Hold |

## Appendix A to Action Package Checklist

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

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) Or it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) Or 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.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) And no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) And all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) Or the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) Or the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

**MEMORANDUM**

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

**DATE:** July 9, 2009

**TO:** Division of Reproductive and Urologic Products  
Attention: Pamela Lucarelli

**FROM:** Pediatric and Maternal Health  
George Greeley

**SUBJECT:** **PeRC PREA Subcommittee Decision**  
NDA 21-998, Plan B One-Step

The following e-mail correspondence is the result of the PeRC PREA Subcommittee review of Plan B One-Step. The committee met on April 8, 2009 and granted a partial wavier for pre-menarcheal patients.

**Lucarelli, Pamela K**

---

**From:** Greeley, George  
**Sent:** Thursday, July 09, 2009 11:49 AM  
**To:** Lucarelli, Pamela K  
**Cc:** Mathis, Lisa; Stowe, Ginneh D.; Christl, Leah A; Addy, Rosemary  
**Subject:** NDA 21-998 Plan B ————— **b(4)**

**Importance:** High

**Follow Up Flag:** Follow up  
**Flag Status:** Purple

Hi Pamela,

The Plan B — (levonorgestrel 1.5 mg) partial waiver and extrapolation application was reviewed by the PeRC PREA Subcommittee on April 08, 2009. The Division recommended a partial waiver for pre-menarcheal patients because pre-menarcheal patients are not at risk of becoming pregnant and the use of this product before menarche is not indicated. The Division also noted that the pediatric study requirement for post-menarcheal pediatric patients by the extrapolation of adult data. The PeRC agreed with the Division. **b(4)**

In addition, the PeRC has asked that the pediatric page be modified at Sections B (Partially Waived Studies) and F (Extrapolation from Other Adult and/or Pediatric Studies) to include an approximate age range for both pre and post-menarcheal pediatric patients. Also the box should be checked to indicate the ages ranges for each are based on Tanner Stage.

Thank you.

George Greeley  
Regulatory Health Project Manager  
Pediatric and Maternal Health Staff  
Office of New Drugs  
FDA/CDER  
10903 New Hampshire Ave.  
Bldg #22, Room 6467  
Silver Spring, MD 20993-0002  
301.796.4025

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this page is the manifestation of the electronic signature.**

/s/

-----  
Pamela Lucarelli  
7/9/2009 12:23:24 PM  
CSO

## Christl, Leah A

---

**From:** Christl, Leah A  
**Sent:** Wednesday, July 08, 2009 10:18 AM  
**To:** 'Hummel, Amy'; 'Walsh, Michele'  
**Subject:** RE: Label Comments Plan B and Plan B One-Step

**Attachments:** IDS Labeling Comments7\_8\_09.doc

Please see attached for small clarification on the labeling comments regarding the statement about use as regular birth control.

Leah



IDS Labeling  
Comments7\_8\_09.doc

Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products

[Leah.Christl@fda.hhs.gov](mailto:Leah.Christl@fda.hhs.gov)

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Submissions:

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---

**From:** Christl, Leah A  
**Sent:** Wednesday, July 08, 2009 8:59 AM  
**To:** 'Hummel, Amy'; Walsh, Michele  
**Subject:** FW: Label Comments Plan B and Plan B One-Step

The reviewers are still looking at the CIL, but I wanted to get this to you ASAP. These comments are in addition to the comments that I sent yesterday regarding removing the '—' language and grouping "72" with "hours"

b(4)

Leah

Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products

[Leah.Christl@fda.hhs.gov](mailto:Leah.Christl@fda.hhs.gov)

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<< File: IDS Labeling Comments7\_8\_09.doc >>

**Labeling Comments July 8, 2009**

**Plan B**

**PDP**

1. Where the two tablets are shown, put a space between 3 and days (i.e., 3 days).

**Blister**

1. Revise the statement ' \_\_\_\_\_ ' to read "Not for regular birth control". **b(4)**

**Drug Facts**

**Under Directions:**

1. Second bulleted statement: put a period at the end of the statement that starts "The sooner you take the first tablet...".
2. Remove the period from the end of the fourth bulleted statement about vomiting.
3. Send us the "font specifications" for the "Drug Facts" labeling.

**Plan B One-Step**

**Carton**

**Blister**

1. Revise the statement ' \_\_\_\_\_ ' to read "Not for regular birth control". **b(4)**

**Drug Facts**

**Under Directions:**

1. Remove the period from the end of the third bulleted statement about vomiting.

**Christl, Leah A**

**From:** Christl, Leah A  
**Sent:** Tuesday, July 07, 2009 4:39 PM  
**To:** Walsh, Michele; Hummel, Amy  
**Subject:** FW: July 7, 2009 Plan B One-Step Labeling Components and CARE Program

Please see comment below...

Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products

Leah.Christl@fda.hhs.gov  
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One minor issue - the "ie" on the PDP in the left lower corner. We asked for "i.e." and the sponsor gave us "ie." On reflection, neither Latin abbreviation is consumer friendly. I have mentioned it to Andrea and we both agree that it could be deleted. It also appears on the Plan B carton.

Could we have the sponsor delete the "ie" from the left lower corner of the PDP for both products?

I have no other comments for Plan B One-Step.

**From:** Hummel, Amy [mailto:Amy.Hummel@barrlabs.com]  
**Sent:** Tuesday, July 07, 2009 3:25 PM  
**To:** Lucarelli, Pamela K; Christl, Leah A; Furness, Melissa  
**Cc:** Walsh, Michele; Reape, Kathleen; Niemann, Amy; Porzio, Andrea; Spinelli, Leah Ann; Forbes, Jack  
**Subject:** July 7, 2009 Plan B One-Step Labeling Components and CARE Program

Hi Pam, Leah, and Melissa,

Attached to this email are the latest versions (dated today, July 7, 2009) of the Plan B One-Step labeling components and CARE program document.

Leah/Melissa: the cartons (trade and \_\_\_\_\_ and CIL were modified incorporating the comments received yesterday (7/6/09).

b(4)

7/9/2009

. am: The PI was modified from the version sent earlier today as follows: TOC merged onto page 1 with the highlights and formatted double-column, footers changed to remove "DRAFT" and include today's date, and the company phone number in the Highlights/Adverse Events section was corrected. The CARE document footer was also changed to today's date and to remove "Draft", and minor changes for grammar and clarity.

The CARE program document will be submitted formally to NDA 21-998 today.

**Attachments:**

Plan B One-Step Duramed label  
Plan B One-Step CARE Program  
Plan B One-Step Trade Carton  
Plan B One-Step  Carton  
Plan B One-Step CIL

**b(4)**

**Amy C. Hummel, MS**

Manager, Clinical Regulatory Affairs  
Teva Women's Health Research, Inc.  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004  
(P) 610-747-2731  
(F) 610-747-6695  
(E) amy.hummel@barriabs.com  
(M) 201-783-4115

7/9/2009

**Christl, Leah A**

**From:** Christl, Leah A  
**Sent:** Tuesday, July 07, 2009 4:17 PM  
**To:** 'Hummel, Amy'  
**Cc:** Walsh, Michele; Reape, Kathleen; Niemann, Amy; Porzio, Andrea; Spinelli, Leah Ann; Forbes, Jack  
**Subject:** RE: July 7, 2009 Plan B Labeling Components and CARE Program

For the carton labels, we need you to send us the "font specifications" for the "Drug Facts" labeling for both cartons, as you have done for Plan B One-Step.

Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
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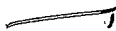
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---

**From:** Hummel, Amy [mailto:Amy.Hummel@barriabs.com]  
**Sent:** Tuesday, July 07, 2009 3:25 PM  
**To:** Lucarelli, Pamela K; Christl, Leah A; Furness, Melissa  
**Cc:** Walsh, Michele; Reape, Kathleen; Niemann, Amy; Porzio, Andrea; Spinelli, Leah Ann; Forbes, Jack  
**Subject:** July 7, 2009 Plan B Labeling Components and CARE Program

Hi Pam, Leah, and Melissa,

Attached to this email are the latest versions (dated today, July 7, 2009) of the Plan B labeling components and CARE program document.

Leah/Melissa: the cartons (trade and ) and CIL were modified incorporating the comments received yesterday (7/6/09).

Pam: The PI was modified from the version sent earlier today as follows: footers added today's date, and tables center-justified. The CARE document footer was also changed to today's date and to remove "Draft", and minor changes for grammar and clarity.

The CARE program document will be submitted formally to NDA 21-045 today.

Attachments:  
Plan B Duramed label  
Plan B CARE Program  
Plan B Trade Carton  
Plan B  Carton  
Plan B CIL

b(4)

b(4)

7/9/2009

**Amy C. Hummel, MS**

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(E) amy.hummel@barrlabs.com  
(M) 201-783-4115

**Christl, Leah A**

**From:** Christl, Leah A  
**Sent:** Tuesday, July 07, 2009 4:58 PM  
**To:** 'Hummel, Amy'  
**Cc:** Walsh, Michele; Reape, Kathleen; Niemann, Amy; Porzio, Andrea; Spinelli, Leah Ann; Forbes, Jack  
**Subject:** RE: July 7, 2009 Plan B Labeling Components and CARE Program

On the right hand side of the trade and ~~cartons'~~ PDP of Plan B, it says, "  
\_\_\_\_\_  
\_\_\_\_\_, should be switched to read "...within 72 hours (3 days) after..."

b(4)

**Leah Christl, Ph.D.**  
Associate Director for Regulatory Affairs  
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**From:** Hummel, Amy [mailto:Amy.Hummel@barrlabs.com]  
**Sent:** Tuesday, July 07, 2009 3:25 PM  
**To:** Lucarelli, Pamela K; Christi, Leah A; Furness, Melissa  
**Cc:** Walsh, Michele; Reape, Kathleen; Niemann, Amy; Porzio, Andrea; Spinelli, Leah Ann; Forbes, Jack  
**Subject:** July 7, 2009 Plan B Labeling Components and CARE Program

**Hi Pam, Leah, and Melissa,**

Attached to this email are the latest versions (dated today, July 7, 2009) of the **Plan B** labeling components and CARE program document.

**Leah/Melissa: the cartons (trade and ~~\_\_\_\_\_~~ and CIL were modified incorporating the comments received yesterday (7/6/09).**

b(4)

**Pam: The PI was modified from the version sent earlier today as follows: footers added today's date, and tables center-justified. The CARE document footer was also changed to today's date and to remove "Draft", and minor changes for grammar and clarity.**

**The CARE program document will be submitted formally to NDA 21-045 today.**

**Attachments:**  
 Plan B Duramed label  
 Plan B CARE Program  
 Plan B Trade Carton  
 Plan B \_\_\_\_\_

**7/9/2009**

an B CIL

**Amy C. Hummel, MS**

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(F) 610-747-6695  
(E) amy.hummel@barrlabs.com  
(M) 201-783-4115

7/9/2009

**Christl, Leah A**

---

**From:** Christl, Leah A  
**Sent:** Tuesday, July 07, 2009 9:41 AM  
**To:** 'Walsh, Michele'  
**Cc:** Hummel, Amy; Porzio, Andrea  
**Subject:** RE: NDA 21-998 and NDA 21-045 Labeling Comments

Michele,

The response from the division is as follows:

Please let Duramed know that we feel vomiting should be in the warnings. It is on the Plan B label and, although the clinical trial for Plan B One-Step did not demonstrate vomiting, we think that it can occur from Plan B One-Step, such that the labeling includes the statement about what to do if it does occur. It makes no sense to have instructions about what to do if vomiting occurs without stating it as a potential AE in warnings.

Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products

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---

**From:** Walsh, Michele [<mailto:Michele.Walsh@barrlabs.com>]  
**Sent:** Monday, July 06, 2009 5:22 PM  
**To:** Furness, Melissa; Christl, Leah A  
**Cc:** Hummel, Amy; Porzio, Andrea  
**Subject:** RE: NDA 21-998 and NDA 21-045 Labeling Comments  
**Importance:** High

Hi Melissa and Leah,

We are working on getting all these changes into the Plan B and Plan B One-Step Cartons and CILs and hope to get them back to you tomorrow.

.now the presentation of the company name is confusing, but the different versions are correct as stated.

7/9/2009

There is **one issue** on the AE list for Plan B One-Step (see the red text below). According to the clinical trial conducted in support of the NDA and the latest version of the PI reviewed by DRUP, "...The most common adverse reactions ( $\geq 10\%$ ) in clinical trials were heavier menstrual bleeding (31%), nausea (14%), lower abdominal pain (13%), fatigue (13%), headache, (10%), and dizziness (10%).

---

I have attached the latest version of the PI for your reference.

b(4)

If there are any further comments, please let me know ASAP.

thanks,  
Michele

Michele G. Walsh  
Director, Clinical Regulatory Affairs  
Duramed Research Inc.  
One Belmont Ave, 11th Floor  
Bala Cynwyd, PA 19004

direct: 610-747-2644  
main: 610-747-2600  
fax: 610-747-6640  
e-mail: Michele.Walsh@barlabs.com

---

From: Furness, Melissa [mailto:Melissa.Furness@fda.hhs.gov]  
Sent: Monday, July 06, 2009 4:00 PM  
To: Walsh, Michele  
Cc: Christl, Leah A  
Subject: NDA 21-998 and NDA 21-045 Labeling Comments

Hi Michelle,

Please find below the following labeling comments regarding the OTC labeling components for NDA 21-998 (Plan B One-Step) and NDA 21-045 (Plan B).

**General comment:** Please ensure that all words are spelled out fully and that contractions are not used in any of the OTC labeling components.

**I. Carton label (For both Products)**

**a. Principal Display Panel**

**i. For Plan B:**

1. Revise the first statement located where Tablet 1 and Tablet 2 are shown to read as follows: "Take the first tablet as soon as possible within 72 hours (3 days) after unprotected sex."
2. At the bottom left corner of the PDP, revise the statements to read "Reduces the chance of pregnancy after unprotected sex — if a regular birth control method fails or after sex without birth control). Not for regular birth control."

b(4)

7/9/2009

ii. For **Plan B One-Step**:

1. Revise the first statement located where it states One Tablet One Dose to read as follows: "[bullet]Take as soon as possible within 72 hours (3 days) after unprotected sex.....".
2. At the bottom left corner of the PDP, revise the statements to read "Reduces the chance of pregnancy after unprotected sex (i.e., if a regular birth control method fails or after sex without birth control). Not for regular birth control."
3. Above the brand name, revise the NEW! product statement to read "NEW! Now only ONE dose"

b. Blister Cards (inner panels)

i. For **Plan B**

1. Move the bullet and the word "\_\_\_\_\_ associated with Plan B Step One to be part of the sentence below it which reads " \_\_\_\_\_

b(4)

c. Other panels:

i. General comments

1. Please revise again the "name and place of business" to reflect the appropriate corporate structure. We are confused about who you are. We are and still are Duramed Pharamceuticals.
2. For **Plan B One-Step** the carton reads "Duramed Pharmaceuticals, Inc. Subsidiary of Barr Pharmaceuticals, Inc". Is this correct? YES
3. For **Plan B**, the carton reads "Mfg by Gedeon Richter Budapest, Hungary for Duramed Pharmaceuticals, Inc. Subsidiary of Barr Pharmaceuticals, Inc." Is this correct? YES - an agreement with Gedeon Richter for the Plan B application
4. For **Plan B**, ensure that the strength of the tablet is included as part of the statement of identity. ok

d. Drug Facts

i. For **Plan B**:

1. Under **When using this product**, delete the adverse event \_\_\_\_\_ b(4)
2. Under **Directions**:
  - a. Revise the second bullet to read: "take the first tablet as soon as possible within 72 hours (3 days) after unprotected sex. The sooner you take the first tablet, the better it will work."
  - b. Revise the third bullet to read "take the second tablet 12 hours after you take the first tablet"
  - c. Revise the fourth bulleted statement to read "if you vomit within 2 hours of taking the medication, call a healthcare professional to find out if you should repeat that dose"

3. Under Other information:

- a. Unbold the third bulleted statements
- b. Delete the last sentence: \_\_\_\_\_

b(4)

ii. For Plan B One Step:

1. Under When using this product, add the adverse event "vomiting".

**II. Consumer Information Leaflet (CIL)**

1. Avoid using contractions in the text of the CIL. For example, on page 2 of the One-Step CIL is the word ~~—~~  
On page 3 of the One-Step CIL are the words you're and won't. Check all pages for contractions, and check the Plan B CIL as well.
2. On the cover of the CILs for both Plan B and Plan B One-Step, do the statements "From the makers of Plan B Duramed Pharmaceuticals, Inc., a subsidiary of Barr Pharmaceuticals, Inc." reflect the correct company structure? Also, on the Plan B CIL cover the company structure statement starts "From the makers of Plan B. Duramed Pharmaceuticals, Inc., ....." whereas on the One-Step CIL there is a comma after "From the makers of Plan B." Either use a comma or a period but be consistent.
3. Page 12 of the One-Step CIL, eliminate the second sentence "\_\_\_\_\_  
\_\_\_\_\_ It is repeated twice. Likewise, delete the second sentence from page 12 of the Plan B CIL which reads: \_\_\_\_\_ It is repeated twice.
4. Page 14, 16 and 24 of the One-Step CIL, add "vomiting" as one of the side effects. To page 14 16 and 24 of the Plan B CIL, delete "\_\_\_\_\_ as a side effect.
5. Page 20 of the One-Step CIL, revise the second paragraph to read as follows: "Remember, Plan B One-Step is only for emergency pregnancy prevention. There are many other products that work for regular birth control that are available by prescription and over-the-counter." Revise the second paragraph on page 20 of the Plan B CIL in the same way to be consistent between products.

b(4)

b(4)

b(4)

Please let me know if you have any questions.

Best regards,

Melissa

Melissa Hancock Furness  
Chief, Project Management Staff  
FDA/CDER/OND/ONP/DNCE

phone: 301-796-0893

e-mail: [Melissa.Furness@fda.hhs.gov](mailto:Melissa.Furness@fda.hhs.gov)

---

From: Walsh, Michele [<mailto:Michele.Walsh@barriabs.com>]  
Sent: Monday, July 06, 2009 3:09 PM

7/9/2009

>: Christl, Leah A; Lucarelli, Pamela K; Hummel, Amy; Furness, Melissa  
**Subject:** RE: just checking in.....

Hi Melissa, do you have an estimate time on when we can expect the OTC comments?

-Michele

---

**From:** Christl, Leah A [mailto:Leah.Christl@fda.hhs.gov]  
**Sent:** Monday, July 06, 2009 1:17 PM  
**To:** Walsh, Michele; Lucarelli, Pamela K; Hummel, Amy; Furness, Melissa  
**Subject:** Re: just checking in.....

There will be some OTC labeling comments coming soon. Melissa will be sending them since I am out of the office still.

Leah

---

Message sent from my BlackBerry Wireless Handheld. Please excuse any typos.

---

**From:** Walsh, Michele <Michele.Walsh@barriabs.com>  
**To:** Lucarelli, Pamela K; Christl, Leah A  
**Sent:** Mon Jul 06 11:00:19 2009  
**Subject:** just checking in.....

Hello Ladies,

Happy Plan B PDUFA week! Just checking in to see if there are any comments on the pieces received last week.

7/9/2009

**Christl, Leah A**

**From:** Furness, Melissa  
**Sent:** Monday, July 06, 2009 4:00 PM  
**To:** 'Walsh, Michele'  
**Cc:** Christl, Leah A  
**Subject:** NDA 21-998 and NDA 21-045 Labeling Comments

Hi Michelle,

Please find below the following labeling comments regarding the OTC labeling components for NDA 21-998 (Plan B One-Step) and NDA 21-045 (Plan B).

**General comment:** Please ensure that all words are spelled out fully and that contractions are not used in any of the OTC labeling components.

**I. Carton label (For both Products)**

**a. Principal Display Panel**

**i. For Plan B:**

1. Revise the first statement located where Tablet 1 and Tablet 2 are shown to read as follows: "Take the first tablet as soon as possible within 72 hours (3 days) after unprotected sex.
2. At the bottom left corner of the PDP, revise the statements to read "Reduces the chance of pregnancy after unprotected sex (i.e., if a regular birth control method fails or after sex without birth control). Not for regular birth control."

**ii. For Plan B One-Step:**

1. Revise the first statement located where it states One Tablet One Dose to read as follows: "[bullet]Take as soon as possible within 72 hours (3 days) after unprotected sex.....".
2. At the bottom left corner of the PDP, revise the statements to read "Reduces the chance of pregnancy after unprotected sex (i.e., if a regular birth control method fails or after sex without birth control). Not for regular birth control."
3. Above the brand name, revise the NEW! product statement to read "NEW! Now only ONE dose"

**b. Blister Cards (inner panels)**

**i. For Plan B**

1. Move the bullet and the word "\_\_\_\_\_ associated with Plan B Step One to be part of the sentence below it which reads "\_\_\_\_\_

b(4)

**c. Other panels:**

7/9/2009

i. General comments

1. Please revise again the "name and place of business" to reflect the appropriate corporate structure. We are confused about who you are.
2. For **Plan B One-Step** the carton reads "Duramed Pharmaceuticals, Inc. Subsidiary of Barr Pharmaceuticals, Inc". Is this correct?
3. For **Plan B**, the carton reads "Mfg by Gedeon Richter Budapest, Hungary for Duramed Pharmaceuticals, Inc. Subsidiary of Barr Pharmaceuticals, Inc." Is this correct?
4. For **Plan B**, ensure that the strength of the tablet is included as part of the statement of identity.

d. Drug Facts

i. For **Plan B**:

1. Under **When using this product**, delete the adverse event \_\_\_\_\_ b(4)
2. Under **Directions**:
  - a. Revise the second bullet to read: "take the first tablet as soon as possible within 72 hours (3 days) after unprotected sex. The sooner you take the first tablet, the better it will work."
  - b. Revise the third bullet to read "take the second tablet 12 hours after you take the first tablet"
  - c. Revise the fourth bulleted statement to read "if you vomit within 2 hours of taking the medication, call a healthcare professional to find out if you should repeat that dose"
3. Under **Other information**:
  - a. Unbold the third bulleted statements
  - b. Delete the last sentence: \_\_\_\_\_ b(4)

ii. For **Plan B One Step**:

1. Under **When using this product**, add the adverse event "vomiting".

II. Consumer Information Leaflet (CIL)

1. Avoid using contractions in the text of the CIL. For example, on page 2 of the One-Step CIL is the word \_\_\_\_\_ b(4)  
On page 3 of the One-Step CIL are the words \_\_\_\_\_ Check all pages for contractions, and check the Plan B CIL as well. b(4)
2. On the cover of the CILs for both Plan B and Plan B One-Step, do the statements "From the makers of Plan B Duramed Pharmaceuticals, Inc., a subsidiary of Barr Pharmaceuticals, Inc." reflect the correct company structure? Also, on the Plan B CIL cover the company structure statement starts "From the makers of Plan B. Duramed Pharmaceuticals, Inc., ....." whereas on the One-Step CIL there is a comma after "From the makers of Plan B," Either use a comma or a period but be consistent.
3. Page 12 of the One-Step CIL, eliminate the second sentence \_\_\_\_\_ b(4)

It is repeated twice. Likewise, delete the second sentence from page 12 of the Plan B CIL which reads: \_\_\_\_\_ It is repeated twice.

b(4)

4. Page 14, 16 and 24 of the One-Step CIL, add "vomiting" as one of the side effects. To page 14 16 and 24 of the Plan B CIL, delete " \_\_\_\_\_ " as a side effect.
5. Page 20 of the One-Step CIL, revise the second paragraph to read as follows: "Remember, Plan B One-Step is only for emergency pregnancy prevention. There are many other products that work for regular birth control that are available by prescription and over-the-counter." Revise the second paragraph on page 20 of the Plan B CIL in the same way to be consistent between products.

Please let me know if you have any questions.

Best regards,

Melissa

Melissa Hancock Furness  
Chief, Project Management Staff  
FDA/CDER/OND/ONP/DNCE

phone: 301-796-0893  
e-mail: Melissa.Furness@fda.hhs.gov

---

**From:** Walsh, Michele [mailto:Michele.Walsh@barriabs.com]  
**Sent:** Monday, July 06, 2009 3:09 PM  
**To:** Christl, Leah A; Lucarelli, Pamela K; Hummel, Amy; Furness, Melissa  
**Subject:** RE: just checking in.....

Hi Melissa, do you have an estimate time on when we can expect the OTC comments?

-Michele

---

**From:** Christl, Leah A [mailto:Leah.Christl@fda.hhs.gov]  
**Sent:** Monday, July 06, 2009 1:17 PM  
**To:** Walsh, Michele; Lucarelli, Pamela K; Hummel, Amy; Furness, Melissa  
**Subject:** Re: just checking in.....

There will be some OTC labeling comments coming soon. Melissa will be sending them since I am out of the office still.

Leah

---

Message sent from my BlackBerry Wireless Handheld. Please excuse any typos.

---

.om: Walsh, Michele <Michele.Walsh@barriabs.com>

7/9/2009

o: Lucarelli, Pamela K; Christl, Leah A  
**Sent:** Mon Jul 06 11:00:19 2009  
**Subject:** just checking in.....

Hello Ladies,

Happy Plan B PDUFA week! Just checking in to see if there are any comments on the pieces received last week.

7/9/2009

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

/s/

-----  
Leah Christl  
7/9/2009 12:17:11 PM  
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

Duramed Research, Inc.  
Attention: Michele Walsh  
Director, Regulatory Affairs  
One Belmont Avenue, 11<sup>th</sup> Floor  
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

We acknowledge receipt on June 29, 2009, of your June 26, 2009, correspondence notifying the Food and Drug Administration of the change of ownership of the following new drug application (NDA):

Name of Drug Product: Plan B One-Step (levonorgestrel 1.5 mg tablet)

NDA Number: 21-998

Name of New Applicant: Duramed Pharmaceuticals, Inc.

Name of Previous Applicant: Gedeon Richter Plc.

Your correspondence provided the information necessary to effect this change, and we have revised our records to indicate Duramed Pharmaceuticals, Inc. as the applicant of record for this application.

All changes in the NDA from those described by the original owner, such as manufacturing facilities and controls, must be reported to us prior to implementation except that changes in the drug product's label or labeling to change the product's brand or the name of its manufacturer, packer, or distributor may be reported in the next annual report. Refer to the *Guidance for Industry: Changes to an Approved NDA or ANDA* for information on reporting requirements. We request that you notify your suppliers and contractors who have DMFs referenced by your application of the change in ownership so that they can submit a new letter of authorization (LOA) to their Drug Master File(s).

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81. In addition, you are responsible for any correspondence outstanding as of the effective date of the transfer.

NDA 21-998

Page 2

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Reproductive and Urologic Products  
5901-B Ammendale Road  
Beltville, MD 20705-1266

If you have any question, please call me at (301) 796-3961.

Sincerely,

*See appended electronic signature*

Pamela Lucarelli  
Regulatory Health Project Manager  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

cc: Gedeon Richter Plc.  
Attention: Dr. Herta Pálfi Goóts  
Manager, Regulatory Affairs  
1103 Budapest  
Gyömrői út 19-21., Hungary

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this page is the manifestation of the electronic signature.**

/s/

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Pamela Lucarelli  
7/7/2009 09:11:43 AM

**Christl, Leah A**

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**From:** Christl, Leah A  
**Sent:** Thursday, July 02, 2009 8:37 AM  
**To:** 'Walsh, Michele'; Hummel, Amy  
**Cc:** Lucarelli, Pamela K; Mercier, Jennifer L  
**Subject:** RE: Age presentation for Plan B and Plan B One Step

**Attachments:** N21-998 Plan B One-Step & NDA 21-045 Plan B OTC labeling comments 7\_2\_09.doc



N21-998 Plan B  
One-Step & NDA ...

Please find attached the labeling comments regarding the OTC labeling components for NDA 21-998 Plan B One-Step and NDA 21-045 Plan B.

Please let me know if you have any questions.

Leah

Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products

Leah.Christl@fda.hhs.gov  
Phone: 301-796-0869  
White Oak Building 22, Room 5300  
Main Office Phone: 301-796-2060  
Fax: 301-796-9899  
Mail:

10903 New Hampshire Ave Room 5300  
Silver Spring, MD 20993

Submissions:  
FDA CDER  
Office of Nonprescription Products  
5901-B Ammendale Rd  
Beltsville, MD 20705-1266

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-----Original Message-----

From: Walsh, Michele [mailto:Michele.Walsh@barrlabs.com]  
Sent: Wednesday, July 01, 2009 6:01 PM  
To: Christl, Leah A  
Cc: Lucarelli, Pamela K; Hummel, Amy  
Subject: Age presentation for Plan B and Plan B One Step

Hi Leah,  
I heard from Pam Lucarelli that you will be in contact with us regarding the age presentation on the cartons and consumer information leaflets for both products. I also understand that you will be accepting the DRUP convention for presenting the age restriction.

Is there any way to get the changes to us tomorrow. We received the latest version of the

PI from DRUP and we are accepting all their proposed changes (that was easy). So, we just need to make the changes to the carton and CIL. If I get your edits by lunchtime (and there are no further changes other than the age) we are prepared to return all the updated labeling components by COB tomorrow. Our people here are motivated to get this final label back to you before the holiday.

Please keep me updated as to when we will receive your comments. Many thanks.

-Michele

NDA 21-045 & NDA 21-998  
OTC labeling comments

**General comment:** Please ensure that all words are spelled out fully and that contractions are not used in any of the OTC labeling components.

**I. Carton label (For both products):**

**a. Principal Display Panel**

- i. Change the "\_\_\_\_\_." to "Rx only for women younger than age 17" **b(4)**

**ii. Plan B**

1. Change "\_\_\_\_\_." to "Take first tablet as soon as possible within 72 hours..." **b(4)**
2. Change "\_\_\_\_\_." To "The sooner you take the first tablet the better Plan B will work."

**ii. Plan B One-Step**

1. Change the bulleted statement from "\_\_\_\_\_." to "...within 72 hours (3 days)...the better Plan B One-Step will work." **b(4)**

**b. Blister Cards (inner panels)**

**i. Plan B One-Step**

1. The statement "\_\_\_\_\_." to "Take ... as soon as possible within 72 hours (3 days)... The sooner you take it, the better [Plan B One-Step] will work". This should be one bulleted statement and read as it appears in the PDP. **b(4)**

**ii. Plan B**

1. Change "\_\_\_\_\_." to "Take first tablet as soon as possible within 72 hours..."

**c. Other panels:**

**i. Plan B One-Step carton end panels**

1. Change the "\_\_\_\_\_." to "Rx only for women younger than age 17" **b(4)**

**ii. General comments**

1. Please revise the "name and place of business" to reflect the appropriate corporate structure

**d. Drug Facts**

**i. Under the Warnings heading, When using this product subheading**

1. The AE listing should be the same as in the Consumer Information Leaflet (CIL) for both products.

2. **Plan B One-Step** – delete \_\_\_\_\_ because this is not one of the AEs listed in the PI.

b(4)

ii. Under the **Directions** heading

1. under the first bullet “women 17 years of age and older”

- a. Change the sub-bullet “ \_\_\_\_\_”

b(4)

\_\_\_\_\_ to “...as soon as possible within 72 hours (3 days)...the better it will work.”

- b. Add the vomiting statement that is appropriate to the specific product as an additional sub-bullet as stated in the CIL.

2. under the second bullet

- a. change “ \_\_\_\_\_”

b(4)

\_\_\_\_\_ to “prescription only for women younger than age 17. If you are younger than age 17, ...”

**II. Consumer Information Leaflet (CIL)**

These comments are based on the Plan B® One-Step CIL submitted on 6/22/09. Any required/recommended revisions apply to both product CILs, unless otherwise noted or are product specific, such as dosing directions. Also the color scheme of each product’s CIL should match the outer carton of the relevant product.

a. Cover (Page 1)

i. **Plan B**

1. The title should be changed from \_\_\_\_\_ to “Plan B Emergency Contraceptive. Because the unexpected happens” to parallel the title of the Plan B One-Step CIL.
2. “For additional information...” statement - delete “Emergency Contraceptive” from the end of the statement.

b(4)

ii. **Plan B One-Step**

1. “For additional information...” add “One-Step” after “Plan B”

iii. **Both products**

1. Revise the “name and place of business” to reflect the appropriate corporate structure

- b. Page 2 - 2<sup>nd</sup> paragraph, revise the last sentence to read “For example, if you were using a condom and it broke or slipped, if you did not use

NDA 21-045 & NDA 21-998  
OTC labeling comments

your regular birth control as you should have, or if you did not use any birth control, [Plan B One-Step] may work for you.”

c. Page 3

- i. Delete the first sentence. Start the second sentence to read as follows: “[Plan B One-Step] will not work if you’re already pregnant...”
- ii. Third sentence: Revise \_\_\_\_\_ to “[Plan B One-Step] should not be used as regular birth control.”

b(4)

d. Page 4 - Second bullet point

- i. Delete the parenthetical phrase “\_\_\_\_\_”

b(4)

e. Page 5 – Add the phrase, “or any other ingredients in [Plan B One-Step]” to the end of the last bullet point to make it consistent with this warnings on pages 16 and 23.

f. Page 7 - Delete the second paragraph starting with the statement “\_\_\_\_\_”

b(4)

g. Page 8:

- i. First sentence - the words “try to” should be added to the statement to read “You have only a few days to try to prevent pregnancy...”
- ii. Third sentence - change to read “...as soon as possible within 72 hours (3 days)...”
- iii. First sentence in the second paragraph - Replace “\_\_\_\_\_” with “The sooner you take [Plan B One-Step], the better it will work. Take [Plan B One-Step] as soon as possible after unprotected sex.”
- iv. Last sentence - delete “\_\_\_\_\_”

b(4)

b(4)

h. Page 10 – Delete the second paragraph and add the following sentence to the end of the first paragraph, “[Plan B One-Step] will not work if you’re already pregnant.”

i. Page 11

- i. Heading - insert “(abdominal)” after the word “stomach” to read “...have severe lower stomach (abdominal) pain...”
- ii. First sentence – revise the sentence to read “...have severe lower stomach (abdominal) pain...”

NDA 21-045 & NDA 21-998  
OTC labeling comments

- iii. First sentence – revise “ \_\_\_\_\_ ” to \_\_\_\_\_  
“...3 to 5 weeks after taking [Plan B One-Step],...” b(4)
- j. Page 12, third sentence – revise “ \_\_\_\_\_ ”  
to “...should not be used as regular birth control.” b(4)
- k. Page 14, second sentence – delete the sentence \_\_\_\_\_ b(4)
- l. Pages 14, 16, and 24 - The adverse events lists on these pages differ from one another. They should reflect the adverse events described in prescription labeling and should be consistent with each other when applicable. Based on the current draft of prescription labeling, we recommend all of the lists be changed to include only menstrual changes, tiredness, lower stomach (abdominal) pain, nausea, vomiting, headache, dizziness, breast pain, and diarrhea (diarrhea on Plan B only). The listing in “Drug Facts” under “When using this product” should also be changed to reflect the same information. “Diarrhea” should not be listed for Plan B One-Step to be consistent with the Plan B One-Step prescription labeling.
- m. Page 17 - The appropriate ages should be changed to be the same as under the **Directions** header of the Drug Facts label..
- n. Page 19 – “Protect yourself in more ways than One!” change the first letter in the word “One” to lower case.
- o. Page 20:
  - i. First paragraph, second, third, and fourth sentences - revise as follows: “For example, if you were using a condom and it broke or slipped, or if you did not use your regular birth control as you should have, or if you did not use any birth control, [Plan B One-Step] may work for you.”
  - ii. Second paragraph
    - 1. Delete the second sentence \_\_\_\_\_ b(4)
    - 2. Delete the words “ \_\_\_\_\_ ” from the third sentence
    - 3. Delete the words \_\_\_\_\_ from the fourth sentence so the sentence reads “These are available...”
    - 4. Revise the fifth sentence to read “Other effective methods are also available...” [emphasis added to note revision]
- p. Page 22 – Delete the final sentence \_\_\_\_\_ b(4)
- q. Page 23 – Change the last paragraph to read “The sooner you take [Plan B One-Step], the better it will work.”

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Leah Christl  
7/2/2009 08:45:55 AM  
CSO

**MEMORANDUM**

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

**DATE:** July 1, 2009

**TO:** Duramed Research Inc.  
Attention: Michele Walsh and Amy Hummel

**FROM:** Division of Reproductive and Urologic Products  
Pamela Lucarelli

**SUBJECT:** Plan B  
NDA 21-998, Plan B One-Step

The following e-mail correspondence is an information request (IR) from the clinical reviewer.

**Lucarelli, Pamela K**

---

**From:** Hummel, Amy [Amy.Hummel@barrlabs.com]  
**Sent:** Wednesday, July 01, 2009 12:40 PM  
**To:** Lucarelli, Pamela K  
**Cc:** Walsh, Michele  
**Subject:** RE: Plan B  
**Attachments:** Medwatch forms 7 serious-medically confirmed events.pdf

Hi Pam,

Please see the below message from the Pharmacovigilance group, identifying the cases comprising the 7 medically confirmed and serious events. Please note that the 5 cases represent all 7 events, as some individuals have multiple serious events. Case narratives can be found in the 55-page document "Pages from 21045 2008-08-28 Periodic Report 7-1-07 to 6-30-08.pdf", submitted on June 11, 2009, as follows:

Case 018247: Narrative summary on page 11

Case 027632: Narrative summary on page 22

Case 022167: Narrative summary on page 24

Case 016183: Narrative summary on page 38 (page 39 of the .pdf file)

Case 007670 was a follow-up report and is noted on page 7 of the submitted report.

Copies of the associated Medwatch forms (Form FDA 3500A) are attached to this message as well for your further convenience.

If you have any questions, please do not hesitate to contact me.

Kind regards,  
Amy

---

**From:** Maher, Erin  
**Sent:** Wednesday, July 01, 2009 12:12 PM  
**To:** Hummel, Amy  
**Cc:** Godshall, Joyce  
**Subject:** Plan B -serious/medically confirmed cases

Hi Amy,

The following five cases are serious and have been medically confirmed. The total of serious events from the cases match the expected/unexpected totals from table 3.1 in the periodic report.

018247  
ectopic pregnancy      serious/expected  
blood in urine          serious/unexpected

7/1/2009

027632  
miscarriage            serious/unexpected

022167  
missed abortion        serious/unexpected

016183  
ectopic pregnancy     serious/expected

007670  
cytomegalovirus        serious/unexpected  
pancreatitis            serious/unexpected

 Right-click here to download pictures. To help protect your privacy, Outlook prevented automatic download of this picture from the Internet.

Best Regards,  
Erin Maher  
Pharmacovigilance  
Drug Safety Associate  
Teva Neuroscience  
Horsham PA 19044  
Phone: 215-293-6356  
Fax: 215-293-6398

---

**From:** Walsh, Michele  
**Sent:** Tuesday, June 30, 2009 8:07 AM  
**To:** Hummel, Amy; Reape, Kathleen  
**Subject:** Fw: Plan B

---

**From:** Lucarelli, Pamela K  
**To:** Walsh, Michele  
**Sent:** Tue Jun 30 06:51:09 2009  
**Subject:** Plan B

Hi Michele,

Below is an information request from our clinical team. Please confirm that you received this and provide a brief narrative by COB on Wednesday (7/1/09). If you have any questions, let me know.

*The 6-11-09 submission included a 55-page Narrative Summary and Analysis from the latest PSUR for Plan B (the two-dose levonorgestrel 0.75 mg product). The summary covers the 12 months from 7-01-07 to 6-30-08. This periodic report contains 9,029 Individual Case Safety Reports with 48 considered as serious. Seven case reports were medically confirmed and serious (two of them were expected and five unexpected).*

*Please identify the 7 medically confirmed and serious cases; a brief narrative of each case will be sufficient.*

7/1/2009

Thanks in advance,  
Pam

Pamela Lucarelli  
Regulatory Health Project Manager  
FDA/Center for Drug Evaluation and Research  
Division of Reproductive and Urologic Products  
WO22 - Room 5323  
10903 New Hampshire Avenue  
Silver Spring, MD 20903

Phone 301.796.3961  
Fax 301.796.9897  
pamela.lucarelli@fda.hhs.gov

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/s/

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Pamela Lucarelli  
7/1/2009 01:33:54 PM  
CSO

Pamela Lucarelli  
7/1/2009 01:34:14 PM  
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-045  
NDA 21-998

Duramed Research, Inc.  
Attention: Michele Walsh  
Director, Clinical Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plan B ® (levonorgestrel, 0.75 mg) Tablets (NDA 21-045) and Plan B One-Step ® (levonorgestrel, 1.5 mg) Tablets (NDA 21-998).

We also refer to the meeting between representatives of your firm and the FDA on June 1, 2009. The purpose of the meeting was to discuss a full OTC switch for both the Plan B ® and Plan B One-Step ® products.

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

If you have any questions, call Leah Christl, Associate Director for Regulatory Affairs, Office of Nonprescription Products, at 301-796-0869, or Pamela Lucarelli, Regulatory Health Project Manager, Division of Reproductive and Urologic Products, at (301) 796-3961.

Sincerely,

*(See appended electronic signature page)*

Andrea Leonard-Segal, M.D.  
Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

Enclosure

**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** Type B

**Meeting Category:** Pre-Supplemental NDA

**Meeting Date and Time:** June 1, 2009  
11:00 a.m. – 12:30 p.m. EST

**Location:** White Oak CDER Office Building 22  
10903 New Hampshire Avenue  
Conference Room 1313  
Silver Spring, MD 20993

**Applications:** NDA 21-045 and NDA 21-998

**Product Names:** Plan B ® (levonorgestrel, 0.75 mg) tablets (NDA 21-045)  
and Plan B One-Step ® (levonorgestrel, 1.5 mg) tablets  
(NDA 21-998)

**Sponsor Name:** Duramed Research, Inc.

**Meeting Requestor:** Michele Walsh  
Director, Clinical Regulatory Affairs

**Meeting Chair:** Andrea Leonard-Segal, M.D.  
Director  
Division of Nonprescription Clinical Evaluation

**Meeting Recorder:** Leah Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products

**Meeting Attendees:**

**FDA Attendees:**

Office of Nonprescription Products

Charles Ganley, M.D., Director

Shaw Chen, M.D., Acting Deputy Director

Leah Christl, Ph.D., Associate Director for Regulatory Affairs

Division of Nonprescription Clinical Evaluation

Andrea Leonard-Segal, M.D., Director

Lesley Furlong, M.D., Clinical Team Leader

Christina Chang, M.D., M.P.H., Medical Officer

Laura Shay, Ph.D., RN, Social Science Analyst

Murewa Oguntimein, Social Science Analyst

Division of Nonprescription Regulation Development

Arlene Solbeck, IDS Reviewer

Office of Drug Evaluation III

Julie Beitz, M.D., Director

Maria Walsh, Acting Associate Director for Regulatory Affairs

Division of Reproductive and Urologic Products

Scott Monroe, M.D., Director

Lisa Soule, M.D., Clinical Team Leader

Daniel Davis, M.D., Medical Officer

Jennifer Mercier, Chief, Project Management Staff

Pamela Lucarelli, Regulatory Project Manager

Office of New Drugs

John Jenkins, M.D., Director

Pediatric and Maternal Health Staff

Lisa Mathis, M.D., Director

Office of Regulatory Policy

Jane Axelrad, J.D., Director

Office of Executive Programs, Executive Operations Staff

Vikki Kinsey, Consumer Safety Officer

FDA - Office of the Chief Counsel

Kim Dettlebach, J.D., Associate Chief Counsel

Donna Katz, J.D., Associate Chief Counsel

**External Constituent Attendees:**

Duramed Research, Inc.

Joseph Carrado, Vice President, Regulatory Affairs

Amy Niemann, Senior Vice President and General Manager

Michele Walsh, Director, Regulatory Affairs

Amy Hummel, Senior Associate, Regulatory Affairs

**1.0 BACKGROUND:**

Plan B® (levonorgestrel, 0.75 mg) is given in 2 doses, 12 hours apart, for emergency contraception. In April 2003, the applicant submitted Efficacy Supplement #011 to market Plan B® as an over-the-counter product. Duramed Research, Inc (Duramed) received approval on August 24, 2006 to market a dual-label product to allow nonprescription availability of Plan B® for women 18 years and older and by prescription only for women 17 years and younger.

On June 24, 2006, Duramed submitted a New Drug Application (NDA) to market Plan B One-Step ® (levonorgestrel tablets, 1.5 mg) as a prescription-only product for women of all ages. Plan B One-Step ® (levonorgestrel, 1.5 mg) is given as a single dose for emergency contraception. Duramed received an approvable letter on November 22, 2006 based on the need to submit revised labeling that meets the requirements of marketing of levonorgestrel tablets, 1.5 mg, as a prescription product for women 17 years of age and younger, and as a nonprescription product for women 18 years of age and older. On January 12, 2009, Duramed submitted a complete response to the November 22, 2006 action letter.

On April 21, 2009, FDA issued a letter to Duramed stating that it had concluded that Plan B may be made available to women 17 years of age and older without a prescription, subject to the submission and approval of revised draft labeling as a prior approval efficacy supplement to NDA 21-045 that would allow for this change in population. The letter also stated that if Duramed wanted to pursue the marketing of Plan B for women 17 years of age and older without a prescription, or other options for marketing Plan B, that a meeting was encouraged to discuss necessary labeling revisions and the content of any submission(s).

On April 28, 2009, Duramed submitted a meeting request to the FDA for an advice meeting to discuss the necessary regulatory and developmental pathway to support full over-the-counter (OTC) status for both Plan B ® and Plan B One-Step ®. In the meeting request, Duramed provided information and specific questions for both Plan B ® and Plan B One-Step ® for discussion.

#### **1.1 MEETING OBJECTIVES:**

To discuss the pathway for full OTC status for Plan B ® and Plan B One-Step ®.

#### **2.0 DISCUSSION:**

b(4)

5 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

       Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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/s/

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Andrea Segal

6/26/2009 12:50:11 PM

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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         | <h2 style="margin: 0;">REQUEST FOR CONSULTATION</h2>                                                                                                        |                                                                                                                                                                      |                                          |
| TO (Office/Division): Division of Drug Marketing, Advertising and Communications (DDMAC)<br>Attention: Janice Maniwang 301-796-3821                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |         | FROM (Name, Office/Division, and Phone Number of Requestor): Division of Reproductive and Urologic Drug Products (HFD-580)<br>Pamela Lucarelli 301-796-3961 |                                                                                                                                                                      |                                          |
| DATE<br>June 5, 2009                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | IND NO. | NDA NO.<br>21-998                                                                                                                                           | TYPE OF DOCUMENT<br>Original                                                                                                                                         | DATE OF DOCUMENT<br>January 9, 2009      |
| NAME OF DRUG<br>Plan B — (levonorgestrel tablet)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         | PRIORITY CONSIDERATION<br>Standard                                                                                                                          | CLASSIFICATION OF DRUG<br>3S                                                                                                                                         | DESIRED COMPLETION DATE<br>June 19, 2009 |
| NAME OF FIRM: Duramed Research, Inc. and Gedeon Richter, Ltd.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <b>REASON FOR REQUEST</b><br><b>I. GENERAL</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <div style="display: flex; flex-wrap: wrap;"> <div style="width: 33%;"> <input type="checkbox"/> NEW PROTOCOL<br/> <input type="checkbox"/> PROGRESS REPORT<br/> <input type="checkbox"/> NEW CORRESPONDENCE<br/> <input type="checkbox"/> DRUG ADVERTISING<br/> <input type="checkbox"/> ADVERSE REACTION REPORT<br/> <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION<br/> <input type="checkbox"/> MEETING PLANNED BY         </div> <div style="width: 33%;"> <input type="checkbox"/> PRE-NDA MEETING<br/> <input type="checkbox"/> END-OF-PHASE 2a MEETING<br/> <input type="checkbox"/> END-OF-PHASE 2 MEETING<br/> <input type="checkbox"/> RESUBMISSION<br/> <input type="checkbox"/> SAFETY / EFFICACY<br/> <input type="checkbox"/> PAPER NDA<br/> <input type="checkbox"/> CONTROL SUPPLEMENT         </div> <div style="width: 33%;"> <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER<br/> <input type="checkbox"/> FINAL PRINTED LABELING<br/> <input type="checkbox"/> LABELING REVISION<br/> <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE<br/> <input type="checkbox"/> FORMULATIVE REVIEW<br/> <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):         </div> </div> |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <b>II. BIOMETRICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <input type="checkbox"/> PRIORITY P NDA REVIEW<br/> <input type="checkbox"/> END-OF-PHASE 2 MEETING<br/> <input type="checkbox"/> CONTROLLED STUDIES<br/> <input type="checkbox"/> PROTOCOL REVIEW<br/> <input type="checkbox"/> OTHER (SPECIFY BELOW):         </div> <div style="width: 50%;"> <input type="checkbox"/> CHEMISTRY REVIEW<br/> <input type="checkbox"/> PHARMACOLOGY<br/> <input type="checkbox"/> BIOPHARMACEUTICS<br/> <input type="checkbox"/> OTHER (SPECIFY BELOW):         </div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <b>III. BIOPHARMACEUTICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <input type="checkbox"/> DISSOLUTION<br/> <input type="checkbox"/> BIOAVAILABILITY STUDIES<br/> <input type="checkbox"/> PHASE 4 STUDIES         </div> <div style="width: 50%;"> <input type="checkbox"/> DEFICIENCY LETTER RESPONSE<br/> <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS<br/> <input type="checkbox"/> IN-VIVO WAIVER REQUEST         </div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <b>IV. DRUG SAFETY</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL<br/> <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES<br/> <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)<br/> <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP         </div> <div style="width: 50%;"> <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY<br/> <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE<br/> <input type="checkbox"/> POISON RISK ANALYSIS         </div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <b>V. SCIENTIFIC INVESTIGATIONS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| <div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <input type="checkbox"/> CLINICAL         </div> <div style="width: 50%;"> <input type="checkbox"/> NONCLINICAL         </div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| COMMENTS / SPECIAL INSTRUCTIONS: Please review the labels for acceptability. The applicable labels are available through EDR. The PDUFA goal date is July 12, 2009. Please review and make recommendations by the above due date.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |                                                                                                                                                             |                                                                                                                                                                      |                                          |
| SIGNATURE OF REQUESTOR<br>Pamela Lucarelli                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |                                                                                                                                                             | METHOD OF DELIVERY (Check one)<br><input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND |                                          |
| PRINTED NAME AND SIGNATURE OF RECEIVER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                                                                                                                                             | PRINTED NAME AND SIGNATURE OF DELIVERER                                                                                                                              |                                          |

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/s/

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Pamela Lucarelli  
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**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

**DISCIPLINE REVIEW LETTER**

Duramed Research, Inc.  
Attention: Michele G. Walsh  
Director, Clinical Regulatory Affairs  
One Belmont Ave., 11th Floor  
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

Please refer to your January 24, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel 1.5 mg tablets.

We also refer to your submission dated January 9, 2009.

Our review of the nonprescription labeling contained in your January 9, 2009 submission is complete, and we have identified the following deficiencies:

**Drug Facts**

1. Under "Directions", for the second bulleted statement which begins ' \_\_\_\_\_' insert the word "tablet" after the word "take" for clarity. b(4)
2. The bulleted statement under "Directions" (for Plan B®) which states ' \_\_\_\_\_' was revised (shortened) for Plan B ® \_\_\_\_\_ to read ' \_\_\_\_\_' We recommend that the original statement as approved for Plan B® be used for Plan B ® \_\_\_\_\_ for clarity. b(4)
3. Under "Other information", the tamper-evident feature statement which begins ' \_\_\_\_\_' should be revised to read "tablet is enclosed..." since Plan B ® \_\_\_\_\_ is a single dose product. b(4)

**Consumer Information Leaflet (CIL)**

4. Cover: The word " \_\_\_\_\_" should be inserted before ' \_\_\_\_\_' in the statement " \_\_\_\_\_" b(4)

- 8. Page 12: Put a period after the storage temperature statement.**

**We also have the following recommendations.**

### Principal Display Panel (PDP)

10. If both the 0.75 mg dual pack and the 1.5 mg single dose products will overlap each other in the marketplace, we recommend that the statement of identity appear more prominently and is distinctly different for each product.

**CIL**

- 11. Page 11: Under the overdose warning, insert the Poison Control Center telephone number.**

**We acknowledge that you submitted a revised carton label on May 19, 2009. The revisions to the carton label in that submission do not affect the deficiencies and recommendations outlined above, except that the proprietary name has changed and the reference to age 17 has changed to age 16.**

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response,

and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle. If you have any questions regarding this letter, call me at 301-796-0869. For any other information regarding this application, contact the Division of Reproductive and Urologic Products Regulatory Project Manager.

Sincerely,

*See appendix {electronic signature page}*

Leah A Christl, Ph.D.  
Associate Director for Regulatory Affairs  
Office of Nonprescription Products  
Office of New Drugs  
Center for Drug Evaluation and Research

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/s/

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Leah Christl

5/29/2009 01:29:41 PM



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Nonprescription Products

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**FAX TRANSMITTAL SHEET**

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**DATE:** May 21, 2009

|                                                                   |                                                                           |
|-------------------------------------------------------------------|---------------------------------------------------------------------------|
| <b>To:</b> Michele Walsh<br>Director, Clinical Regulatory Affairs | <b>From:</b> Leah Christl<br>Associate Director for Regulatory<br>Affairs |
| <b>Company:</b> Duramed Research, Inc.                            | Office of Nonprescription Products                                        |
| <b>Email address:</b><br>Michele.Walsh@barrlabs.com               | <b>Email address:</b> leah.christl@fda.hhs.gov                            |
| <b>Phone number:</b> (610) 747-2644                               | <b>Phone number:</b> (301) 796-0869                                       |

**Subject:** Preliminary responses for NDA 21-045 and 21-998 – Meeting on June 1, 2009

**Total no. of pages including cover:** 6

**Drug Name:** Plan B (0.75 mg levonorgestrel) tablet and Plan B One Step (1.5 mg levonorgestrel) tablet

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**Document to be mailed:** YES ☒ NO

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**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2080. Thank you.

NDA 21-045 and NDA 21-998  
Plan B and Plan B One-Step  
Duramed Research, Inc.  
Type A meeting June 1, 2009

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for June 1, 2009 at 11:00 am EST between Duramed Research, Inc., the Division of Nonprescription Clinical Evaluation and the Division of Reproductive and Urologic Products. This material is shared to promote a collaborative and successful discussion at the meeting. If there is anything in it that you do not understand or with which you do not agree, we expect you to communicate such questions and disagreements. The minutes of the meeting will reflect the discussion that takes place during the meeting and may not be identical to these preliminary comments following substantive discussion at the meeting. If these answers and comments are clear to you and you determine that further discussion is not required, you have the option of canceling the meeting (contact the Regulatory Project Manager). It is important to remember that some meetings, particularly milestone meetings, are valuable even if pre-meeting communications seem to have answered the principal questions. It is our experience that the discussion at meetings often raises important new issues. If you choose to cancel the meeting, this document will represent the official record of response to your questions. If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda and/or changing the format of the meeting (e.g., from face to face to teleconference). Please note that if there are any major changes to your development plan, the purpose of the meeting, or to the questions (based on our responses herein), we may not be prepared to discuss or reach agreement on such changes at the meeting, but we will be glad to discuss them to the extent possible. If any modifications to the development plan or additional questions for which you would like FDA feedback arise prior to the meeting, contact the Regulatory Project Manager to discuss the possibility of including these for discussion at the meeting.

Duramed Research, Inc. should provide a hardcopy or electronic version of any materials (e.g. slides, or handouts) to be presented and/or discussed at the meeting to the Regulatory Project Manager to be appended to the meeting minutes.

Duramed Research, Inc. will be responsible for providing a verbal summary of the key discussion points, agreements and action items at the close of the meeting.

Plan B

1. Duramed believes that the information already submitted to the Agency in the original Rx-to-OTC supplement (S-011) submitted by Women's Capital Corporation on April 21, 2003 is sufficient to support full OTC status for Plan B, and that only revised labeling is required to be submitted. Therefore, in light of the Advice Letter of April 21, 2009, Duramed would like guidance from the Divisions as to what, if any, additional information they envision would be required to be submitted to constitute a complete reviewable supplement to achieve full OTC status for Plan B.

*FDA preliminary response:*

b(4)

b(4)

b(4)

b(4)

3 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

       Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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/s/

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Leah Christl  
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CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

**PROPRIETARY NAME REQUEST  
- CONDITIONALLY ACCEPTABLE**

Duramed Research, Inc.  
ATTENTION: Michele G. Walsh  
Director, Clinical Regulatory Affairs  
One Belmont Avenue, 11<sup>th</sup> Floor  
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

Please refer to your New Drug Application (NDA) dated and received January 24, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel tablet, 1.5 mg.

We also refer to your submission dated April 20, 2009, received April 21, 2009, requesting review of your proposed proprietary name, Plan B One-Step. We have completed our review of the proposed proprietary name, Plan B One-Step, and have concluded that it is acceptable.

If any of the proposed product characteristics as stated in your April 20, 2009, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Darrell Jenkins, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0558. For any other information regarding this application contact Pamela Lucarelli, Regulatory Project Manager in the Division of Reproductive and Urologic Products, at 301-796-2130.

Sincerely,

*{See appended electronic signature page}*

Scott Monroe, M.D.  
Director  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Andrea Leonard-Segal, M.D.  
Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

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/s/

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Scott Monroe  
5/13/2009 09:19:23 AM

Andrea Segal  
5/13/2009 09:22:40 AM

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| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |         |                                                                                                                                                                                         | REQUEST FOR CONSULTATION                                                                                  |                                         |
| TO (Division/Office):<br>Mail: OSE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                                                                                                                                                                         | FROM: Jennifer Mercier, Chief, project Management Staff<br>Division of Reproductive and Urologic Products |                                         |
| DATE<br>May 12, 2009                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | IND NO. | NDA NO.<br>21-045<br>21-998                                                                                                                                                             | TYPE OF DOCUMENT                                                                                          | DATE OF DOCUMENT                        |
| NAME OF DRUG<br>Plan B (levonorgestrel)<br>Plan B One-Step (levonorgestrel)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         | PRIORITY CONSIDERATION                                                                                                                                                                  | CLASSIFICATION OF DRUG                                                                                    | DESIRED COMPLETION DATE<br>June 1, 2009 |
| NAME OF FIRM: Duramed Pharmaceutical Research                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| REASON FOR REQUEST                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| I. GENERAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| <input type="checkbox"/> NEW PROTOCOL<br><input type="checkbox"/> PROGRESS REPORT<br><input type="checkbox"/> NEW CORRESPONDENCE<br><input type="checkbox"/> DRUG ADVERTISING<br><input type="checkbox"/> ADVERSE REACTION REPORT<br><input type="checkbox"/> MANUFACTURING CHANGE/ADDITION<br><input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> RESUBMISSION<br><input type="checkbox"/> SAFETY/EFFICACY<br><input type="checkbox"/> PAPER NDA<br><input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER<br><input type="checkbox"/> FINAL PRINTED LABELING<br><input type="checkbox"/> LABELING REVISION<br><input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE<br><input type="checkbox"/> FORMULATIVE REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW): |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| II. BIOMETRICS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| STATISTICAL EVALUATION BRANCH                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         | STATISTICAL APPLICATION BRANCH                                                                                                                                                          |                                                                                                           |                                         |
| <input type="checkbox"/> TYPE A OR B NDA REVIEW<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> CONTROLLED STUDIES<br><input type="checkbox"/> PROTOCOL REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |         | <input type="checkbox"/> CHEMISTRY REVIEW<br><input type="checkbox"/> PHARMACOLOGY<br><input type="checkbox"/> BIOPHARMACEUTICS<br><input type="checkbox"/> OTHER (SPECIFY BELOW):      |                                                                                                           |                                         |
| III. BIOPHARMACEUTICS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| <input type="checkbox"/> DISSOLUTION<br><input type="checkbox"/> BIOAVAILABILITY STUDIES<br><input type="checkbox"/> PHASE IV STUDIES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE<br><input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS<br><input type="checkbox"/> IN-VIVO WAIVER REQUEST                            |                                                                                                           |                                         |
| IV. DRUG EXPERIENCE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL<br><input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES<br><input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)<br><input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY<br><input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE<br><input type="checkbox"/> POISON RISK ANALYSIS |                                                                                                           |                                         |
| V. SCIENTIFIC INVESTIGATIONS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| <input type="checkbox"/> CLINICAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |         | <input type="checkbox"/> PRECLINICAL                                                                                                                                                    |                                                                                                           |                                         |
| COMMENTS/SPECIAL INSTRUCTIONS:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| The Division of Reproductive and Urologic Products would like to request an AERS consult for the Plan B and Plan B One-Step. We would like an update since the 2006 dual Rx/OTC approval of Plan B, but would also like data on SAEs/deaths since the original approval of Plan B. Please contact Jennifer Mercier at 301-796-0957 if you have any question pertaining to this consult.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |                                                                                                                                                                                         |                                                                                                           |                                         |
| SIGNATURE OF REQUESTER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         | METHOD OF DELIVERY (Check one)<br><input type="checkbox"/> MAIL <input type="checkbox"/> HAND                                                                                           |                                                                                                           |                                         |
| SIGNATURE OF RECEIVER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         | SIGNATURE OF DELIVERER                                                                                                                                                                  |                                                                                                           |                                         |

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/s/

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Jennifer L. Mercier  
5/12/2009 01:59:43 PM



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

**PROPRIETARY NAME REQUEST  
- WITHDRAWN**

Duramed Research, Inc.  
Attention: Michele G. Walsh  
Director, Clinical Regulatory Affairs  
One Belmont Avenue, 11<sup>th</sup> Floor  
Bala Cynwyd, Pennsylvania 19004

Dear Ms. Walsh:

Please refer to your New Drug Application (NDA) dated and received January 24, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel 1.5 mg Tablets.

We acknowledge receipt of your April 20, 2009, correspondence received on April 21, 2009, notifying us that you are withdrawing your request for a review of the proposed proprietary name Plan B ———. his proposed proprietary name request is considered withdrawn as of April 21, 2009.

b(4)

We note that you have proposed an alternate proprietary name, Plan B One-Step, in your submission dated April 20, 2009. We will begin our review of the alternate proposed name.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Darrell Jenkins, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0558. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

*See appendix - electronic signature on page 1*

Scott Monroe, M.D.  
Director  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Scott Monroe  
5/8/2009 01:34:14 PM



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-045  
NDA 21-998

Duramed Research, Inc.  
Attention: Michele Walsh  
Director, Clinical Regulatory Affairs  
One Belmont Avenue, 11<sup>th</sup> Floor  
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plan B (levonorgestrel, 0.75 mg) Tablets (NDA 21-045) and Plan B One-Step (levonorgestrel, 1.5 mg) Tablets.

We also refer to your April 28, 2009, correspondence, received April 29, 2009, requesting a meeting to discuss a full OTC switch for both the Plan B and Plan B One-Step products.

Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type B meeting as described in our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDUFA Products* (February 2000). The meeting is scheduled for:

Date: June 1, 2009  
Time: 11:00 – 12:30 PM  
Location: TBA

Please have all attendees bring photo identification and allow 15-30 minutes to complete security clearance. If there are additional attendees, email that information to me at [jennifer.mercier@fda.hhs.gov](mailto:jennifer.mercier@fda.hhs.gov) so that I can give the security staff time to prepare temporary badges in advance. Upon arrival at FDA, give the guards either of the following numbers to request an escort to the conference room: Jennifer Mercier, 301-796-0957; the division secretary, 301-796-2130.

NDA 21-045  
NDA 21-998  
Page 2

If you have any questions, call me at (301) 796-0957.

Sincerely,

*(See attached electronic signature page)*

Jennifer Mercier  
Chief, Project Management Staff  
Division of Reproductive and Urologic  
Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Jennifer L. Mercier  
5/6/2009 11:25:17 AM

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                    |                                 |                                                                                                                                                                                                  |                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                    | <b>REQUEST FOR CONSULTATION</b> |                                                                                                                                                                                                  |                                     |
| TO (Office/Division): CDER OSE Consults<br>Attention: Cherye Milburn, Regulatory Health Project Manager                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                    |                                 | FROM (Name, Office/Division, and Phone Number of Requestor): Division of Reproductive and Urologic Drug Products, HFD-580<br>Pamela Lucarelli, Regulatory Health Project Manager<br>301-796-3961 |                                     |
| DATE<br>February 4, 2009                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | IND NO.                            | NDA NO.<br>21-998               | TYPE OF DOCUMENT<br>Original                                                                                                                                                                     | DATE OF DOCUMENT<br>January 9, 2009 |
| NAME OF DRUG<br>Plan R <del>levonorgestrel</del> tablet)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | PRIORITY CONSIDERATION<br>Standard | CLASSIFICATION OF DRUG<br>3S    | DESIRED COMPLETION DATE<br>April 30, 2009                                                                                                                                                        |                                     |
| NAME OF FIRM: Duramed Research, Inc. and Gedeon Richter, Ltd.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <b>REASON FOR REQUEST</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <b>I. GENERAL</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <input type="checkbox"/> NEW PROTOCOL<br><input type="checkbox"/> PROGRESS REPORT<br><input type="checkbox"/> NEW CORRESPONDENCE<br><input type="checkbox"/> DRUG ADVERTISING<br><input type="checkbox"/> ADVERSE REACTION REPORT<br><input type="checkbox"/> MANUFACTURING CHANGE / ADDITION<br><input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING<br><input type="checkbox"/> END-OF-PHASE 2a MEETING<br><input type="checkbox"/> END-OF-PHASE 2 MEETING<br><input type="checkbox"/> RESUBMISSION<br><input type="checkbox"/> SAFETY / EFFICACY<br><input type="checkbox"/> PAPER NDA<br><input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER<br><input type="checkbox"/> FINAL PRINTED LABELING<br><input type="checkbox"/> LABELING REVISION<br><input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE<br><input type="checkbox"/> FORMULATIVE REVIEW<br><input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <b>II. BIOMETRICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <input type="checkbox"/> PRIORITY P NDA REVIEW<br><input type="checkbox"/> END-OF-PHASE 2 MEETING<br><input type="checkbox"/> CONTROLLED STUDIES<br><input type="checkbox"/> PROTOCOL REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW): <input type="checkbox"/> CHEMISTRY REVIEW<br><input type="checkbox"/> PHARMACOLOGY<br><input type="checkbox"/> BIOPHARMACEUTICS<br><input type="checkbox"/> OTHER (SPECIFY BELOW):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <b>III. BIOPHARMACEUTICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <input type="checkbox"/> DISSOLUTION<br><input type="checkbox"/> BIOAVAILABILITY STUDIES<br><input type="checkbox"/> PHASE 4 STUDIES <input type="checkbox"/> DEFICIENCY LETTER RESPONSE<br><input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS<br><input type="checkbox"/> IN-VIVO WAIVER REQUEST                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <b>IV. DRUG SAFETY</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL<br><input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES<br><input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)<br><input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY<br><input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE<br><input type="checkbox"/> POISON RISK ANALYSIS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <b>V. SCIENTIFIC INVESTIGATIONS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                    |                                 |                                                                                                                                                                                                  |                                     |
| <input type="checkbox"/> CLINICAL <input type="checkbox"/> NONCLINICAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                    |                                 |                                                                                                                                                                                                  |                                     |
| COMMENTS / SPECIAL INSTRUCTIONS: Please review the labels for acceptability. The applicable labels are available through EDR. The PDUFA goal date is July 12, 2009. Please review and make recommendations by the above due date.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                    |                                 |                                                                                                                                                                                                  |                                     |
| SIGNATURE OF REQUESTOR<br>Pamela Lucarelli                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                    |                                 | METHOD OF DELIVERY (Check one)<br><input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND                             |                                     |
| PRINTED NAME AND SIGNATURE OF RECEIVER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                    |                                 | PRINTED NAME AND SIGNATURE OF DELIVERER                                                                                                                                                          |                                     |

b(4)

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/s/

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Pamela Lucarelli  
2/5/2009 01:25:12 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

Duramed Research, Inc.  
Attention: Michele Walsh  
Director, Clinical Regulatory Affairs  
One Belmont Avenue, 11<sup>th</sup> Floor  
Bala Cynwyd, PA 19004

Dear Ms. Walsh:

We acknowledge receipt on January 12, 2009, of your January 9, 2009, resubmission to your new drug application for levonorgestrel 1.5 mg tablets.

We consider this a complete, class 2 response to our November 22, 2006, action letter. Therefore, the user fee goal date is July 12, 2009.

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 requirement. We are waiving the requirement for pediatric studies for this application.

If you have any questions, please call Pamela Lucarelli, Regulatory Health Project Manager, at (301) 796-3961.

Sincerely,

*See appended electronic signature*

Jennifer Mercier  
Chief, Project Management Staff  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Jennifer L. Mercier  
1/22/2009 05:18:48 PM

**NDA REGULATORY FILING REVIEW**  
(Including Memo of Filing Meeting)

NDA # 21-998

Supplement #

Efficacy Supplement Type SE-

Proprietary Name: TO BE DETERMINED

Established Name: levonorgestrel

Strengths: 1.5 mg tablet

Applicant: Gedeon Richter, Ltd.

Agent for Applicant (if applicable): Duramed Research, Inc.

Date of Application: January 24, 2006

Date of Receipt: January 24, 2006

Date clock started after UN:

Date of Filing Meeting: February 23, 2006

Filing Date: March 25, 2006

Action Goal Date (optional): November 22, 2006

User Fee Goal Date: November 24, 2006

Indication(s) requested: Emergency Contraception

Type of Original NDA: (b)(1) ☒

(b)(2) ☐

AND (if applicable)

Type of Supplement: (b)(1) ☐

(b)(2) ☐

**NOTE:**

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.

Review Classification: S ☒

P ☐

Resubmission after withdrawal? ☐

Resubmission after refuse to file? ☐

Chemical Classification: (1,2,3 etc.) 1

Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted:

YES ☒ NO ☐

User Fee Status: Paid ☒

Exempt (orphan, government) ☐

Waived (e.g., small business, public health) ☐

**NOTE:** If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES ☒ NO ☐  
If yes, explain: NDA 21-045 Plan B (levonorgestrel), 0.75 mg tablets, approved on 8/24/06.

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity 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 ☐

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- 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 ☐

- Does the submission contain an accurate comprehensive index? YES ☒ NO ☐  
If no, explain:

- 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:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES ☐

2. This application is an eNDA or combined paper + eNDA YES ☐

This application is: All electronic ☐ Combined paper + eNDA ☒  
This application is in: NDA format ☐ CTD format ☐  
Combined NDA and CTD formats ☐

Does the eNDA, follow the guidance?  
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES ☒ NO ☐

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format? All except for the administrative documents.

Additional comments:

3. This application is an eCTD NDA. YES ☐

**If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.**

Additional comments:

- Patent information submitted on form FDA 3542a? 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 should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge . . ."*

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES ☒ NO ☐
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES ☒ NO ☐
- Is this submission a partial or complete response to a pediatric Written Request? YES ☐ NO ☒

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES ☒ NO ☐  
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)  
*NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.*
- Field Copy Certification (that it is a true copy of the CMC technical section) YES ☒ NO ☐
- PDUFA and Action Goal dates correct in tracking system? YES ☒ NO ☐  
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: none
- Are the trade, established/proper, and applicant names correct in COMIS? YES ☐ NO ☒  
If no, have the Document Room make the corrections.
- End-of-Phase 2 Meeting(s)? Date(s) \_\_\_\_\_ NO ☒

If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) January 13, 2006 NO ☐  
If yes, distribute minutes before filing meeting.
- Any SPA agreements? Date(s) \_\_\_\_\_ NO ☒  
If yes, distribute letter and/or relevant minutes before filing meeting.

### Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES ☒ NO ☐  
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:  
Was the PI submitted in PLR format? YES ☐ NO ☒  
  
If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request: NO
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES ☒ NO ☐
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES ☒ NO ☐
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS? N/A ☐ YES ☒ NO ☐
- Risk Management Plan consulted to OSE/IO? N/A ☒ YES ☐ NO ☐
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA ☒ YES ☐ NO ☐

### If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES ☐ NO ☐
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? 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 | <input type="checkbox"/>            | NO | <input type="checkbox"/> |
| If EA submitted, consulted to EA officer, OPS?                   | YES | <input type="checkbox"/>            | NO | <input type="checkbox"/> |
| • Establishment Evaluation Request (EER) submitted to DMPQ?      | YES | <input checked="" type="checkbox"/> | NO | <input type="checkbox"/> |
| • If a parenteral product, consulted to Microbiology Team?       | YES | <input type="checkbox"/>            | NO | <input type="checkbox"/> |

# ATTACHMENT

## MEMO OF FILING MEETING

DATE: February 23, 2006

NDA #: 21-998

DRUG NAMES: levonorgestrel 1.5 mg Tablet

APPLICANT: Gedeon Richter, Ltd.

### BACKGROUND:

Levonorgestrel 1.5 mg tablet is a single-dose progestin-only emergency contraceptive that can be used to prevent pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the tablet should be taken as soon as possible within 72 hours of unprotected intercourse. Levonorgestrel 1.5 mg tablet is the single-dose version of the currently marketed Plan B® (levonorgestrel) tablets, 0.75 mg approved under NDA 21-045 on July 28, 1999.

### ATTENDEES:

Lisa Soule, M.D. – Clinical Team Leader, DRUP  
Daniel Davis, M.D. - Medical Officer, DRUP  
Myong Jin Kim, Ph.D. – Clinical Pharmacology and Biopharmaceutics Reviewer, Office of Clinical Pharmacology and Biopharmaceutics (OCPB)  
Donna Christner, Ph.D.–Pharmaceutical Assessment Lead, Office of New Drug Quality Assessment (ONDQA), Division II, Branch III  
Monica Cooper, Ph.D. – Chemist, ONDQA, Division II, Branch III  
Mahboob Sobhan, Ph.D. – Statistician, Division of Biometrics II (DBII)  
Sonia Castillo, M.S. – Statistician, DBII  
Jennifer Mercier – Chief, Project Management Staff, DRUP

### ASSIGNED REVIEWERS (including those not present at filing meeting) :

#### Discipline/Organization

Medical:  
Secondary Medical:  
Statistical:  
Pharmacology:  
Statistical Pharmacology:  
Chemistry:  
Environmental Assessment (if needed):

#### Reviewer

Daniel Davis  
Lisa Soule  
Sonia Castillo  
Lynnda Reid  
None  
Donna Christner

Biopharmaceutical: Myong Jin Kim  
Microbiology, sterility: None  
Microbiology, clinical (for antimicrobial products only): None  
DSI:  
OPS:  
Regulatory Project Management: Nenita Crisostomo  
Other Consults:

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

CLINICAL FILE ☒ REFUSE TO FILE ☐  
• Clinical site audit(s) needed? YES ☐ NO ☒  
If no, explain:  
• Advisory Committee Meeting needed? YES, date if known \_\_\_\_\_ NO ☒  
• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A ☒ YES ☐ NO ☐

CLINICAL MICROBIOLOGY N/A ☒ FILE ☐ REFUSE TO FILE ☐

STATISTICS N/A ☐ FILE ☒ REFUSE TO FILE ☐

BIOPHARMACEUTICS FILE ☒ REFUSE TO FILE ☐

• Biopharm. study site audits(s) needed? ☒ YES ☐ NO

PHARMACOLOGY/TOX N/A ☐ FILE ☒ REFUSE TO FILE ☐

• GLP audit needed? YES ☐ NO ☒

CHEMISTRY FILE ☒ REFUSE TO FILE ☐

• Establishment(s) ready for inspection? YES ☒ NO ☐  
• Sterile product? YES ☐ NO ☒  
If yes, was microbiology consulted for validation of sterilization? YES ☐ NO ☐

ELECTRONIC SUBMISSION:  
Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:  
(Refer to 21 CFR 314.101(d) for filing requirements.)

- ☐ The application is unsuitable for filing. Explain why:
- ☒ The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.

- ☐ No filing issues have been identified.
- ☒ Filing issues to be communicated by Day 74. List (optional):

**ACTION ITEMS:**

1. ☒ Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2. ☐ If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. ☐ If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4. ☒ If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. ☒ Convey document filing issues/no filing issues to applicant by Day 74.

Nenita Crisostomo, R.N.  
Regulatory Health Project Manager

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/s/

-----  
Nenita Crisostomo  
11/22/2006 12:10:38 PM  
CSO



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

Duramed Research, Inc.  
Attention: Joseph Carrado, M.Sc., R.Ph  
Senior Director, Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your new drug application (NDA) for levonorgestrel tablet, 1.5 mg.

We also refer to your submissions dated August 16, 2006, received August 17, 2006, containing the dissolution profiles. We further refer to your submission dated October 13, 2006, received October 16, 2006, containing the additional dissolution data from the primary and supportive stability studies. Furthermore, we refer to our written communication to you dated October 16, 2006, containing our recommendation to revise your dissolution specifications.

We also refer to the teleconference on October 17, 2006,

BETWEEN:

**Duramed Research/Gideon Richter:**

Michelle Walsh – Manager, Regulatory Affairs

Mr. Balázs Lázár, Regulatory Affairs

Ms. Emese Korbuly, Manager of Department, Regulatory Affairs

AND

**Food and Drug Administration:**

Donna Christner, Ph.D. - Pharmaceutical Assessment Lead, Division of Premarketing  
Assessment II (DPMA II), Branch III, Office of New Drug Quality Assessment  
(ONDQA)

Monica Cooper, Ph.D. - Chemist, DPMA II, Branch III, ONDQA

Nenita Crisostomo, R.N. - Regulatory Health Project Manager, Division of Regulatory  
Health Project Manager

As discussed during the teleconference, based on the dissolution data and profiles provided, the Agency commented that the 30-minute time point is appropriate for evaluating dissolution of your drug product. The teleconference concluded with your agreement to submit to the NDA your revised drug product dissolution specifications to reflect an acceptance criterion of not less than Q at 30 minutes.

**b(4)**

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager at 301-796-0875.

Sincerely,

*{See appended electronic signature page}*

Donna Christner, Ph.D.  
Pharmaceutical Assessment Lead  
Division of Premarketing Assessment II, Branch III  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

-----  
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/s/

-----  
Donna Christner  
11/14/2006 04:08:34 PM  
I concur



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

**INFORMATION REQUEST LETTER**

Duramed Research, Inc.  
Attention: Joseph Carrado, M.Sc., R.Ph.  
Vice President, Clinical Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your January 24, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel tablets, 1.5 mg.

We also refer to your amendment to the Statistical Report on WHO Study 97902 dated June 13, 2006.

We are reviewing the Clinical 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.

Recalculate the following tables from the Summary of Clinical Efficacy, restricting the population analyzed to the subset of women who presented for emergency contraception from 0 to 72 hours after unprotected intercourse:

Tables 1, 5 - 8, (Table 8 may be recalculated for full ITT population only), Table 9

We presume that the first three tables (pages 2-3) of the Final Study Report Amendment 1, dated June 13, 2006, represent the data from Tables 2-4 in the Summary of Clinical Efficacy when analysis is restricted to those women presenting within 72 hours of unprotected intercourse. If this is not the case, please provide recalculated Tables 2-4 as described above.

In addition, populate the following cells or tables we have derived from your summary, based on the subset of women who presented for emergency contraception from 0 to 72 hours after unprotected intercourse:

**Clinical Studies Populations**

| Trial               | WHO Study 97902 |           | Nigerian Study |          |
|---------------------|-----------------|-----------|----------------|----------|
|                     | Single dose     | Two dose  | Single dose    | Two dose |
| Safety population   | 1,356           | 1,356     | 550            | 600      |
| Efficacy population | (fill in)       | (fill in) | 545            | 573      |
|                     |                 |           |                |          |

**Patient Populations**

| Patient Populations          | Group 1<br>Single dose | Group 2<br>Two dose |
|------------------------------|------------------------|---------------------|
|                              |                        |                     |
| Enrolled initially           |                        |                     |
| Lost or non-evaluable        |                        |                     |
|                              |                        |                     |
| Full ITT (completed study)   |                        |                     |
| Protocol Violations          |                        |                     |
| >120 hrs post coitus         | N/A                    | N/A                 |
| Abnormal cycle length        |                        |                     |
| Rhythm method used           |                        |                     |
| Further acts of coitus       |                        |                     |
|                              |                        |                     |
| Restricted ITT               |                        |                     |
| Treatment non-compliance     |                        |                     |
|                              |                        |                     |
| Per Protocol Population (PP) |                        |                     |

**Efficacy Results by Age Groups (Full ITT Population)**

|                                | N | Observed Pregnancies |          |          | Expected Pregnancies |         |          |
|--------------------------------|---|----------------------|----------|----------|----------------------|---------|----------|
|                                |   | n                    | Rate (%) | 95% C.I. | n                    | PF* (%) | 95% C.I. |
| <b>35 Years of Age or Less</b> |   |                      |          |          |                      |         |          |
| Levonorgestrel 1.5 mg × 1      |   |                      |          |          |                      |         |          |
| Levonorgestrel 0.75 mg × 2     |   |                      |          |          |                      |         |          |
| <b>36 Years of Age or More</b> |   |                      |          |          |                      |         |          |
| Levonorgestrel 1.5 mg × 1      |   |                      |          |          |                      |         |          |
| Levonorgestrel 0.75 mg × 2     |   |                      |          |          |                      |         |          |

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at 301-796-0875.

Sincerely,

*{See appended electronic signature page}*

Jennifer Mercier  
Chief, Project Management Staff  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Jennifer L. Mercier  
11/7/2006 04:27:01 PM

**Crisostomo, Nenita**

---

**From:** Crisostomo, Nenita  
**Sent:** Monday, November 06, 2006 4:19 PM  
**To:** 'Walsh, Michele'  
**Subject:** RE: NDA 21998 3-month safety update

Michele,

As discussed on the phone earlier, I will look forward to your submission. Here is an additional advise I got that might help with this Safety Update submission:

The sponsor is required to submit a 120 safety update prior to the action date but no older than 4 months for their product. In that update the sponsor is required to submit any additional safety information pertaining to their product. They can cross reference the NDA for the original product (Plan B) to give information on levonorgestrel. They are also required to send us information on ongoing trials with this (1.5) product and anything that could be useful to assess the safety of the product and active ingredient.

Pls call if you have any questions.

Thanks!  
nita

---

**From:** Walsh, Michele [mailto:MWalsh@barriabs.com]  
**Sent:** Monday, November 06, 2006 3:21 PM  
**To:** Crisostomo, Nenita  
**Subject:** RE: NDA 21998 3-month safety update

21998 is not approved. There is no 3-month safety update.

-----Original Message-----

**From:** Crisostomo, Nenita [mailto:nenita.crisostomo@fda.hhs.gov]  
**Sent:** Monday, November 06, 2006 3:04 PM  
**To:** Walsh, Michele  
**Subject:** NDA 21998 3-month safety update

Michelle,

I can't seem to find the official submission for this. Please help & advise if has been submitted. If not, could you please submit it to the NDA?

Thanks so much for all your help, Michele.

--nita

*Nenita Crisostomo, RN  
Regulatory Health Project Manager  
U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Reproductive and Urologic Products  
Telephone: 301-796-0875*

11/19/2006

***Fax: 301-796-9897***

**11/19/2006**



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

Duramed Research, Inc.  
Attention: Joseph A. Carrado, M.Sc., R.Ph  
Senior Director, Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your January 24, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel 1.5 mg.

We also refer to your submission dated July 14, 2006, containing your proposed trade names.

In conjunction with the Division of Medication Errors and Technical Support (DMETS), we have reviewed your submission, and we have the following comments. We also acknowledge that many of these comments may need to be modified should the Agency take the position that levonorgestrel 1.5 mg cannot be a prescription product for women 18 years of age and older.

**A. TRADE NAME**

1. Plan B and Plan B

b(4)

There is concern that 'Plan B' or 'Plan B' may be confused with the currently marketed product 'Plan B'. This potential confusion can occur as long as Plan B continues to be marketed. The modifiers or may not convey to patients and healthcare providers that what is intended to be prescribed is a different drug product (levonorgestrel 1.5 mg) with a higher strength per tablet (1.5 mg levonorgestrel vs. 0.75 mg) and a different dosing frequency (one tablet vs. two tablets taken 12 hours apart). Since the dosage strengths and dosing regimen vary between the existing marketed product (Plan B) and the proposed product (levonorgestrel 1.5 mg), a woman dispensed Plan B might take a subtherapeutic dose, were she told to take a single tablet as soon as possible. The ramifications of this error would be that the woman might not obtain the desired effect of emergency contraception.

2.

b(4)

The name  may be confused with dosage instructions, such as "STAT." Utilizing a name that is associated with a common administration term may produce confusion. Additionally, according to DMETS, the Agency has not allowed sponsors to use names that are "instructional". A pharmacist who receives a prescription for

b(4)

—— UD [as directed]” may be led to believe that the prescriber omitted the drug name by mistake. DMETS is concerned that this will necessitate further clarification with the prescriber and might lead to a delay in administration. Failure to receive the drug within 72 hours may increase the likelihood of an unwanted pregnancy.

For the aforementioned reasons, DMETS does not recommend the use of the proposed proprietary names, ‘Plan B —— or ‘Plan B ——.

b(4)

3. Alternative Proposal:

We recommend that you consider retaining the name “Plan B” for the 1.5 mg, single dose product. The strength (1.5 mg) should appear prominently on labels and labeling to differentiate this product from the 0.75 mg Plan B product, which is available over the counter (OTC) for women over 18 and by prescription (Rx) for women 18 and under. The packaging of the 1.5 mg product should also be distinctly different from the OTC/Rx packaging of the 0.75 mg product. We further recommend that the labeling for the 0.75 mg product be revised to give increased prominence to the dosage strength; however, this change in labeling may wait until the next print date.

B. LABELING

1. General Comment

- a. Revise the labels, including carton, and insert labeling so that the stated name. ——  
—— is replaced with the proprietary name approved with this application.

b(4)

2. Carton Labeling

- a. The purple font color used for the text, contrasted with the bluish background color is difficult to read. Revise the background color to improve the readability or use a darker font color so that the background color is contrasted with the color used for the text.
- b. The product strength and dosage form “tablet” is printed in smaller font beneath the established name and is difficult to read. Increase the prominence of the strength and dosage form so that it appears as the same size as “Levonorgestrel.”
- c. The strength appears with the proprietary and established name. In its current presentation, the “1.5 mg” looks as if it is part of the proprietary name. Revise the labeling so that the strength appears immediately following the established name, not the proposed proprietary name.
- d. A graphic design is present on the label. This graphic item appears more prominent than the proprietary and established names, whereas the names and strength should appear most prominently on the labels and labeling. Therefore, we recommend removing this graphic design or at a minimum, decreasing the size so that the proprietary and established names and strength are the most prominent information on the labels and labeling.
- e. A purple oval-like circle appears on the back panel of the carton labeling with the instructions, ——

We recommend adding “Recommended dosage:” in the oval

b(4)

immediately preceding the administration instructions.



b(4)

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at 301-796-0875.

Sincerely,

*{See appended electronic signature page}*

Jennifer Mercier  
Chief, Project Management Staff  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

-----  
Jennifer L. Mercier  
11/6/2006 10:09:01 AM

**Crisostomo, Nenita**

---

**From:** Walsh, Michele [MWalsh@barriabs.com]  
**Sent:** Wednesday, November 01, 2006 1:43 PM  
**To:** Crisostomo, Nenita  
**Subject:** RE: NDA 21998: Debarment Certification  
**Attachments:** 21-998 Revised Debarment Cert.pdf

Here is it.... I will make an official paper submission to the NDA today

-----Original Message-----

**From:** Crisostomo, Nenita [mailto:nenita.crisostomo@fda.hhs.gov]  
**Sent:** Wednesday, November 01, 2006 1:42 PM  
**To:** Walsh, Michele  
**Subject:** NDA 21998: Debarment Certification

Hi Michelle,

Last week, Jen spoke to Joe Carrado regarding the need to revise the Debarment Certification to include the signature of both Joe & Gedeon Richter. It has only Joe's right now. So Joe said he'll to send a revised one. Just following up on the status on when we may be expecting the submission. Thanks so much and have a nice day!

--nita

*Nenita Crisostomo, RN  
Regulatory Health Project Manager  
U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Reproductive and Urologic Products  
Telephone: 301-796-0875  
Fax: 301-796-9897*



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

**NDA 21-998**

**INFORMATION REQUEST LETTER**

Duramed Research, Inc.  
Attention: Joseph A. Carrado, M.Sc., R.Ph  
Senior Director, Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your January 24, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for levonorgestrel 1.5 mg tablets.

We are reviewing the Clinical 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.

For the full intent to treat (ITT) and the restricted ITT populations in both the single dose and two dose levonorgestrel groups, for each 24 hr interval (from 1 through 5 days), provide the following information:

- the number of subjects in the time interval,
- the expected number of pregnancies,
- the observed number of pregnancies, and
- the prevented fraction with the 95% confidence intervals.

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at 301-796-0875.

Sincerely,

*{See appended electronic signature page}*

Jennifer Mercier  
Chief, Project Management Staff  
Division of Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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-----  
Jennifer L. Mercier  
10/25/2006 01:00:49 PM

**END OF DOCUMENT INFORMATION PAGE**

The Fax begins on the next page.



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation ODEIII

**FACSIMILE TRANSMITTAL SHEET****DATE: October 16, 2006**

**To:** Joseph A. Carrado, M.Sc., R.Ph.  
Vice President, Clinical Regulatory Affairs  
C/O Michelle Walsh

**From:** Nenita Crisostomo, R.N.  
Regulatory Health Project Manager

**Company:** Duramed Research, Inc.

Division of Reproductive and Urologic  
Products

**Fax number:** 610-747-2979

**Fax number:** 301-796-0875

**Phone number:** 610-747-2910

**Phone number:** 301-796-0875

**Subject:** Discipline Review Completed for NDA 21-998  
NDA 21998: levonorgestrel 1.5 mg--CMC Advice regarding Dissolution

**Total no. of pages including cover:** 3

**Comments:**

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

**Document to be mailed:**☐ YES☒ NO

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If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2130. Thank you.

**NDA 21-998 Levenorgestrel 1.5 mg  
Recommendations  
Chemistry, Manufacturing and Controls  
October 16, 2006**

- Based on the dissolution profiles provided in your Amendment dated August 16, 2006, and on the additional dissolution data provided from the primary and supportive stability studies in your Amendment dated October 13, 2006, the 30-minute time point is the appropriate time point for evaluating dissolution of your drug product. Revise your drug product dissolution specifications to reflect an acceptance criterion of not less than ~~Q~~ (Q) at 30 minutes. A copy of the revised drug product specification table should be submitted showing this change. Please reply on or before October 20, 2006.

b(4)

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/s/

-----  
Nenita Crisostomo

10/16/2006 02:43:03 PM

CSO

**Crisostomo, Nenita**

---

**From:** Walsh, Michele [MWalsh@barrlabs.com]  
**Sent:** Wednesday, September 27, 2006 9:45 AM  
**To:** Crisostomo, Nenita  
**Cc:** Carrado, Joseph; Pakulski, John; Hummel, Amy; Coriolan, Markens; Faries, Wendy; Smith, Tamara  
**Subject:** RE: NDA 21998: Request for WORD documents  
**Attachments:** 2.7.3 summary of clinical efficacy updated 1-17-2006.doc; 2.7.4 summary of clinical safety re-updated 1-17-2006.doc

As requested.....

-----Original Message-----

**From:** Crisostomo, Nenita [mailto:nenita.crisostomo@fda.hhs.gov]  
**Sent:** Tuesday, September 26, 2006 6:42 PM  
**To:** Walsh, Michele  
**Subject:** NDA 21998: Request for WORD documents

Hi Michelle,

We'd like to ask you a big favor. Could you please send a Word copy of 2.7.3 and 2.7.4, the Summaries of Clinical Efficacy and Clinical Safety?

We'd appreciate it very much...

Thanks & Regards,  
nita

*Nenita Crisostomo, RN  
Regulatory Health Project Manager  
U.S. Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Reproductive and Urologic Products  
Telephone: 301-796-0875  
Fax: 301-796-9897*

11/19/2006



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: September 25, 2006

|                                                                                                                                                                         |                                                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| To: Joseph A. Carrado, M.Sc., R.Ph.—Vice President,<br>Clinical Regulatory Affairs<br>C/O Michelle Walsh—Manager, Regulatory Affairs<br>Company: Duramed Research, Inc. | Nenita Crisostomo, R.N.<br>From: Regulatory Health Project Manager<br>Division of Reproductive and Urologic<br>Products |
| Fax number: 610-747-2979                                                                                                                                                | Fax number: 301-796-9897                                                                                                |
| Phone number: 610-747-2600                                                                                                                                              | Phone number: 301-796-0875                                                                                              |
| Subject: Discipline Review Completed for NDA 21-998<br>NDA 21-998: Levonorgestrel 1.5 mg--ClinPharm Information Request                                                 |                                                                                                                         |

Total no. of pages including cover: 3

Dear Mr. Carrado:

We are currently reviewing your NDA submission and, as attached, we have the following requests for additional information. Please respond on or before September 26, 2006. If you have any questions, please contact me at 301-796-0875.

Thank you very much,

Nenita Crisostomo, RN  
Regulatory Health Project Manager

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

Document to be mailed: ☐ YES ☒ NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2130. Thank you.

**NDA 21-998 Levonorgestrel 1.5 mg  
Information Requests  
Clinical Pharmacology  
September 25, 2006**

- 1) Study 2990 was a bioequivalence study of LNG 1 x 1.5 mg tablet (without gelatin) versus Plan B 2 x 0.75 mg tablets in healthy female subjects. The currently approved Plan B product contains gelatin. Confirm that the Plan B 0.75 mg product used in this bioequivalence study contains gelatin and that they are the same product as the currently approved Plan B product.
- 2) Study 02162 was a relative bioavailability study of LNG 1 x 1.5 mg tablet (without gelatin) versus Postinor-2 1 x 0.75 mg given twice daily in healthy female subjects. On March 2006, you confirmed that Postinor-2 and Plan B are the same products. Confirm that the Postinor-2 product used in Study 02162 contains gelatin.

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/s/

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Nenita Crisostomo  
9/25/2006 12:03:14 PM  
CSO



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: September 8, 2006

|                                                                                                   |                                                                     |
|---------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|
| <b>To:</b> Joseph A. Carrado<br>Vice President, Clinical Regulatory Affairs<br>C/O Michelle Walsh | <b>From:</b> Nenita Crisostomo<br>Regulatory Health Project Manager |
| <b>Company:</b> Duramed Research, Inc.                                                            | Division of Reproductive and Urologic<br>Products                   |
| <b>Fax number:</b> 610-747-2979                                                                   | <b>Fax number:</b> 301-796-9897                                     |
| <b>Phone number:</b> 610-747-2910                                                                 | <b>Phone number:</b> 301-796-0875                                   |

**Subject:** NDA 21998: Levonorgestrel 1.5 mg: Request for Information--Dissolution Data

**Total no. of pages including cover:** 2

Dear Mr. Carrado:

- On or before the end of September 2006, please provide all available dissolution data at the 30-minute time point for the primary drug product batches (T36296, T36297, and T36298) and supportive drug product batches (T24157, T24158, T24159) collected throughout the stability studies.

If you have any questions, please feel free to contact me by phone @ 301-796-0875 or email @ [nenita.crisostomo@fda.hhs.gov](mailto:nenita.crisostomo@fda.hhs.gov).

Thank you very much,

Nenita Crisostomo

We are requesting for these additional information from you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these requests do not reflect a final decision on the information reviewed and should not be construed to do so. These are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

**Document to be mailed:**

☐ YES

☒ NO

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If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2130. Thank you.

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Nenita Crisostomo  
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|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|------------------------------------|
| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |         | <h2 style="margin: 0;">REQUEST FOR CONSULTATION</h2>                                                                                                                                    |                                              |                                    |
| TO (Division/Office):<br><b>Director, Division of Medication Errors and Technical Support (DMETS), HFD-420<br/>         WO22, RM 4447</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         | FROM: Nenita Crisostomo, R.N.<br>Division of Reproductive and Urologic Products<br>HFD 580, Ph: 301-796-0875                                                                            |                                              |                                    |
| DATE<br>8/4/06                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | IND NO. | NDA NO.<br>21-998                                                                                                                                                                       | TYPE OF DOCUMENT<br>Trade Name Proposal      | DATE OF DOCUMENT<br>7/14/06        |
| NAME OF DRUG<br>Levonorgestrel 1.5 mg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         | PRIORITY CONSIDERATION                                                                                                                                                                  | CLASSIFICATION OF DRUG<br>Oral Contraceptive | DESIRED COMPLETION DATE<br>10/4/06 |
| NAME OF FIRM: Gedeon Richter, Ltd (Regulatory Agent: Duramed Research)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         |                                                                                                                                                                                         |                                              |                                    |
| <b>REASON FOR REQUEST</b><br><b>I. GENERAL</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |                                                                                                                                                                                         |                                              |                                    |
| <div style="display: flex; flex-wrap: wrap;"> <div style="width: 33%;"> <input type="checkbox"/> NEW PROTOCOL<br/> <input type="checkbox"/> PROGRESS REPORT<br/> <input type="checkbox"/> NEW CORRESPONDENCE<br/> <input type="checkbox"/> DRUG ADVERTISING<br/> <input type="checkbox"/> ADVERSE REACTION REPORT<br/> <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION<br/> <input type="checkbox"/> MEETING PLANNED BY         </div> <div style="width: 33%;"> <input type="checkbox"/> PRE-NDA MEETING<br/> <input type="checkbox"/> END OF PHASE II MEETING<br/> <input type="checkbox"/> RESUBMISSION<br/> <input type="checkbox"/> SAFETY/EFFICACY<br/> <input type="checkbox"/> PAPER NDA<br/> <input type="checkbox"/> CONTROL SUPPLEMENT         </div> <div style="width: 33%;"> <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER<br/> <input type="checkbox"/> FINAL PRINTED LABELING<br/> <input type="checkbox"/> LABELING REVISION<br/> <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE<br/> <input type="checkbox"/> FORMULATIVE REVIEW<br/> <input type="checkbox"/> OTHER (SPECIFY BELOW): <b>Trade name review</b> </div> </div> |         |                                                                                                                                                                                         |                                              |                                    |
| <b>II. BIOMETRICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |                                                                                                                                                                                         |                                              |                                    |
| STATISTICAL EVALUATION BRANCH                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         | STATISTICAL APPLICATION BRANCH                                                                                                                                                          |                                              |                                    |
| <input type="checkbox"/> TYPE A OR B NDA REVIEW<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> CONTROLLED STUDIES<br><input type="checkbox"/> PROTOCOL REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |         | <input type="checkbox"/> CHEMISTRY REVIEW<br><input type="checkbox"/> PHARMACOLOGY<br><input type="checkbox"/> BIOPHARMACEUTICS<br><input type="checkbox"/> OTHER (SPECIFY BELOW):      |                                              |                                    |
| <b>III. BIOPHARMACEUTICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |         |                                                                                                                                                                                         |                                              |                                    |
| <input type="checkbox"/> DISSOLUTION<br><input type="checkbox"/> BIOAVAILABILITY STUDIES<br><input type="checkbox"/> PHASE IV STUDIES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE<br><input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS<br><input type="checkbox"/> IN-VIVO WAIVER REQUEST                            |                                              |                                    |
| <b>IV. DRUG EXPERIENCE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |                                                                                                                                                                                         |                                              |                                    |
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL<br><input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES<br><input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)<br><input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY<br><input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE<br><input type="checkbox"/> POISON RISK ANALYSIS |                                              |                                    |
| <b>V. SCIENTIFIC INVESTIGATIONS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                                                                                                                                                                         |                                              |                                    |
| <input type="checkbox"/> CLINICAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |         | <input type="checkbox"/> PRECLINICAL                                                                                                                                                    |                                              |                                    |
| COMMENTS/SPECIAL INSTRUCTIONS: Please review the Sponsor's proposal for Trade Names listed in order of preference, as per attached submission: 1) Plan B —, 2) Plan B — 3) — Please note the PDUFA Goal Date for this NDA is November 17, 2006. For your convenience, the attached container label and the Package Insert, similar to those provided to you on 3/30/06, are also located in EDR: \\CDSESUB1\N21998\N_000\2006-01-24. If you have any questions, please feel free to contact me at 301-796-0875.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |         |                                                                                                                                                                                         |                                              |                                    |
| Thank you,<br>Nita Crisostomo, RPM                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                                                                                                                                                                         |                                              |                                    |
| PDUFA DATE: 11/17/06<br>ATTACHMENTS: Draft Package Insert, Container and Carton Labels<br>CC: Archival IND/NDA 21998<br>HFD-580/Division File<br>HFD-580/RPM<br>HFD-580/Reviewers and Team Leaders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                                                                                                                                                                         |                                              |                                    |

b(4)

|                                    |                                                                                                                                            |
|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| NAME AND PHONE NUMBER OF REQUESTER | METHOD OF DELIVERY (Check one)<br><input checked="" type="checkbox"/> DFS ONLY <input type="checkbox"/> MAIL <input type="checkbox"/> HAND |
| SIGNATURE OF RECEIVER              | SIGNATURE OF DELIVERER                                                                                                                     |

5/28/05



A subsidiary of Barr Pharmaceuticals, Inc.

**Duramed Research, Inc.**  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004  
(610) 747-2600

July 14, 2006

Scott Monroe, MD  
Acting Director, Division of Reproductive and Urologic Products  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Central Document Room  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

**NDA 21-998**  
**Levonorgestrel 1.5mg Tablet**

Other: Submission of Proposed Trade Names

Dear Dr. Monroe:

Reference is made to NDA 21-998 Levonorgestrel 1.5 mg tablet for Emergency Contraception, NDA 21-998 filed to the Division of Reproductive and Urologic Products on January 24, 2006 by Duramed Research, Inc, a subsidiary of Barr Pharmaceuticals, Inc. and regulatory agent for Gedeon Richter, Ltd of Budapest, Hungary.

The following are the proposed choices for the Levonorgestrel 1.5 mg Tablet Trade Name:

1. Plan B \_\_\_\_\_
  2. Plan B \_\_\_\_\_
  3. \_\_\_\_\_
- b(4)

Please contact Michele Walsh (610-747-2644) or the undersigned at (610) 747-2910 if you have any questions or comments.

Sincerely,  
**Duramed Research, Inc.**

A handwritten signature in black ink, appearing to read "J. Carrado".

Joseph A. Carrado, M.Sc., R.Ph.  
Vice President  
Clinical Regulatory Affairs

10 Page(s) Withheld

       Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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/s/

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Nenita Crisostomo  
8/5/2006 02:45:18 PM



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-998

**INFORMATION REQUEST LETTER**

Duramed Research, Inc.  
Agent for: Gedeon Richter, Ltd.  
Attention: Joseph A. Carrado, M.Sc., R.Ph  
Vice-President, Clinical Regulatory Affairs  
One Belmont Avenue, 11th Floor  
Bala Cynwyd, PA 19004

Dear Mr. Carrado:

Please refer to your January 24, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Levonorgestrel 1.5 mg Tablets.

We also refer to your submission dated June 20, 2006.

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. Please provide a commitment to place annual production batches of the drug product on stability studies according to your long-term stability protocol.
2. With respect to the container/carton label, the list of inactive ingredients includes gelatin. Since the new formulation does not contain gelatin, please correct this error. In addition, there is a typo under the section "How effective is \_\_\_\_\_" – on the last line, the word "unprotected" is misspelled. Also, please indicate where the lot number and expiration date will be printed.
3. We received your response to the CMC item in the 74-Day Letter regarding dissolution profile data. However, the information that you referenced in the pharmaceutical development report was not the information we were requesting. On page 3 of Section 3.2.P.5.6 *Justification of Specifications*, you state that the new dissolution specifications for Levonorgestrel 1.5 mg tablets were based on dissolution profile data obtained from three batches of Levonorgestrel 1.5 mg tablets. Please provide the dissolution profile data from these three batches to support the dissolution release specification of NLT \_\_\_\_\_ (Q) at \_\_\_\_\_

b(4)

b(4)

**If you have any questions, call Kassandra Sherrod, R.Ph., Regulatory Project Manager, at 301-796-2130.**

**Sincerely,**

**Moo-Jhong Rhee, Ph.D.**  
**Chief, Branch III**  
**Pre-Marketing Assessment Division II**  
**Office of New Drug Quality Assessment**  
**Center for Drug Evaluation and Research**

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/s/

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Moo-Jhong Rhee  
7/11/2006 12:14:38 PM  
Chief, Branch III



**Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation ODEIII**

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** June 12, 2006

|                                                                                                 |                                                                           |
|-------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| <b>To:</b> Joseph A. Carrado, c/o Michelle Walsh<br>Vice President, Clinical Regulatory Affairs | <b>From:</b> Nenita Crisostomo, R.N.<br>Regulatory Health Project Manager |
| <b>Company:</b> Duramed Research, Inc.                                                          | Division of Reproductive and Urologic<br>Products                         |
| <b>Fax number:</b> 610-747-2979                                                                 | <b>Fax number:</b> 301-796-9897                                           |
| <b>Phone number:</b> 610-747-2910                                                               | <b>Phone number:</b> 301-796-0875                                         |
| <b>Subject:</b> NDA 21-998 levonorgestrel 1.5 mg tablet: Statistical Information Request        |                                                                           |

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**Total no. of pages including cover:** 2

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**Comments:**

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

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**Document to be mailed:**

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**Information Request for NDA 21,998 Levonorgestrel 1.5 mg Tablet**  
**June 12, 2006**

1. Provide subgroup analyses of the primary efficacy outcomes for the following two groups:
  - Subjects 35 years of age or less
  - Subjects 36 years of age or more
2. Provide the rationale for classifying the following subjects as not "on treatment pregnancies" even though their follow-up urine pregnancy test results were positive:

Subject numbers (SAS dataset variable SUBJNN) - 10023, 10222, 13260378

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/s/

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Nenita Crisostomo  
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Nenita Crisostomo  
6/12/2006 05:49:29 PM  
CSO

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| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         |                                    | <h2 style="margin: 0;">REQUEST FOR CONSULTATION</h2>                                                                                                                                    |                                          |
| TO (Division/Office):<br><b>Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 WO22, RM 4447</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                    | FROM: Nenita Crisostomo, RN, Regulatory Health Project Manager, Division of Reproductive and Urologic Products---Ph: 301-796-0875                                                       |                                          |
| DATE<br>March 30, 2006                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | IND NO. | NDA NO.<br>21-998                  | TYPE OF DOCUMENT<br>Package Insert, container & carton labeling                                                                                                                         | DATE OF DOCUMENT<br>January 24, 2006     |
| NAME OF DRUG<br>Levonorgestrel 1.5 mg Tablet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         | PRIORITY CONSIDERATION<br>standard | CLASSIFICATION OF DRUG<br>Progestin--oral contraceptive                                                                                                                                 | DESIRED COMPLETION DATE<br>June 30, 2006 |
| NAME OF FIRM: Gedeon Richter, Ltd.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |         |                                    |                                                                                                                                                                                         |                                          |
| <b>REASON FOR REQUEST</b><br><b>I. GENERAL</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |         |                                    |                                                                                                                                                                                         |                                          |
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| <b>II. BIOMETRICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |                                    |                                                                                                                                                                                         |                                          |
| STATISTICAL EVALUATION BRANCH                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                    | STATISTICAL APPLICATION BRANCH                                                                                                                                                          |                                          |
| <input type="checkbox"/> TYPE A OR B NDA REVIEW<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> CONTROLLED STUDIES<br><input type="checkbox"/> PROTOCOL REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |                                    | <input type="checkbox"/> CHEMISTRY REVIEW<br><input type="checkbox"/> PHARMACOLOGY<br><input type="checkbox"/> BIOPHARMACEUTICS<br><input type="checkbox"/> OTHER (SPECIFY BELOW):      |                                          |
| <b>III. BIOPHARMACEUTICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> DISSOLUTION<br><input type="checkbox"/> BIOAVAILABILITY STUDIES<br><input type="checkbox"/> PHASE IV STUDIES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |                                    | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE<br><input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS<br><input type="checkbox"/> IN-VIVO WAIVER REQUEST                            |                                          |
| <b>IV. DRUG EXPERIENCE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL<br><input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES<br><input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)<br><input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |         |                                    | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY<br><input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE<br><input type="checkbox"/> POISON RISK ANALYSIS |                                          |
| <b>V. SCIENTIFIC INVESTIGATIONS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> CLINICAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |                                    | <input type="checkbox"/> PRECLINICAL                                                                                                                                                    |                                          |
| COMMENTS/SPECIAL INSTRUCTIONS:<br><br>Attached are the Package Insert, Container and Carton Labels for your review. The documents can also be found in EDR at this site: \\Cdsub1\n21998\N_000\2006-01-24\labeling. If you have any questions, please feel free to contact me.<br><br>Thank you very much for your kind assistance.<br><br>Nita Crisostomo<br><br><b>PDUFA DATE: 11/24/06</b><br><b>ATTACHMENTS:</b> Draft Package Insert, Container and Carton Labels<br><b>CC:</b> Archival IND/NDA 21-998<br>HFD-580/Division File                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |                                    |                                                                                                                                                                                         |                                          |

|                                                                               |                                                                                                                                            |
|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| HFD-580/RPM<br>HFD-580/Reviewers and Team Leaders                             |                                                                                                                                            |
| NAME AND PHONE NUMBER OF REQUESTER<br>Nenita Crisostomo, RN--Ph: 301-796-0875 | METHOD OF DELIVERY (Check one)<br><input checked="" type="checkbox"/> DFS ONLY <input type="checkbox"/> MAIL <input type="checkbox"/> HAND |
| SIGNATURE OF RECEIVER                                                         | SIGNATURE OF DELIVERER                                                                                                                     |

5/28/05

10 Page(s) Withheld

       Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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

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Nenita Crisostomo  
3/30/2006 02:17:01 PM

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |         |                                    |                                                                                                                                                                                         |                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |         |                                    | <b>REQUEST FOR CONSULTATION</b>                                                                                                                                                         |                                          |
| TO (Division/Office):<br><b>Mail: ODS: Division of Surveillance, Research, and Communication Support</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |                                    | FROM: Nenita Crisostomo, Regulatory Health Project Manager<br>Division of Reproductive and Urologic Products<br>Ph. 301-796-0875                                                        |                                          |
| DATE<br>March 24, 2006                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | IND NO. | NDA NO.<br>21-998                  | TYPE OF DOCUMENT<br><b>Patient Information</b>                                                                                                                                          | DATE OF DOCUMENT<br>January 24, 2006     |
| NAME OF DRUG<br>Levonorgestrel 1.5 mg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         | PRIORITY CONSIDERATION<br>Standard | CLASSIFICATION OF DRUG<br>Oral Contraception                                                                                                                                            | DESIRED COMPLETION DATE<br>June 24, 2006 |
| NAME OF FIRM: Gedeon Richter, Ltd.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                    |                                                                                                                                                                                         |                                          |
| <b>REASON FOR REQUEST</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |                                    |                                                                                                                                                                                         |                                          |
| <b>I. GENERAL</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> NEW PROTOCOL<br><input type="checkbox"/> PROGRESS REPORT<br><input type="checkbox"/> NEW CORRESPONDENCE<br><input type="checkbox"/> DRUG ADVERTISING<br><input type="checkbox"/> ADVERSE REACTION REPORT<br><input type="checkbox"/> MANUFACTURING CHANGE/ADDITION<br><input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> RESUBMISSION<br><input type="checkbox"/> SAFETY/EFFICACY<br><input type="checkbox"/> PAPER NDA<br><input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER<br><input type="checkbox"/> FINAL PRINTED LABELING<br><input type="checkbox"/> LABELING REVISION<br><input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE<br><input type="checkbox"/> FORMULATIVE REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW): |         |                                    |                                                                                                                                                                                         |                                          |
| <b>II. BIOMETRICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         |                                    |                                                                                                                                                                                         |                                          |
| STATISTICAL EVALUATION BRANCH                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |                                    | STATISTICAL APPLICATION BRANCH                                                                                                                                                          |                                          |
| <input type="checkbox"/> TYPE A OR B NDA REVIEW<br><input type="checkbox"/> END OF PHASE II MEETING<br><input type="checkbox"/> CONTROLLED STUDIES<br><input type="checkbox"/> PROTOCOL REVIEW<br><input type="checkbox"/> OTHER (SPECIFY BELOW):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                    | <input type="checkbox"/> CHEMISTRY REVIEW<br><input type="checkbox"/> PHARMACOLOGY<br><input type="checkbox"/> BIOPHARMACEUTICS<br><input type="checkbox"/> OTHER (SPECIFY BELOW):      |                                          |
| <b>III. BIOPHARMACEUTICS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> DISSOLUTION<br><input type="checkbox"/> BIOAVAILABILITY STUDIES<br><input type="checkbox"/> PHASE IV STUDIES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         |                                    | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE<br><input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS<br><input type="checkbox"/> IN-VIVO WAIVER REQUEST                            |                                          |
| <b>IV. DRUG EXPERIENCE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL<br><input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES<br><input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)<br><input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |                                    | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY<br><input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE<br><input type="checkbox"/> POISON RISK ANALYSIS |                                          |
| <b>V. SCIENTIFIC INVESTIGATIONS</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |         |                                    |                                                                                                                                                                                         |                                          |
| <input type="checkbox"/> CLINICAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |         |                                    | <input type="checkbox"/> PRECLINICAL                                                                                                                                                    |                                          |
| COMMENTS/SPECIAL INSTRUCTIONS:<br><br><b>Please review the Patient Information, printed on the carton container, as attached. The PDUFA Goal date is November 24, 2006. The submission is fully electronic and may be found in this website: \\Cdsub1\21998\N_000\2006-01-24\labeling</b><br><br><b>If you have any questions, please do not hesitate to contact me at 301-796-0875. Thank you very much for your assistance.</b><br><br><b>Nenita Crisostomo, RN</b><br><b>Project Manager</b>                                                                                                                                                                                                                                                                                                                                                                                                                                     |         |                                    |                                                                                                                                                                                         |                                          |
| SIGNATURE OF REQUESTER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |                                    | METHOD OF DELIVERY (Check one)<br><input type="checkbox"/> MAIL <input checked="" type="checkbox"/> ELECTRONIC <input type="checkbox"/> HAND                                            |                                          |
| SIGNATURE OF RECEIVER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         |                                    | SIGNATURE OF DELIVERER                                                                                                                                                                  |                                          |