

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-214

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

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

NDA NUMBER

22-214

NAME OF APPLICANT / NDA HOLDER

AstraZeneca UK Limited

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

TRADE NAME (OR PROPOSED TRADE NAME)

ARIMIDEX anastrozole Tablets

ACTIVE INGREDIENT(S)

anastrozole

STRENGTH(S)

1 mg

DOSAGE FORM

Tablets

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) 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 pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

GENERAL

a. United States Patent Number RE36,617	b. Issue Date of Patent 3/14/2000	c. Expiration Date of Patent 12/27/2009
--	--------------------------------------	--

d. Name of Patent Owner AstraZeneca UK Ltd.	Address (of Patent Owner) 15 Stanhope Gate	
	City/State London, UK	
	ZIP Code W1K 1LN	FAX Number (if available) +44 (0)20 7304 5151
	Telephone Number +44 (0)20 7304 5000	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) Glenn M. Engelmann, Vice President, Policy, Legal & Scientific Affairs & General Counsel AstraZeneca Pharmaceuticals LP	Address (of agent or representative named in 1.e.) 1800 Concord Pike	
	City/State Wilmington, DE	
	ZIP Code 19850-5437	FAX Number (if available)
	Telephone Number (800) 456-3669	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 the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No*

* Certain claims may cover at least one additional polymorph in addition to claiming the drug substance of the pending NDA, amendment or supplement, but the patent is not being listed on that basis.

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). Yes 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 active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes 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.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes 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.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit Indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and 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. Yes

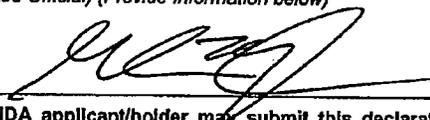
6. Declaration (Certification)

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending 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.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



7/19/07

NOTE: 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.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Glenn Engelmann, Vice President, Policy, Legal & Scientific Affairs & General Counsel

Address

1800 Concord Pike

City/State

Wilmington, DE

ZIP Code

19803

Telephone Number

(302) 886-3244

FAX Number (if available)

(302) 886-1578

E-Mail Address (if available)

glenn.engelmann@astrazeneca.com

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:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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.

12/4/08

EXCLUSIVITY SUMMARY

NDA # 22-214

SUPPL # N/A

HFD # N/A

Trade Name Arimidex

Generic Name anastrozole

Applicant Name AstraZeneca Pharmaceuticals LP

Approval Date, If Known December 5, 2008

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES NO

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

505(b)(1)

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

YES NO

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

N/A

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:

N/A

d) Did the applicant request exclusivity?

YES NO

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

Pediatric exclusivity determination requested (6 months); sponsor not seeking an indication or other type of exclusivity

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?

yes

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# 20-541

Arimidex (anastrozole) Tablets, 1 mg (parent NDA)

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

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

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

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

YES NO

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

N/A

(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:

N/A

(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:

N/A

- (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:

Investigation 1: Study 1033US/0006 (A double-blind, placebo-controlled study to assess the safety and efficacy of anastrozole versus placebo for the treatment of gynecomastia in pubertal boys)

Investigation 2: Study D5394C00001 (An open-label PK and pharmacodynamic (PD) study of anastrozole used to treat pubertal boys with gynecomastia of recent onset)

Investigation 3: Study 1033IL/0046 (An open-label study evaluating the safety and efficacy of anastrozole in the treatment of precocious puberty in girls with McCune-Albright Syndrome)

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 <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #3	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>

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

N/A

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 <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #3	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

N/A

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"):

Investigation 1: Study 1033US/0006 (A double-blind, placebo-controlled study to assess the safety and efficacy of anastrozole versus placebo for the treatment of gynecomastia in pubertal boys)

Investigation 2: Study D5394C00001 (An open-label PK and pharmacodynamic (PD) study of anastrozole used to treat pubertal boys with gynecomastia of recent onset)

Investigation 3: Study 1033IL/0046 (An open-label study evaluating the safety and efficacy of anastrozole in the treatment of precocious puberty in girls with McCune-Albright Syndrome)

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 # 62,138	YES <input checked="" type="checkbox"/>	! NO <input type="checkbox"/>
		! Explain:

Investigation #2
IND # 62,138 YES ! NO
! Explain:

Investigation #3
IND # 62,138 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:

Investigation #2
YES ! NO
Explain: ! Explain:

Investigation #3
IND # 62,138 YES ! 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:

N/A

Name of person completing form: Jennifer Johnson
Title: Regulatory Project Manager
Date: December 4, 2008

Name of Office/Division Director signing form: Mary H. Parks, M.D.
Title: Director, Division of Metabolism and Endocrinology Products

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

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

/s/

Mary Parks
12/4/2008 09:10:01 PM

1/14/08

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 22-214 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: September 5, 2007 PDUFA Goal Date: March 5, 2008

HFD 510 Trade and generic names/dosage form: Arimidex (anastrozole) Tablets

Applicant: AstraZeneca Pharmaceuticals Therapeutic Class: Developmental Disorders

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): _____

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

Number of indications for this application(s): 2

Indication #1: For use in male pubertal patients with gynecomastia

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: _____

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. 0 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. <11 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 (in the specified waived age range above)
- 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. 11 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 18 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.

Attachment A

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

Indication #2: For use in female pediatric patients with McCune-Albright syndrome with progressive precocious puberty

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: _____

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. 0 AND >11 Tanner Stage _____
 Max _____ kg _____ mo. _____ yr. 3 AND 18 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 (*in the specified waived age range above*)
- 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. 3 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 11 Tanner Stage _____

Comments:

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

This page was completed by:

{See appended electronic signature page}
Jennifer Johnson
Regulatory 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/

Jennifer Johnson
1/14/2008 06:30:54 PM

AstraZeneca 

Internal Memorandum

US Regulatory Affairs

Date: 22 March 2007

To: E. Jane Valas

cc: N. J. Troise

From: Donna M. Dea

Re: ARIMIDEX[®] (anastrozole) - Debarment Response Memo

I hereby certify on behalf AstraZeneca Pharmaceuticals LP that no individual who has been debarred by the FDA as published in the Federal Register through 19 March 2007, has been used in any capacity during the conduct of studies or trials included in the ARIMIDEX Pediatric NDA submission. This applies to current and past employees of AstraZeneca, as well as, consultants, contractors, investigators, and any other agents or assigns.



Date: 6/12/07

SIGNED ON BEHALF OF FUNCTIONAL/DEPARTMENT

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

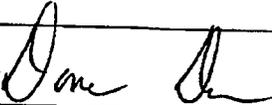
Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	SEE ATTACHED REPORT(S)	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Donna Dea	TITLE Vice President, Regulatory Affairs
FIRM / ORGANIZATION AstraZeneca Pharmaceuticals	
SIGNATURE 	DATE 3/17/07

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

4 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

Withheld Track Number: *Admin* ~~Other Action Letter~~ 1

December 9, 2008

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22-214	NDA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A
Proprietary Name: Arimidex Established/Proper Name: anastrozole Dosage Form: Tablets		Applicant: AstraZeneca Pharmaceuticals LP Agent for Applicant (if applicable): N/A
RPM: Jennifer Johnson		Division: Metabolism and Endocrinology Products, HFD-510
NDA's: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (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.)		505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)): N/A Provide a brief explanation of how this product is different from the listed drug. N/A <input type="checkbox"/> If no listed drug, check here and explain: N/A 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. <input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: 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. On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.
❖ User Fee Goal Date Action Goal Date (if different)		March 5, 2008 December 5, 2008
❖ Actions		
<ul style="list-style-type: none"> • Proposed action 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		X None
❖ Promotional Materials (<i>accelerated approvals only</i>) 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 www.fda.gov/cder/guidance/2197dft.pdf). If not submitted, explain _____		<input type="checkbox"/> Received

¹ 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 ² Characteristics	
Review priority: <input type="checkbox"/> Standard <input checked="" type="checkbox"/> Priority Chemical classification (new NDAs only): 6 <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies Comments: <u>Application submitted in response to Pediatric Written Request issued April 8, 2005</u>	
❖ Date reviewed by PeRC (<i>required for approvals only</i>) If PeRC review not necessary, explain: _____	March 5, 2008
❖ 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 checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

² 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"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> 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> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (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> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (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> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (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> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDA 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> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> 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. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> 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. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III 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). 	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV 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> 	<input type="checkbox"/> N/A (no paragraph IV certification) <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>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
---	--

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	Included
Officer/Employee List	
❖ 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>)	X Included
Documentation of consent/non-consent by officers/employees	X Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Approval letter: December 5, 2008
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	October 29, 2008 (by parent NDA 20-541 in the Division of Drug Oncology Products – pediatric language finalized by DMEP on March 3, 2008)
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	November 4, 2008 (to parent NDA 20-541 in the Division of Drug Oncology Products)
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	September 4, 2007
<ul style="list-style-type: none"> • 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 <input checked="" type="checkbox"/> Patient Package Insert

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

	<input checked="" type="checkbox"/> Instructions for Use <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	October 29, 2008 (by parent NDA 20-541 in the Division of Drug Oncology Products)
<ul style="list-style-type: none"> Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	November 4, 2008 (to parent NDA 20-541 in the Division of Drug Oncology Products)
<ul style="list-style-type: none"> Original applicant-proposed labeling 	September 4, 2007
<ul style="list-style-type: none"> Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	N/A
❖ Labels (full color carton and immediate-container labels) (write submission/communication date at upper right of first page of each submission)	
<ul style="list-style-type: none"> Most-recent division proposal for (only if generated after latest applicant submission) 	Approved under NDA 20-541
<ul style="list-style-type: none"> Most recent applicant-proposed labeling 	Approved under NDA 20-541
❖ Labeling reviews (indicate dates of reviews and meetings) ❖ Please note that the Physicians Labeling Rule (PLR) conversion of the package insert was handled by the Division of Drug Oncology Products	<input type="checkbox"/> RPM N/A <input type="checkbox"/> DMEDP N/A <input checked="" type="checkbox"/> DRISK May 2, 2008 <input type="checkbox"/> DDMAC N/A <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
❖ Proprietary Name <ul style="list-style-type: none"> Review(s) (indicate date(s)) Acceptability/non-acceptability letter(s) (indicate date(s)) 	Approved under NDA 20-541 N/A
Administrative / Regulatory Documents	
❖ Administrative Reviews (e.g., RPM Filing Review⁴/Memo of Filing Meeting) (indicate date of each review)	January 14, 2008
❖ NDAs only: Exclusivity Summary (signed by Division Director)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents www.fda.gov/ora/compliance_ref/aip_page.html	
<ul style="list-style-type: none"> Applicant in on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> 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"/> Yes <input checked="" type="checkbox"/> No N/A N/A <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
<ul style="list-style-type: none"> Outgoing communications (if located elsewhere in package, state where located) Incoming submissions/communications 	
❖ Postmarketing Commitment (PMC) Studies	<input checked="" type="checkbox"/> None

⁴ Filing reviews for other disciplines should be filed behind the discipline tab.

<ul style="list-style-type: none"> Outgoing Agency request for postmarketing commitments (<i>if located elsewhere in package, state where located</i>) 	N/A
<ul style="list-style-type: none"> Incoming submission documenting commitment 	N/A
❖ Outgoing communications (<i>letters (except previous action letters), emails, faxes, telecons</i>)	February 1, 2008; November 15 (2), 2, October 11, 2007, and November 20, 2006
❖ Internal memoranda, telecons, etc.	None
❖ Minutes of Meetings	
<ul style="list-style-type: none"> PeRC (<i>indicate date; approvals only</i>) 	<input type="checkbox"/> Not applicable
<ul style="list-style-type: none"> Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) 	<input type="checkbox"/> Not applicable None
<ul style="list-style-type: none"> Regulatory Briefing (<i>indicate date</i>) 	X No mtg
<ul style="list-style-type: none"> Pre-NDA/BLA meeting (<i>indicate date</i>) 	X No mtg Written responses issued by Agency on November 29, 2006 in lieu of formal meeting
<ul style="list-style-type: none"> EOP2 meeting (<i>indicate date</i>) 	X No mtg
<ul style="list-style-type: none"> Other (e.g., EOP2a, CMC pilot programs) 	Pediatric Exclusivity Board: March 30, 2008
❖ Advisory Committee Meeting(s)	X No AC meeting
<ul style="list-style-type: none"> Date(s) of Meeting(s) 	
<ul style="list-style-type: none"> 48-hour alert or minutes, if available 	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	X None
Division Director Summary Review (<i>indicate date for each review</i>)	X None
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	X None
Clinical Information⁵	
❖ Clinical Reviews	
<ul style="list-style-type: none"> Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	Concurrence by Team Leader on primary review on February 20, 2008
<ul style="list-style-type: none"> Clinical review(s) (<i>indicate date for each review</i>) 	February 20, 2008
<ul style="list-style-type: none"> Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	X None
❖ Safety update review(s) (<i>indicate location/date if incorporated into another review</i>)	See page 76 of clinical review
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	February 20, 2008
❖ Clinical reviews from other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	X None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	X Not needed
❖ Risk Management <ul style="list-style-type: none"> 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>) 	X None N/A

⁵ Filing reviews should be filed with the discipline reviews.
Version: 9/5/08

<ul style="list-style-type: none"> REMS Memo (<i>indicate date</i>) REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) 	N/A
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	X None requested
Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	X None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	X None (Concurrence by Team Leader on primary review on March 5, 2008)
Statistical Review(s) (<i>indicate date for each review</i>)	March 5, 2008
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	X None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	X None Concurrence by Team Leader on primary reviews dated March 25 and February 28, 2008, and November 9, 2007
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	March 25 and February 28, 2008; November 9, 2007
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	X None
Nonclinical <input checked="" type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
<ul style="list-style-type: none"> ADP/T Review(s) (<i>indicate date for each review</i>) 	<input type="checkbox"/> None
<ul style="list-style-type: none"> Supervisory Review(s) (<i>indicate date for each review</i>) 	<input type="checkbox"/> None
<ul style="list-style-type: none"> Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>) 	<input type="checkbox"/> None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input type="checkbox"/> None requested
CMC/Quality <input type="checkbox"/> None	
❖ CMC/Quality Discipline Reviews	
<ul style="list-style-type: none"> ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>) 	<input type="checkbox"/> None
<ul style="list-style-type: none"> Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>) 	X None Concurrence by Team Leader on primary review dated February 28, 2008
<ul style="list-style-type: none"> CMC/product quality review(s) (<i>indicate date for each review</i>) 	<input type="checkbox"/> None February 28, 2008
<ul style="list-style-type: none"> BLAs only: Facility information review(s) (<i>indicate dates</i>) 	X None N/A

<ul style="list-style-type: none"> ❖ Microbiology Reviews <ul style="list-style-type: none"> • NDAs: Microbiology reviews (sterility & pyrogenicity) <i>(indicate date of each review)</i> • BLAs: Sterility assurance, product quality microbiology <i>(indicate date of each review)</i> 	<p>X Not needed N/A</p>
<ul style="list-style-type: none"> ❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i> 	<p>X None</p>
❖ Environmental Assessment (check one) (original and supplemental applications)	
<p>X Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i></p>	<p>February 28, 2008</p>
<p><input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i></p>	
<p><input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i></p>	
<ul style="list-style-type: none"> ❖ NDAs: Methods Validation 	<p><input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed</p>
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> • NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date)</i> 	<p>Date completed: N/A <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation</p>
<ul style="list-style-type: none"> • BLAs: <ul style="list-style-type: none"> ○ TBP-EER ○ 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> 	<p>Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation Date completed: <input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold</p>

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.

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

/s/

Jennifer Johnson
12/9/2008 12:42:05 PM

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Friday, February 01, 2008 4:55 PM
To: 'Valas, E Jane'
Cc: Johnson, Jennifer
Subject: NDA 22-214 (Arimidex): Review Team Information Request

Dear Jane,

We have a request for information regarding NDA 22-214, Arimidex (see below for specific questions). Please respond as an official amendment to this NDA, and feel free to contact me with any questions or concerns.

Many thanks,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

1) Provide descriptive statistics at baseline, Month 3 and Month 6 in each of the 3 clinical studies for the following hormonal parameters: estradiol, testosterone, LH and FSH. Include absolute and percent change from baseline to each time point. Specify the normal range of values for each assay. An example of such a table is provided below:

Descriptive statistics	Baseline or screening	Month 6	Change from baseline at Month 6	% change from baseline at Month 6
Study 1033IL/0046				
Estradiol				
Testosterone				
LH				
FSH				
Study 1033US/0006				
Estradiol				
Testosterone				
LH				
FSH				
Study D5394C00001				
Estradiol				
Testosterone				
LH				
FSH				

2) Confirm if the data provided in Table 14 (reproduced below) is correct, especially with respect to "percent change from baseline to Month 6".

Table 14 Change in calculated volume of gynecomastia from Visit 1 to Month 6/Final visit (ITT population)

		Randomized treatment	
		Anastrozole 1 mg (N=39)	Placebo (N=35)
Baseline	n	38	33
	Mean (SD)	439.5 (596.2)	574.5 (722.4)
	Range	4 to 2066	2 to 2687
Month 6/Final visit	n	38	34
	Mean (SD)	309.2 (540.5)	369.0 (450.3)
	Range	0 to 2376	1 to 1932
Change from baseline to Month 6/Final visit	n	38	33
	Mean (SD)	-130.3 (353.5)	-216.1 (565.8)
	Range	-1581 to 415	-2333 to 1106
Percent change from baseline to Month 6/Final visit	n	38	33
	Mean (SD)	-23.5 (66.1)	-5.9 (118.3)
	Range	-100 to 266	-96 to 593

SD standard deviation

3) Confirm if the data provided in Table 16 (reproduced below) is correct, especially with respect to “percent change from baseline”.

Table 16 Hormone levels and change from baseline – ITT population

	Randomized treatment					
	Anastrozole 1 mg (N=39)			Placebo (N=35)		
	n	Mean (SD)	Range	n	Mean (SD)	Range
Serum estradiol (pmol/L)						
Baseline	38	65.1 (35.5)	18.4 to 165.2	34	68.3 (32.8)	36.7 to 146.8
Month 3	38	54.0 (29.3)	36.7 to 161.5	34	64.4 (33.8)	36.7 to 139.5
Change from baseline to Month 3	37	-9.7 (24.4)	-62.5 to 33.0	33	-4.3 (30.4)	-102.7 to 51.4
Percent change from baseline to Month 3 (%)	37	-6.5 (35.7)	-63.0 to 99.5	33	0.9 (42.1)	-70.0 to 140.1
Month 6/Final visit	37	48.0 (21.0)	18.4 to 102.8	29	57.7 (21.8)	36.7 to 102.8
Change from baseline to Month 6/ Final visit	36	-18.4 (29.1)	-77.1 to 36.7	28	-11.3 (28.6)	-55.0 to 40.4
Percent change from baseline to Month 6/ Final visit (%)	36	-15.4 (40.0)	-70.5 to 100.0	28	-4.5 (41.4)	-56.5 to 100.0
Testosterone (nmol/L)						
Baseline	38	9.2 (7.3)	1.0 to 32.1	34	9.3 (6.2)	0.5 to 30.7
Month 3	37	15.6 (7.1)	0.7 to 28.5	34	9.7 (5.9)	0.8 to 24.8
Change from baseline to Month 3	36	6.2 (5.3)	-5.8 to 15.7	33	0.3 (5.5)	-12.2 to 14.3
Percent change from baseline to Month 3 (%)	36	169.2 (226.4)	-85.8 to 819.8	33	23.2 (86.0)	-64.5 to 365.0
Month 6/Final visit	39	13.9 (7.1)	3.4 to 28.6	34	10.1 (5.9)	1.6 to 27.1
Change from baseline to Month 6/ Final visit	38	4.9 (5.9)	-12.5 to 18.5	33	0.8 (3.8)	-5.5 to 10.4
Percent change from baseline to Month 6/ Final visit (%)	38	153.2 (204.4)	-69.2 to 830.7	33	52.9 (129.9)	-47.3 to 537.5

4) Provide a description of the distribution of the testicular volume changes in each arm of the two pubertal gynecomastia studies and a correlation analysis with the changes in FSH values for the same patients.

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

/s/

Jennifer Johnson
2/1/2008 05:00:59 PM
CSO

January 14, 2008

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-214 Supplement # N/A Efficacy Supplement Type SE- N/A

Proprietary Name: Arimidex Tablets
Established Name: anastrozole
Strengths: 1 mg

Applicant: AstraZeneca UK Limited
Agent for Applicant (if applicable): AstraZeneca Pharmaceuticals LP

Date of Application: September 4, 2007
Date of Receipt: September 5, 2007
Date clock started after UN: N/A
Date of Filing Meeting: October 15, 2007
Filing Date: November 4, 2007
Action Goal Date (optional): User Fee Goal Date: March 5, 2008

Indication(s) requested: for use in male pubertal patients with gynecomastia and female pediatric patients with McCune-Albright syndrome with progressive precocious puberty

Type of Original NDA: (b)(1) X (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 X
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 6
Other (orphan, OTC, etc.)

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

User Fee Status: Paid X Exempt (orphan, government)
UFID
3007624
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 X
If yes, explain:

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 X
- 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)]? N/A 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 X
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES NO
- Does the submission contain an accurate comprehensive index? YES X NO
If no, explain:
- Was form 356h included with an authorized signature? YES X NO
If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES X 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 NO X
2. This application is an eNDA or combined paper + eNDA YES X NO
This application is: All electronic X Combined paper + eNDA
This application is in: NDA format CTD format X
Combined NDA and CTD formats

Does the eNDA, follow the guidance?
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES X 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? N/A

Additional comments: N/A

3. This application is an eCTD NDA. YES X NO
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments: N/A

- Patent information submitted on form FDA 3542a? YES X NO
- Exclusivity requested? YES X NO

NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required. (Applicant has requested 6 months of pediatric exclusivity in this application.)

- Correctly worded Debarment Certification included with authorized signature? YES X 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 X NO

Note: The applicant should have, but did not, submit a waiver request for the age groups not studied to satisfy PREA requirements. The applicant was under the impression that these age groups did not have to be addressed due to this application being submitted in response to a Pediatric Written Request issued by FDA. The applicant was informed that in the future such a waiver request should be submitted in the original application submission, but will not be required to do so in this application. The clinical review will document the age ranges to be waived for the indications being studied. See Pediatric Page.

- 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)? N/A X YES NO

- Is this submission a partial or complete response to a pediatric Written Request? YES X NO

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES X 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 X

- PDUFA and Action Goal dates correct in tracking system? YES X 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: 62,138

- 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) November 20, 2006: Meeting denial and responses to sponsor's questions issued 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: N/A
- 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: N/A

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? N/A 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? N/A YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to EA officer, OPS? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team? N/A YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: October 15, 2007

NDA #: 22-214

DRUG NAMES: Arimidex (anastrozole) Tablets

APPLICANT: AstraZeneca Pharmaceuticals LP

BACKGROUND:

Arimidex was approved in the Division of Drug Oncology Products under NDA 20-541 on December 29, 1995, for the treatment of advanced breast cancer in postmenopausal women who have progressed following tamoxifen therapy.

The sponsor submitted IND 62,138 on February 27, 2001, to the Division of Metabolism and Endocrinology Products (DMEP), for the purpose of studying anastrozole in pediatric patients. On May 9, 2001, DMEP issued a Pediatric Written Request to the sponsor for the study of anastrozole in pediatric patients with pubertal gynecomastia and McCune-Albright syndrome. This Written Request was subsequently reissued on July 2, 2002, and amended on November 19, 2002, December 19, 2003, and April 8, 2005.

b(4)

Because of this agreement, it was decided by DMEP that the Written Request did not need to be amended further.

On September 4, 2007, the sponsor submitted this Type 6 NDA in response to the last-issued Written Request for the purpose of pediatric exclusivity determination. As required for all NDAs and efficacy supplements submitted after June 30, 2006, this NDA included updated labeling in the Physicians Labeling Rule (PLR) format.

ATTENDEES: Jennifer Johnson, Lina AlJuburi, Mary Parks, Dragos Roman, Sally Choe, Manoj Khurana, Karen Davis Bruno, Cynthia Liu

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

Discipline/Organization

Reviewer

Medical:	Dragos Roman
Secondary Medical:	Mary Parks
Statistical:	Cynthia Liu
Pharmacology:	Karen Davis Bruno
Statistical Pharmacology:	N/A
Chemistry:	Julia Pinto
Environmental Assessment (if needed):	Julia Pinto
Biopharmaceutical:	Manoj Khurana
Microbiology, sterility:	N/A
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	N/A
OPS:	N/A
Regulatory Project Management:	Jennifer Johnson
Other Consults:	None at this time

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

CLINICAL FILE X REFUSE TO FILE

- Clinical site audit(s) needed? YES NO X
If no, explain: *any concerns that arise will be captured in application review*
- Advisory Committee Meeting needed? YES, date if known _____ NO X
- 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 X YES NO

CLINICAL MICROBIOLOGY N/A X FILE REFUSE TO FILE

STATISTICS N/A FILE X REFUSE TO FILE

BIOPHARMACEUTICS FILE X REFUSE TO FILE

- Biopharm. study site audits(s) needed? YES NO X

PHARMACOLOGY/TOX N/A FILE X REFUSE TO FILE
(no P/T review needed – no new nonclinical data)

- GLP audit needed? YES NO X

CHEMISTRY FILE X REFUSE TO FILE

- Establishment(s) ready for inspection? YES X NO
- Sterile product? YES NO X
- 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:
- X 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.
- X Filing issues to be communicated by Day 74. List (optional):
Filing Letter issued on November 15, 2007

ACTION ITEMS:

1. X 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. X If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. X Convey document filing issues/no filing issues to applicant by Day 74.

Jennifer Johnson
Regulatory Project Manager

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

/s/

Jennifer Johnson
1/14/2008 06:31:52 PM
CSO

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

/s/

Jennifer Johnson
11/15/2007 02:53:11 PM
CSO

11/15/07



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-214

AstraZeneca Pharmaceuticals LP
Attention: E. Jane Valas, Ph.D.
Associate Director, Regulatory Affairs
1800 Concord Pike, P.O. Box 8355
Wilmington, DE 19803-8355

Dear Dr. Valas:

Please refer to your new drug application (NDA) dated September 4, 2007, received September 5, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Arimidex (anastrozole) Tablets, 1 mg.

We also refer to your submission dated September 5, 2007.

As previously communicated in a letter we issued to your attention on November 2, 2007, we have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Priority**. Therefore, the user fee goal date is **March 5, 2008**.

During our filing review of your application, we identified the following potential review issues, and request that you submit the following information:

Clinical

1. Indicate the location of the financial disclosure information for Study 1033US/0006 titled "A Randomized, Double-blind, Placebo-controlled Trial to Assess the Safety and Efficacy of Anastrozole (ZD1033, ARIMIDEX™) versus Placebo for the Treatment of Gynecomastia in Pubertal Boys".
2. For the same study, indicate if the numerical results of Table 14 titled "Change in calculated volume of gynecomastia from Visit 1 to Month 6/Final visit (ITT population)" are correct (for instance, a 216.1 change from a baseline value of 574.5 in the placebo group is listed as a 5.9% change).
3. Specify the normal range for estradiol and testosterone in each of the three clinical studies:

- Study 0006: A Randomized, Double-blind, Placebo-controlled Trial to Assess the Safety and Efficacy of Anastrozole (ZD1033, ARIMIDEX™) versus Placebo for the Treatment of Gynecomastia in Pubertal Boys
- Study 0001: An Open-label Pharmacokinetic and Pharmacodynamic Study of Anastrozole (ARIMIDEX™) used to Treat Pubertal Boys with Gynecomastia of Recent Onset
- Study 0046: An Open-label Study Evaluating the Safety and Efficacy of Anastrozole (ARIMIDEX™) in the Treatment of Precocious Puberty in Girls with McCune-Albright Syndrome

Clinical Pharmacology

For Study 0046 titled, "An Open-label Study Evaluating the Safety and Efficacy of Anastrozole (ARIMIDEX™) in the Treatment of Precocious Puberty in Girls with McCune-Albright Syndrome (MAS)", the pharmacokinetic sample analysis was conducted in three parts by _____ on _____ following dates:

b(4)

<i>Part</i>	<i>Start Analysis</i>	<i>End Analysis</i>
1	15-Jan-2004	21-Jan-2004
2	14-Jan-2005	27-Jan-2005
3	08-Nov-2005	11-Nov-2005

The analysis date for Part 1 falls under the period (January 2000 to December 2004) for which Agency issued the letter (February 1, 2007) to Sponsors regarding the significant concerns about the validity of the bioanalytical studies conducted by _____ Therefore, the Agency requests that you address this concern by conducting one of the following, in order of preference:

b(4)

- repeat Study 0046,
- re-assay the samples for anastrozole at a different bioanalytical facility. For this option, the integrity of the original samples must be demonstrated for the frozen storage period, or
- commission a scientific audit by a qualified independent expert, who is knowledgeable in the area of clinical pharmacology studies and bioanalytical data, and selected by you rather than by _____ to verify the results obtained by _____

b(4)

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

NDA 22-214

Page 3

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this application.

If you have any questions, please call Jennifer Johnson, Regulatory Project Manager, at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Lina AlJuburi, Pharm.D., M.S.
Chief, Project Management Staff
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Jennifer Johnson
11/15/2007 01:08:06 PM
Signing on behalf of Lina AlJuburi, CPMS



Date: 29 August 2007

US Food and Drug Administration (360909)
Mellon Client Service Center
Room 670
500 Ross Street
Pittsburgh, PA 15262-0001

RE: NDA 22-214
ARIMIDEX[®] (anastrozole) Tablets
Prescription Drug User Fee Payment: User Fee I.D. No. PD3007624

Dear Madam/Sir:

In accordance with section 736 of the Federal Food, Drug and Cosmetic Act, AstraZeneca Pharmaceuticals LP (AstraZeneca) is providing a Prescription User Fee payment for a Type 6 NDA for the use of Arimidex in Request for Pediatric Exclusivity Determination.

The User Fee payment is made in the amount of \$896,200 and represents the total NDA application fee for fiscal year 2007. A copy of the User Fee Cover Sheet, Form FDA 3397, is enclosed.

Please direct any questions or requests for additional information to me, or in my absence, to Nicholas Troise, Director, Regulatory Affairs, at 302-886-8016.

Sincerely,

A handwritten signature in black ink that reads "E. Jane Valas, Ph.D." in a cursive style.

E. Jane Valas, Ph.D.
Associate Director
Regulatory Affairs
Telephone: 302-886-2122
Fax: 302-886-2822

EJV

Enclosure

Form FDA 3397 – User Fee Cover Sheet
User Fee Check No. PD3007624
Check Number 1500163562

US Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See instructions for OMB Statement, below.

DEPARTMENT OF HEALTH AND HUMAN
SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVERSHEET

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

1. APPLICANT'S NAME AND ADDRESS ASTRAZENECA PHARMACEUTICALS LP Cindy Lancaster 1800 CONCORD PIKE PO BOX 8355 WILMINGTON DE 198038355 US		4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER 22-214	
2. TELEPHONE NUMBER 302-885-1348		5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:	
3. PRODUCT NAME ARIMIDEX Tablets (anastrozole)		6. USER FEE I.D. NUMBER PD3007624	
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act			
<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY			
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO			
OMB Statement: Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Department of Health and Human Services Food and Drug Administration CBER, HFM -99 1401 Rockville Pike Rockville, MD 20852-1448 Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852 An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.			
SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 		TITLE Executive Director	DATE August 29, 2007
9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$896,200.00			
Form FDA 3397 (03/07)			

Close Print Cover sheet

8/27/2007

11/15/07

Johnson, Jennifer

From: Johnson, Jennifer
Sent: Thursday, November 15, 2007 2:49 PM
To: 'Valas, E Jane'
Cc: Johnson, Jennifer
Subject: NDA 22-214: Pediatric Exclusivity Determination for anastrozole

Dear Dr. Valas,

This email serves as the formal notification that Pediatric Exclusivity has been granted. Please let me know if you have any questions.

Kind Regards,
Jennifer

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food & Drug Administration
301-796-2194 phone
301-796-9712 fax
jennifer.johnson@fda.hhs.gov

Pediatric Exclusivity Notification

Pediatric Exclusivity has been granted for studies conducted on anastrozole, effective November 14, 2007, under section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a), as amended by the Best Pharmaceuticals for Children Act (BPCA). This information will be reflected on CDER's pediatric web site and in the monthly update of the *Orange Book*. For additional information, please see the "Guidance for Industry - Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act." <http://www.fda.gov/cder/guidance/2891fnl.pdf>

In addition, the FDA Amendments Act of 2007, Title V: BPCA of 2007, enacted on September 27, 2007, mandates that all adverse event reports must be referred to the Office of Pediatric Therapeutics one year after a labeling change is approved for applications and supplements submitted under subsection (i). The Director of that Office will provide for a review of the adverse event reports by the Pediatric Advisory Committee (PAC) and will obtain recommendations from that Committee on action FDA should take.

For most products, the presentation at the PAC meeting will be one of the following:

- 1) "Abbreviated" presentation: brief comments presented to the PAC concerning the lack of any safety signal.
- 2) "Standard" presentation: a review of Adverse Event Reporting Systems (AERS) data, use data, the exclusivity trials with a focus on the safety reporting, and any additional information thought to be pertinent to the review and discussion.
- 3) "In-depth" presentation: "standard" presentation noted above plus safety issues identified as requiring a more in-depth discussion and review. This may involve external experts and presentations and discussion by Office of Surveillance and Epidemiology and the review division staff.

The type of presentation will depend on the adverse event data and other issues under review at the time. The

11/15/2007

Agency will not determine the type of presentation until after we have reviewed the relevant data and information. Irrespective of the type of presentation, the PAC will receive a briefing package which includes the Adverse Event review, product use review, the exclusivity review summaries and the current labeling.

If you have questions relating to the Pediatric Advisory Committee, please call Ann Myers, R.Ph., in the Office of Pediatric Therapeutics at 301-827-9379.

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST

PART I - TO BE COMPLETED BY THE REVIEWING DIVISION.

Date of Written Request from FDA 05/09/01
 WR 1 Amendment 1 11/19/02 WR 1 Amendment 2 12/19/03
 WR 1 Reissued (No Amendment #) 07/02/02 WR 1 Amendment 4 04/08/05
 Application Written Request was made to: IND 62,138
 Timeframe Noted in Written Request for Submission of Studies 10/31/07.
 NDA# 22-214 Supplement # N/A Choose one: SB1 SE2 SE3 SE4 SE5 SE6 SE7 SE8 SLR
 Sponsor AstraZeneca Pharmaceuticals LP
 Generic Name anastrozole Trade Name Arimidex
 Strength 1 mg Dosage Form/Route Tablets
 Date of Submission of Reports of Studies 09/04/07.
 Pediatric Exclusivity Determination Due Date (60 or 90 days from date of submission of studies) 12/04/07.

Was a formal Written Request made for the pediatric studies submitted?	Y <u>X</u>	N
Were the studies submitted after the Written Request?	Y <u>X</u>	N
Were the reports submitted as a supplement, amendment to an NDA, or NDA?	Y <u>X</u>	N
Was the timeframe noted in the Written Request for submission of studies met?	Y <u>X</u>	N
If there was a written agreement, were the studies conducted according to the written agreement? OR If there was no written agreement, were the studies conducted in accord with good scientific principles?	Y <u>X</u>	N
Did the studies fairly respond to the Written Request?	Y <u>X</u>	N

SIGNED *Drayn Roman* DATE 11/5/07
 (Reviewing Medical Officer)

SIGNED *Mary Clark* DATE 11/5/07
 (Division Director)

Do not enter in DFS - FORWARD TO PEDIATRIC EXCLUSIVITY BOARD, HFD-960.

PART II - TO BE COMPLETED BY THE PEDIATRIC EXCLUSIVITY BOARD

Pediatric Exclusivity **Granted** **Denied**

Existing Patent or Exclusivity Protection:

NDA/Product #	Eligible Patents/Exclusivity	Current Expiration Date
<u>20-541</u>	<u>RE 36617</u>	<u>Dec 29, 2009</u>

SIGNED *[Signature]* DATE 11/14/07
 (Last revised Jan 11, 2005)

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

/s/

John Jenkins
11/14/2007 04:45:42 PM

11/2/07



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-214

PRIORITY REVIEW DESIGNATION

AstraZeneca Pharmaceuticals LP
Attention: E. Jane Valas, Ph.D.
Associate Director, Regulatory Affairs
1800 Concord Pike, P.O. Box 8355
Wilmington, DE 19803-8355

Dear Dr. Valas:

Please refer to your new drug application (NDA) dated September 4, 2007, received September 5, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Arimidex (anastrozole) Tablets, 1 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Priority**. Therefore, the user fee goal date is March 5, 2008.

While conducting our filing review, we identified potential review issues and will communicate them to you on or before November 18, 2007.

If you have any questions, please call Jennifer Johnson, Regulatory Project Manager, at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Mary Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Eric Colman
11/2/2007 03:26:34 PM
Eric Colman for Mary Parks

10/11/07



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-214

NDA ACKNOWLEDGMENT

AstraZeneca Pharmaceuticals LP
Attention: E. Jane Valas, Ph.D.
Associate Director, Regulatory Affairs
1800 Concord Pike, P.O. Box 8355
Wilmington, DE 19803-8355

Dear Dr. Valas:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Arimidex (anastrozole) Tablets, 1 mg

Date of Application: September 4, 2007

Date of Receipt: September 5, 2007

Our Reference Number: NDA 22-214

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on November 4, 2007, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be March 5, 2008.

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(1)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must be in the Prescribing Information (physician labeling rule) format.

The NDA number provided above shown above be cited 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:

NDA 22-214
Page 2

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrinology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, please call me at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Jennifer Johnson
Regulatory Project Manager
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Jennifer Johnson
10/11/2007 03:40:14 PM

11/20/06



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

IND 62,138

AstraZeneca Pharmaceuticals LP
Attention: E. Jane Valas, Ph.D.
Associate Director, Regulatory Affairs
1800 Concord Pike, P.O. Box 8355
Wilmington, DE 19803

Dear Dr. Valas:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for ARIMIDEX® (anastrozole) Tablets.

We also refer to your September 18, 2006 correspondence, received September 19, 2006, requesting a meeting to discuss your plans to submit an NDA by October 31, 2007. We have considered your request and concluded that the meeting is unnecessary. However, in order to assist you in your drug development program, we are providing the following information in response to questions included in your meeting request.

Your questions are repeated below and the responses are bolded.

Draft Labeling Text

Question 1:

Does FDA agree that these are the appropriate sections of the ARIMIDEX label to be updated?

Before the NDA data are reviewed, the Division cannot comment on which specific sections of the label will be changed.

Pharmacology and Toxicology

Question 2:

Does the Agency agree that cross-reference statements within Modules 2.4, 2.6 and 4, to the Non-Clinical Pharmacology and Toxicology Reports filed to NDA 20-541 are acceptable?

Yes, cross reference of nonclinical pharmacology and toxicology data from NDA 20-541 is acceptable.

Chemistry, Manufacturing and Controls

Question 3:

Does the Agency agree that cross-reference statements to NDA 20-541 for Modules 2.3 and 3 of the pediatric NDA are acceptable?

Yes, we agree that cross-reference statements to NDA 20-541 for Module 2.3 and 3 of the pediatric NDA are acceptable. In addition, for the purpose of documentation, provide the following in the new NDA: current drug substance and drug product specifications, and a table of composition of the drug product.

Human Pharmacology/Pharmacodynamics, Pharmacokinetics and Bioavailability

Question 4:

Does the Agency agree that cross-reference statements to NDA 20-541, as needed, for Modules 2.5 (Clinical Overview), 2.7 (Clinical Summary) and 5.3.1 Reports of biopharmaceutics studies, 5.3.2 Reports of studies pertinent to pharmacokinetics using human biomaterials, 5.3.3 Reports of human pharmacokinetic (PK) studies, and 5.3.4 Reports of human pharmacodynamic (PD) studies of the pediatric NDA are acceptable?

Referencing this future NDA's clinical pharmacology information to that of NDA 20-541 is acceptable. Please submit the following data and datasets to support the population pharmacokinetic analysis of anastrozole:

- All NONMEM datasets used for model development and validation in SAS transport files (*.xpt). A description of each data item should be provided in a Define.pdf file. Any concentrations and/or subjects that have been excluded from the analysis should be maintained in the datasets.
- NONMEM control streams and output files should be provided in ASCII (*.txt) format for all major model building steps; e.g., base structural model, covariates models, final model, and validation model.
- A model development decision tree and/or table which gives an overview of modeling steps.

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

For the "Summary of Clinical Pharmacology Studies", please also submit the Associated Bioanalytical Methods and Validation for anastrozole in clinical pharmacology studies. The bioanalytical methods used to measure anastrozole should be consistent between the pharmacokinetic study for pubertal boys with gynecomastia and the pharmacokinetic study for girls with McCune-Albright Syndrome.

Question 5:

Is inclusion of the specific plasma concentration data from trial D5394C0001 in the population PK analysis acceptable to FDA?

It is always commendable to have a prospectively developed analysis plan. The adequacy of analysis is a review issue upon filing the NDA.

Question 6:

Does FDA accept the analysis plan including the draft data definition table for the NONMEM dataset as provided in Appendix C?

Please see the response to Question 5.

Clinical/Statistical

Question 7:

Does FDA agree that a cross-reference to report 1033IL/0006 as archived to NDA 20-541 will be acceptable in lieu of resubmitting the report in this NDA?

Yes, this is acceptable.

Question 8:

Does the FDA agree that the datasets as described above (content and format) for 1033IL/0046 and D5394C00001 will be adequate for review of the NDA?

Yes, this will be adequate for review of the NDA.

Question 9:

Does the Agency agree that the Efficacy sections within each Clinical Study Report will suffice to report on efficacy of ARIMIDEX in the pediatric populations studied and, therefore, will agree to grant AstraZeneca a waiver against the standard requirements of the ISE?

We agree that there is not a need for an Integrated Summary of Efficacy (ISE) and therefore a waiver for submitting an ISE is granted.

Question 10:

Does the Agency agree that the Safety sections within each clinical study report and the proposal described above for presenting safety data (within Module 2.7.4, Clinical Summary of Safety) from the three study reports will suffice to report on safety of ARIMIDEX in the pediatric populations studied and, will therefore, agree to grant AstraZeneca a waiver against the standard requirements of the ISS and any subsequent safety update report?

We agree that there is not a need for an Integrated Summary of Safety (ISS) and therefore a waiver for submitting an ISS is granted. However, add to one of the clinical study reports a section that includes incidence tables of adverse events from all the patients with gynecomastia treated with Arimidex (i.e. patients from Study 1 and Study 3 combined) relative to placebo. The requirement for a 4-month safety update will also be waived.

IND 62,138

Page 4

Contents of NDA Submission

Question 11:

Does FDA agree that the contents of the submission as detailed in this draft TOC will be sufficient to accept the NDA for filing?

The proposed draft Table of Contents is acceptable.

Format of Submission

Question 12:

Does the Agency agree to the proposed format of NDA as an electronic submission?

Yes, this proposed format is acceptable.

Pediatric Exclusivity Determination

Question 13:

Can the Agency confirm that AstraZeneca will be notified within 90 days of submission as to the acceptability of qualification for Pediatric Exclusivity for ARIMIDEX?

The determination of Pediatric Exclusivity will be made by the Pediatric Exclusivity Board, not by the Division.

Review of ARIMIDEX NDA

Question 14:

Can the Agency confirm that AstraZeneca's interpretation of the requirements for the determination of Pediatric Exclusivity indicates that the review of a labeling supplement containing pediatric data will occur on a separate timeline from the determination of Pediatric Exclusivity?

The efficacy supplement submission in response to a Written Request has a PDUFA goal date of 6 months. The timeline for the determination of Pediatric Exclusivity is 90 days. See response to Question #13 above.

If you have any questions, call Jennifer Johnson, Regulatory Project Manager, at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Mary Parks
11/20/2006 09:21:26 PM