

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
022460Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 022460

SUPPL #

HFD # 580

Trade Name Jalyn™

Generic Name dutasteride and tamsulosin

Applicant Name GlaxoSmithKline (GSK)

Approval Date, If Known 6/14/10

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)(2)

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.

Study #3: Bioequivalence study ARI109882 titled "An Open-Label, Randomized, Single Dose Three-Period Partial Crossover Study to Determine the Bioequivalence and Food Effect of a Combination Capsule Formulation of dutasteride and tamsulosin Hydrochloride (0.5mg/0.4mg) Compared to Concomitant Dosing of AVODART® 0.5mg and Flomax 0.4mg Commercial Capsules in Healthy Male Subjects" was the only new study submitted to NDA 022460 that was critical to review for the approval of NDA 022460.

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

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

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

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA#

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA# 21-319 Avodart (dutasteride)

NDA# 20-579 Flomax (tamsulosin)

ANDA# 090377 tamsulosin

ANDA# 090408 tamsulosin

ANDA# 078015 tamsulosin

ANDA# 078801 tamsulosin

ANDA# 077630 tamsulosin

ANDA# 078938 tamsulosin

ANDA# 078225 tamsulosin

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

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

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

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

YES
Explain:

! NO
! Explain:

Investigation #2

!
!

YES
Explain:

! NO
! Explain:

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

YES NO

If yes, explain:

=====
Name of person completing form: Olga Salis
Title: Project Manager
Date: 6/14/10

Name of Office/Division Director signing form: George Benson, MD
Title: Deputy Director

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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

/s/

OLGA SALIS
06/14/2010

GEORGE S BENSON
06/14/2010

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-460

Supplement Number: _____

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

Division Name: Division of
Reproductive and Urologic
Products

PDUFA Goal Date: January
20, 2010

Stamp Date: March 20, 2009

Proprietary Name: Flodart

Established/Generic Name: dutasteride and tamsulosin

Dosage Form: 0.5 mg dutasteride and 0.4 mg tamsulosin, Capsules

Applicant/Sponsor: GlaxoSmithKline (GSK)

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

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

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

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

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

Indication: To treat symptomatic BPH in men with an enlarged prostate

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

No Please proceed to Question 2.

If Yes, NDA/BLA#: _____

Supplement #: _____

PMR #: _____

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

Yes. Please proceed to Section D.

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

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

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

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

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

Q3: Does this indication have orphan designation?

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

No. Please proceed to the next question.

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

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

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

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

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

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

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

† Ineffective or unsafe:

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

Δ Formulation failed:

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

Justification attached.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 6/2008)

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

Attachment A

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

Indication #2: _____

Q1: Does this indication have orphan designation?

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

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

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

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

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

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

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

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

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):
 Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

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

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

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

- # Not feasible:
 - Necessary studies would be impossible or highly impracticable because:
 - Disease/condition does not exist in children
 - Too few children with disease/condition to study
 - Other (e.g., patients geographically dispersed): _____
- * Not meaningful therapeutic benefit:
 - Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).
- † Ineffective or unsafe:
 - Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
 - Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
 - Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Δ Formulation failed:
 - Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.*)
 - Justification attached.

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

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additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

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

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

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

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

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

* Other Reason: _____

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

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

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

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

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

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

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

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

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

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

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

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

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

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

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

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

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

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

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

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

This page was completed by:

{See appended electronic signature page}

Olga Salis
Regulatory Project Manager

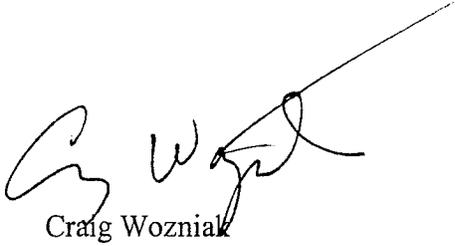
FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 6/2008)

m1.3.3 Debarment Certification

DEBARMENT CERTIFICATION

GlaxoSmithKline 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 (NDA 022460).



Craig Wozniak

October 2008

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 022460 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Jalyn Established/Proper Name: dutasteride and tamsulosin Dosage Form: 0.5 mg dutasteride and 0.4 mg tamsulosin		Applicant: GlaxoSmithKline Agent for Applicant (if applicable):
RPM: Olga Salis		Division: Division of Reproductive and Urologic Products
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		
<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u> Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>NDA 021319 Avadart (dutasteride) NDA 020579 Flomax (tamsulosin)</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>NDA 022460 proposes a new combination of tamsulosin and dutasteride. The combination capsule is produced by over-encapsulating the intermediates of the 2 active drug products.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>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.</p> <p><input type="checkbox"/> No changes <input checked="" type="checkbox"/> Updated Date of check: June 4, 2010</p> <p>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.</p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p>		
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>6/14/10</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input type="checkbox"/> None 1/20/10 (TA Letter)

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.

<p>❖ If accelerated approval, were promotional materials received? Note: For 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 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics²</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><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</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request</p> <p>Comments:</p>	
<p>❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes, date
<p>❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • 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 Answer all questions in all sections in relation 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 BLAs: 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 checked="" 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 checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires: PED June 22, 2013 and M-54, December 22, 2012 (does not effect this b2 action)
<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 checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<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 checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input checked="" 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 4/27/07
<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 checked="" 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?

(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)?

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?

(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)?

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).

Yes No

Yes No

Yes No

Yes No

<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>)	<input checked="" type="checkbox"/> Included
---	--

Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
--	--

Action Letters

❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) 1/20/10 and 6/14/10
---	---

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 draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	6/14/10
--	---------

<ul style="list-style-type: none"> • Original applicant-proposed labeling 	Second Review Cycle: 4/14/10
--	------------------------------

<ul style="list-style-type: none"> • Example of class labeling, if applicable 	NDA 20579 Flomax and NDA 21319 Avodart
--	---

³ Fill in blanks with dates of reviews, letters, etc.
Version: 12/4/09

❖ 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 <input type="checkbox"/> Instructions for Use <input type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in ttrack-changes format. 	6/14/10
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	April 14,2010-2 nd review cycle
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	NDA 21319 Avodart NDA 20579 Flomax
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> • Most-recent draft labeling 	6-10-10
❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) 	<p>not acceptable letters: 9/8/09, 12/16/09, 5/3/10 and 5/10/10</p> <p>Reviews: Reviews: 9/8/09, 12/11/09 2/2/10, 5/3/10 and 5/11/10</p>
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input type="checkbox"/> RPM <input type="checkbox"/> DMEDP <input checked="" type="checkbox"/> DRISK 11/25/09 <input checked="" type="checkbox"/> DDMAC 11/25/09 <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews Drug Usage date (OSE) 9/10/09 and 11/24/09
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	5/12/09 (from first review cycle)
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<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 (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>9/29/09</u> If PeRC review not necessary, explain: _____ • Pediatric Page (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 12/4/09

❖ 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 (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)	1 st and 2 nd review cycle included in the package
❖ Internal memoranda, telecons, etc.	n/a
❖ Minutes of Meetings	
• Pre-Approval Safety Conference (<i>indicate date of mtg; approvals only</i>)	Not applicable
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> Not applicable
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilot programs) (<i>indicates dates</i>)	none
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/19/10 and 6/14/10
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/19/10 and 6/14/10
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	1/19/10, 6/14/10
• Clinical review(s) (<i>indicate date for each review</i>)	Filing 5/7/09 NDA 1/19/10 and 6/14/10
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	Page 12 of MO review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable

⁵ Filing reviews should be filed with the discipline reviews.

❖ Risk Management <ul style="list-style-type: none"> REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) REMS Memo (<i>indicate date</i>) Risk management 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>) 	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None Filing 5/6/09 NDA Review 10/23/09
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None Filing 6/3/09 NDA Review 1/6/09, 1/15/09, and 6/4/10
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	<input type="checkbox"/> None 1/14/10
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None Filing 5/6/09 NDA Review 11/18/10
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None

<ul style="list-style-type: none"> Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>) 	<input type="checkbox"/> None filing 5/7/09 NDA Review 1/4/10 Biopharm 10/7/09 NDA 6/10/10
<ul style="list-style-type: none"> ❖ Microbiology Reviews <ul style="list-style-type: none"> <input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (<i>indicate date of each review</i>) 	<input type="checkbox"/> Not needed 10/1/09 and 12/23/09
<ul style="list-style-type: none"> ❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>) 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> ❖ Environmental Assessment (check one) (original and supplemental applications) 	
<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>) 	1/4/10 Page 141 of CMC review
<ul style="list-style-type: none"> <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) 	
<ul style="list-style-type: none"> <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) 	
<ul style="list-style-type: none"> ❖ Facilities Review/Inspection 	
<ul style="list-style-type: none"> <input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) 	Date completed: 1/4/10 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> <input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) 	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> ❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>) 	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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

/s/

OLGA SALIS
06/14/2010



NDA 022460

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

SmithKline Beecham Corporation
d/b/a GlaxoSmithKline
5 Moore Drive
Research Triangle Park, NC 27709

ATTENTION: Sherman N. Alfors
Director, Antiviral/Antibacterial
US Regulatory Affairs

Dear Mr. Alfors:

Please refer to your New Drug Application (NDA) dated March 20, 2009, received March 20, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dutasteride and Tamsulosin Hydrochloride Capsules, 0.4 mg/0.5 mg.

We also refer to your May 7, 2010, correspondence, received May 7, 2010, requesting review of your proposed proprietary name, Jalyn. We have completed our review of the proposed proprietary name, Jalyn and have concluded that it is acceptable.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Karen Townsend, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5413. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Olga Salis, at (301) 796-0837.

Sincerely,
{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

CAROL A HOLQUIST
06/11/2010



FOOD AND DRUG ADMINISTRATION

Meeting Date: June 6, 2010

Meeting Type: Teleconference

Application Number: NDA 022460

Product Name: dutasteride/tamsulosin combination capsule

Received Briefing Package N/A

Sponsor Name: GlaxoSmithKline (GSK)

Meeting Recorder: Olga Salis, Project Manager, Division of Reproductive and Urologic Products (DRUP)

GSK Attendees:

- Sherman Alfors, PhD, US Regulatory Affairs

FDA Attendees (DRUP):

- Olga Salis, Project Manger

Background:

The Division of Reproductive and Urologic Products (DRUP) provided an “Information Request” letter to the sponsor on June 4, 2010 containing the following comment:

1. Provide declaration of presence of [REDACTED]^{(b) (4)} and/or FD&C Yellow No. 6 as stated in 21 CFR 201.20.

On June 8, 2010, the sponsor responded to the Division and did not agree with the Division and provided the following clarification:

Sponsor: The leaflet indicates that one of the inactive ingredients is FD&C Yellow No. 6. It is our understanding that 21 CFR 201.20(c) which referenced FD&C Yellow No. 6 was suspended December 6, 1988. As far as we can determine, no further action was taken on this regulation. The inactive ingredient will be listed in our product information under Section 11, so the container labeling will not show any reference to FD&C yellow No. 6.

Discussion:

On June 10, 2010, Olga Salis, Regulatory Project Manager (DRUP), held a teleconference with the GSK, who agreed that if the Division at a latter time implements 21 CFR 201.20 for NDA 022460, they agree to submit a supplement for this change.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22460

ORIG-1

SMITHKLINE
BEECHAM CORP
DBA
GLAXOSMITHKLIN
E

DUTASTERIDE/ TAMSULOSIN
HYDROCHLORIDE

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

/s/

OLGA SALIS
06/10/2010



NDA 022460

INFORMATION REQUEST

GlaxoSmithKline LLC
Attention: Sherman N. Alfors
Director, Antiviral/Antibacterial U.S. Regulatory Affairs
5 Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Alfors:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for dutasteride 0.5 mg/tamsulosin hydrochloride 0.4 mg capsules.

We also refer to your February 2, and May 7, 2010, submissions containing requests for proprietary name reviews and product labels.

The Division of Reproductive and Urologic Products (DRUP) along with the Division of Division of Medication Error Prevention and Analysis (DMEPA) is reviewing the Carton and Container Labels, and have the following comments regarding the current labels without consideration to the proprietary name. Once a decision has been made on an acceptable proprietary name, you must revise the labels and labeling accordingly and submit them for review. Alternatively, you can submit labels and labeling that incorporate the recommendations below using "Trademark" as a placeholder for the proprietary name until an acceptable proprietary name is determined. We request a prompt written response in order to continue our evaluation of your NDA.

Container Label (30 and 90 count bottles)

1. Relocate and increase the prominence of the strength statement on the principal display panel (i.e. 0.5 mg/0.4 mg), to appear below the dosage form statement. As currently presented, it is difficult to distinguish and identify the strength.
2. Increase the prominence of the statement "Capsules should be swallowed whole...." As currently presented there is limited white space on the side panel. Thus, it is difficult to read, because it is embedded in the storage, distributor, and usual dosage information.

3. Relocate the statement “Each capsule contains...” from the front principal display panel to the side panel to allow for the implementation of comment 1. As currently presented, the principal display panel appears crowded.
4. Relocate the net quantity statement away from the strength statement (e.g. below the “Rx only” statement). To achieve this we recommend you consider reducing the size of the double arrow graphic.

Container Label (7 count bottles)

1. Relocate and increase the prominence of the strength statement on the principal display panel (i.e. 0.5 mg/0.4 mg), to appear below the dosage form statement. As currently presented it is difficult to distinguish and identify the strength.
2. Increase the prominence of the statement “Capsules should be swallowed whole....” As currently presented there is limited white space on the side panel. Thus, it is difficult to read because it is embedded in the storage, distributor, and usual dosage information.

Additional Comments

1. Provide declaration of presence of [REDACTED]^{(b) (4)} and/or FD&C Yellow No. 6 as stated in 21 CFR 201.20.
2. Clarify the location of “Lot Number” and “Expiration Date” on the container labels.

If you have any questions, call Olga Salis, Regulatory Project Manager, at (301) 796-0837.

Sincerely,

{See appended electronic signature page}

George Benson, M.D.
Deputy Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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

/s/

GEORGE S BENSON
06/04/2010

Salis, Olga

From: Salis, Olga
Sent: Friday, June 04, 2010 2:58 PM
To: 'Andrew Gustafson'
Subject: FW: NDA 022460 IR LTR

Attachments: ScanDoc.PDF

If you are in the office today can you pass this along to appropriate team, since we are getting so close to the PDUFA goal date I would hate for it not to reach the right folks today.

Thanks,
Olga

From: Salis, Olga
Sent: Friday, June 04, 2010 2:53 PM
To: Sherman Alfors
Subject: NDA 022460 IR LTR



ScanDoc.PDF (111
KB)

Please respond officially as soon as possible.

Salis, Olga

From: Salis, Olga
Sent: Friday, June 11, 2010 9:54 AM
To: 'Sherman Alfors'
Subject: RE: GSK - NDA 022460 - FDC (TRADENAME Container Labels)

Not a problem, I will wait for the final submission. Please make sure they the labels comply with comments sent by FDA and all the comments we proposed are implemented.

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Friday, June 11, 2010 9:44 AM
To: Salis, Olga
Subject: RE: GSK - NDA 022460 - FDC (TRADENAME Container Labels)

Olga – Sorry the labels I just sent you still have Jalyn on them in places. I will send you the correct ones in a few minutes.

Thanks,

Sherman

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Friday, June 11, 2010 9:26 AM
To: Sherman Alfors
Subject: RE: GSK - NDA 022460 - FDC (TRADENAME Container Labels)

Sherman,

Is this all the container labels that GSK has?

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Friday, June 11, 2010 9:03 AM
To: Salis, Olga
Subject: GSK - NDA 022460 - FDC (TRADENAME Container Labels)

Olga,

Here are the container labels with 'TRADENAME'. We will send these in an official submission to the NDA today, however I thought you would like these so that you could keep on with your review.

Thank you,

Sherman

Sherman N. Alfors
Global Regulatory Affairs (GRA) – Antivirals (US)
GlaxoSmithKline
☎ 8-703-6030 / 919-483-6030 ✉ sherman.n.alfors@gsk.com

6/11/2010

Salis, Olga

From: Salis, Olga
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To: 'Sherman Alfors'
Subject: RE: GSK - NDA 022460 - FDC (TRADENAME Container Labels)

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To: Salis, Olga
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Thank you,

Sherman

Sherman N. Alfors
Global Regulatory Affairs (GRA) – Antivirals (US)
GlaxoSmithKline
☎ 8-703-6030 / 919-483-6030 ✉ sherman.n.alfors@gsk.com

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Monday, June 07, 2010 2:52 PM
To: 'Andrew Gustafson'
Subject: FW: NDA 022460 Sponsorship/Ownership Name

Mary has given me the information regarding name change so no need to provide me with anything additional.

From: Mary Martinson [mailto:mary.e.martinson@gsk.com]
Sent: Monday, June 07, 2010 2:25 PM
To: Salis, Olga
Subject: NDA 022460 Sponsorship/Ownership Name

Olga,

Per your request via telephone this morning, and the letter you referenced dated May 14, 2010 (with accompanying 356h form dated May 19, 2010), I can verify that the sponsorship/ownership of NDA 022460 has been changed from:

SmithKline Beecham Corporation
One Franklin Plaza
200 North 16th Street
Philadelphia, PA 19102

To:

GlaxoSmithKline LLC
Corporation Service Company
2711 Centerville Road, Suite 400
Wilmington, DE 19808

Please send the acknowledgement letter for this corporate name change to:

Randal Batenhorst, PharmD
Vice President Regulatory Affairs
GlaxoSmithKline
PO Box 13398
5 Moore Drive
Research Triangle Park, NC 27709

Also, with regard to your feedback about subsequent 356h forms having the correct sponsor name and address, GlaxoSmithKline will ensure future FDA forms reflect the correct name and address.

Thank you.

Mary

6/11/2010

Mary E Martinson
Director, Neurosciences
Global Regulatory Affairs
GlaxoSmithKline
Office Phone: 919 483 3763
Mobile Phone: 919 810 1177
RTP - 5.5206
email: mary.e.martinson@gsk.com

Trade secret and/or confidential information contained in this message (including any attachments) is exempt from public disclosure to the full extent provided under law. If you are not the intended recipient of this message, or if you are not responsible for delivering it to the intended recipient(s), do not use, disclose, reproduce, or distribute this message (including any attachments). If you have received this message in error, please erase all copies (including any attachments) and notify me immediately. Thank you.

Salis, Olga

From: Salis, Olga
Sent: Monday, June 07, 2010 2:05 PM
To: 'Andrew Gustafson'
Subject: RE: NDA 022460 IR LTR

Andrew,

Thanks for the response. I need one more item clarified. On May 19, I received a change of corporate name letter from GSK.

Can you clarify for me what the exact name/address used to be prior to the change.

Thanks,
Olga

From: Andrew Gustafson [mailto:andy.n.gustafson@gsk.com]
Sent: Monday, June 07, 2010 9:30 AM
To: Salis, Olga
Subject: RE: NDA 022460 IR LTR

Hi Olga,

Sherman and the Avodart FDC Team are currently working on his.

Thank you.

Andy

Andrew N. Gustafson, Ph.D.
Vice President, Regulatory Affairs, Avodart
GlaxoSmithKline
Work Phone: (919) 483-4461
Work FAX: (919) 315-0033
Mobile Phone: (919) 602-4445
Email: andy.n.gustafson@gsk.com

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Friday, June 04, 2010 2:58 PM
To: Andrew Gustafson
Subject: FW: NDA 022460 IR LTR

If you are in the office today can you pass this along to appropriate team, since we are getting so close to the PDUFA goal date I would hate for it not to reach the right folks today.

Thanks,
Olga

6/11/2010

From: Salis, Olga
Sent: Friday, June 04, 2010 2:53 PM
To: Sherman Alfors
Subject: NDA 022460 IR LTR

<<ScanDoc.PDF>>

Please respond officially as soon as possible.

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Friday, June 11, 2010 8:45 AM
To: 'Sherman Alfors'
Cc: Tiffany Kenney
Subject: RE: Avodart labeling items

Yes, the letter we sent clearly outlines the we need and container labels with TRADENAME. We agree that your formatting is correct and you complied with all the agencies comments but we need this with the TRADENAME placeholder or we can not approve the NDA since JALYN has not yet been approved.

Please send this in this morning, since now we have 1 day to re-view the new container labels.

Thanks,
Olga

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Friday, June 11, 2010 8:41 AM
To: Salis, Olga
Cc: Tiffany Kenney
Subject: RE: Avodart labeling items

Morning Olga,

We sent the revised professional and patient inserts to you yesterday for both Avodart and FDC. Do you want me to send you the container labels with 'TRADENAME' on them?

Thanks,

Sherman

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Thursday, June 10, 2010 12:58 PM
To: Sherman Alfors
Cc: Tiffany Kenney; Zandria King
Subject: RE: Avodart labeling items

Dear All,

The outstanding issues are as follows:

1. As provided via e-mailed the following statement in the ADVERSE REACTIONS section into for 21319 S018 should be placed back. NDA 022460, has this statement and just needs the removal of the last verbiage as indicated below.

Adverse reaction information over the first 2 years of treatment is presented below; information for years 2 to 4 is not yet available (b) (4)

2. In case we do not have tradename by Monday I will need you to resubmit Carton and Container labels, similar to the submission dated 6/8, however, the letter from FDA indicated to use a place holder "TRADE NAME"

6/11/2010

If we do not have a decision regarding JALYN, or in the case it will be dined, we will need to use the "TRADENAME" place holder version to attach to the action letter. We can not approve an NDA without labels and currently, the once with JALYN can not be used.

3. NDA 022460- Remove extra statement in line 1064 that was meant as a comment during labeling negotiations. Please confirm that spacing in the PPI is correct.

Please feel free to call me or e-mail me anytime. Since time in not on our side, please respond officially as soon as possible so we can proceed with the review of both application.

Thanks,

Olga Salis

301-796-0837

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Thursday, June 10, 2010 10:49 AM
To: Salis, Olga
Cc: Tiffany Kenney; Zandria King
Subject: RE: Avodart labeling items

Olga,

Thanks for your patience. I have conferred with our Labeling Group, they are copied on this note, and we can provide you with the following information and decisions:

Registered and Trademark Identification

Avodart is Registered, so the correct identification is the circle R. FDA has informed us that for the XML format labeling that we submit, we should not place the Registered Mark in the Highlights section, but it should appear with the first mention of the name in the Full Prescribing Information section. The manufactured PI, which accompanies the drug product, will also show the Registered Mark on the Title Panel. So the XML versions that we sent to you are correct.

Patient PI

The statement, "General information about AVODART." currently ends with a period. We are fine with that format. It is consistent with all the other statements appearing as sentences. So we believe that it is fine to leave the period at the end of this statement.

Version Tracking Code

The identifier that you asked about, "AVT:5PI" is our internal version tracking code for this version of the PI and PIL. AVT stands for Avodart, the number represents the version and the PI or PIL identifies the Package Insert or Patient Information Leaflet.

Hope this is helpful. We do not believe that another version of the labeling needs to be resubmitted. Our Team has reviewed the labeling for FDC and Avodart and we have no further revisions to make. Call me if you have any questions.

Thank you,

Sherman

6/11/2010

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Thursday, June 10, 2010 9:39 AM
To: Sherman Alfors
Subject: Avodart labeling items

Sherman,

Have you heard back from the labeling team if you will need to re-submit the labeling submitted on June 8, 2010, updating some of the items we discussion this morning. Please let me know ASAP since I do not have much time to re-review the label.

Thanks,
Olga

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Thursday, June 10, 2010 12:58 PM
To: 'Sherman Alfors'
Cc: Tiffany Kenney; Zandria King
Subject: RE: Avodart labeling items

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The outstanding issues are as follows:

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If we do not have a decision regarding JALYN, or in the case it will be dined, we will need to use the "TRADENAME" place holder version to attach to the action letter. We can not approve an NDA without labels and currently, the once with JALYN can not be used.

3. NDA 022460- Remove extra statement in line 1064 that was meant as a comment during labeling negotiations. Please confirm that spacing in the PPI is correct.

Please feel free to call me or e-mail me anytime. Since time in not on our side, please respond officially as soon as possible so we can proceed with the review of both application.

Thanks,

Olga Salis

301-796-0837

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Thursday, June 10, 2010 10:49 AM
To: Salis, Olga
Cc: Tiffany Kenney; Zandria King
Subject: RE: Avodart labeling items

Olga,

Thanks for your patience. I have conferred with our Labeling Group, they are copied on this note, and we can provide you with the following information and decisions:

Registered and Trademark Identification

6/11/2010

Avodart is Registered, so the correct identification is the circle R. FDA has informed us that for the XML format labeling that we submit, we should not place the Registered Mark in the Highlights section, but it should appear with the first mention of the name in the Full Prescribing Information section. The manufactured PI, which accompanies the drug product, will also show the Registered Mark on the Title Panel. So the XML versions that we sent to you are correct.

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The identifier that you asked about, "AVT:5PI" is our internal version tracking code for this version of the PI and PIL. AVT stands for Avodart, the number represents the version and the PI or PIL identifies the Package Insert or Patient Information Leaflet.

Hope this is helpful. We do not believe that another version of the labeling needs to be resubmitted. Our Team has reviewed the labeling for FDC and Avodart and we have no further revisions to make. Call me if you have any questions.

Thank you,

Sherman

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Sent: Thursday, June 10, 2010 9:39 AM

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Sherman,

Have you heard back from the labeling team if you will need to re-submit the labeling submitted on June 8, 2010, updating some of the items we discussed this morning. Please let me know ASAP since I do not have much time to re-review the label.

Thanks,
Olga

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Tuesday, June 08, 2010 4:21 PM
To: 'Sherman Alfors'
Subject: RE: 022460-change

Sherman,

According to 21 CFR 201.20(c), the presence of FD&C Yellow No. 6 needs to be declared. Listing all the excipients does not serve the purpose of declaring a specific ingredient such as FD&C Yellow No. 6 .

Therefore, a separate statement still needs to be added.

Thanks,
Olga

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Tuesday, June 08, 2010 3:46 PM
To: Salis, Olga
Subject: RE: 022460-change

Thanks Olga.

Our Labeling Team is also checking on this. If the FDA CMC Team want us to list it separately, this is precedent setting and is something we would have to consider for all our other products.

Thanks,

Sherman

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Tuesday, June 08, 2010 3:43 PM
To: Sherman Alfors
Subject: RE: 022460-change

I am trying to contact the CMC review team that requested the change. They may have left for the day but I will get in touch with you soon and either way, this can be resolved tomorrow.

Thanks,
Olga

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Tuesday, June 08, 2010 3:39 PM
To: Salis, Olga
Subject: FW: 022460-change

Olga,

6/11/2010

It is also listed in the Patient Labeling section as well.

Thanks,

Sherman

From: Sherman Alfors
Sent: Tuesday, June 08, 2010 3:31 PM
To: 'Salis, Olga'
Subject: RE: 022460-change

Olga,

The official submissions have already gone out.

FD&C Yellow No. 6 is already listed in line 460 (or 461). Why does it need to be listed separately again? If this change is needed, we can get it to you early tomorrow.

Thank you,

Sherman

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Tuesday, June 08, 2010 3:16 PM
To: Sherman Alfors
Subject: 022460-change
Importance: High

Sherman,

We have one additional edit that we will need you to correct and re-submit officially. Hopefully it's not too late to go out with the submission today.

The only change is to line 479.

According to 21 CFR 201.20(c), FD&C Yellow No. 6 only needs to be declared in the labeling (PI) not on the container labels. Therefore, I added a statement in Section 11 of the PI to indicate the presence of FD&C Yellow No. 6 in the drug product.

Attached please find the PI with the added statement.

Please let me know if you have any questions.

Thank you.

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Tuesday, June 08, 2010 1:34 PM
To: Salis, Olga
Subject: FW: JALYN

6/11/2010

Olga,

Here are the Word copies for FDC. Again these are being officially submitted today.

Thank you,

Sherman

From: Melissa Beaman
Sent: Tuesday, June 08, 2010 1:01 PM
To: Sherman Alfors
Subject: JALYN

Melissa Beaman
Manager, US
Global Regulatory Affairs (GRA)
919-483-9316



GLOBAL REGULATORY AFFAIRS

6/11/2010

Salis, Olga

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Thank you,

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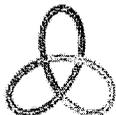
From: Melissa Beaman

Sent: Tuesday, June 08, 2010 1:01 PM

To: Sherman Alfors

Subject: JALYN

Melissa Beaman
Manager, US
Global Regulatory Affairs (GRA)
919-483-9316



GLOBAL REGULATORY AFFAIRS

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Tuesday, June 08, 2010 11:40 AM
To: 'Sherman Alfors'
Cc: Andrew Gustafson; Melissa Beaman
Subject: RE: LABELING FROM FDA

For Both NDAs

Please submit an official cover letter stating you agree to all of our change. Submit a word version of the labeling as you agree for it to appear.

It would be very helpful if this can happen today.

Thanks,
Olga

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Tuesday, June 08, 2010 11:35 AM
To: Salis, Olga
Cc: Andrew Gustafson; Melissa Beaman
Subject: RE: LABELING FROM FDA

Olga,

Thanks for the labeling. We accept them as sent to us for both Avodart and FDC – we have no further revisions. What do you need from us now? Our Labeling folks think you have everything you need since we are not making any further revisions – but we will be glad to send you whatever you need.

Thanks,

Sherman

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Monday, June 07, 2010 3:09 PM
To: Andrew Gustafson; Sherman Alfors
Subject: LABELING FROM FDA

<<DRUP NDA 22-460 label June 7 10.doc>> <<DRUP NDA21319-S018 label June 7 2010.doc>>

Sherman and Andrew,

Attached please see our response to your last labeling negotiations for both 021319/S-018 and 022460.

6/11/2010

We will do our best to take action the same day on both products, so please respond ASAP if you agree and accept the changes, I will need an e-mail followed by an official submission.

Let me know if you have any questions,

-Olga

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Monday, May 24, 2010 5:41 PM
To: 'Sherman Alfors'
Subject: Patient information for NDA 22460

Attachments: DRUP NDA 22-460 Patient Information Format.doc



DRUP NDA 22-460
Patient Inform...

I also wanted to send you this document for your team to work on.

Salis, Olga

From: Salis, Olga
Sent: Monday, May 24, 2010 4:21 PM
To: 'Sherman Alfors'
Subject: LABEL NDA 22460
Attachments: DRUP NDA 22-460 PI and PPI.5.24.doc

Thanks for your response. I will share it with my team.

Attached is the label I promised you today. Please respond as soon as you can, no later than one week from today.

Thanks,
Olga

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Monday, May 24, 2010 4:05 PM
To: Salis, Olga
Cc: Andrew Gustafson
Subject: GSK - Avodart - Establishment and Registration Numbers

Re: NDA 021319 Avodart (dutasteride) Soft Gelatin Capsules
[REDACTED] (b) (4)
Submitted March 12, 2010

Olga,

In response to your question earlier today, this is a clinical supplement. There was no submission of CMC information and no reference to manufacturing facilities, so there are no establishment or registration numbers applicable to this application. Call me or Andy if you have further questions.

Thank you,

Sherman

Sherman Alfors
Global Regulatory Affairs
GlaxoSmithKline
RTP 5.5418
w: (919) 483-6030
f: (919) 483-5756

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Monday, May 24, 2010 11:43 AM
To: 'Sherman Alfors'
Subject: RE: Avodart- information from t-con

Not yet, we will send something soon.

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Monday, May 24, 2010 11:15 AM
To: Salis, Olga
Subject: RE: Avodart- information from t-con

Hi Olga,

Did the team finalize labeling to send to us? I did not received anything last week.

Thank you,

Sherman

From: Salis, Olga [mailto:OLGA.SALIS@fda.hhs.gov]
Sent: Thursday, May 13, 2010 3:29 PM
To: Sherman Alfors
Cc: Andrew Gustafson
Subject: Avodart- information from t-con

<<DRUP Cardiac Failure SLR.doc>>

Sherman and Andrew,

The attached documents reflect proposed labeling language for Cardiac Failure in the Adverse Reactions section of the PI. We will follow up with the actual draft label sometime next week, which will show you the exact placement of these proposed changes.

Also attached is the table of adjudicated cases for your information.

Thanks,
Olga

Fyi- I will be on leave next week but I will have someone send you the labeling once we are done with it.

6/11/2010

Salis, Olga

From: Salis, Olga
Sent: Monday, April 19, 2010 7:25 AM
To: 'Sherman Alfors'
Subject: RE: GSK - NDA 022460 Fixed Dose Combination (dutasteride and tamsulosin)

Sherman,

I looked into this issue last week and basically the PDUFA goal date for the name is May 3, 2010.

You direct contact is:

Karen F. Townsend

Safety and Regulatory Project Manager

FDA/CDER/OSE

301-796-5413

Thanks,

Olga

From: Sherman Alfors [mailto:sherman.n.alfors@gsk.com]
Sent: Tuesday, April 13, 2010 1:59 PM
To: Salis, Olga
Subject: GSK - NDA 022460 Fixed Dose Combination (dutasteride and tamsulosin)

Hi Olga,

I wonder if you might be able to give me update information as to when we will hear from the Review Team on our Proprietary Name submission on February 2, 2010. Any information is appreciated.

Thank you,

Sherman

Sherman Alfors
Global Regulatory Affairs
GlaxoSmithKline
RTP 5.5418
w: (919) 483-6030
f: (919) 483-5756

6/11/2010

3 Page(s) has been Withheld in Full as
B4 (CCI/TS) immediately following
this page

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 022460 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: dutasteride and tamsulosin Dosage Form: 0.5 mg dutasteride and 0.4 mg tamsulosin		Applicant: GlaxoSmithKline Agent for Applicant (if applicable):
RPM: Olga Salis		Division: Division of Reproductive and Urologic Products
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		
<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u> Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>NDA 021319 Avadart (dutasteride) NDA 020579 Flomax (tamsulosin)</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>NDA 022460 proposes a new combination of tamsulosin and dutasteride. The combination capsule is produced by over-encapsulating the intermediates of the 2 active drug products.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>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.</p> <p><input type="checkbox"/> No changes <input checked="" type="checkbox"/> Updated Date of check: 1/19/10</p> <p>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.</p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p>		
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>1/20/10</u> 		<input type="checkbox"/> AP <input checked="" type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None

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.

<p>❖ If accelerated approval, were promotional materials received? Note: For 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 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics²</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><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</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request</p> <p>Comments:</p>	
<p>❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes, date
<p>❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • 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 Answer all questions in all sections in relation 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 type="checkbox"/> No <input checked="" type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: 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 checked="" 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 checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires: PED June 22, 2013 and M-54, December 22, 2012 (does not effect this b2 action)
<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 checked="" type="checkbox"/> Yes If yes, NDA # 020579 and date exclusivity expires: 4/27/10
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<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 checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input checked="" 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 4/27/07
<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 checked="" 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?

(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)?

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?

(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)?

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).

Yes No

Yes No

Yes No

Yes No

<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>
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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>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) 1/20/10
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 draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	NDA 20579 Flomax and NDA 21319 Avodart

³ Fill in blanks with dates of reviews, letters, etc.
Version: 12/4/09

❖ 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 <input type="checkbox"/> Instructions for Use <input type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in ttrack-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	March 20, 2009
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	NDA 21319 Avodart NDA 20579 Flomax
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> • Most-recent draft labeling 	pending review
❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) 	not acceptable letters: 9/8/09 and 12/16/09 Reviews: 9/8/09 and 12/11/09
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input type="checkbox"/> RPM <input type="checkbox"/> DMEDP <input checked="" type="checkbox"/> DRISK 11/25/09 <input checked="" type="checkbox"/> DDMAC 11/25/09 <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews Drug usage data 7/23/09 and 12/6/09 Division of Epidemiology Office of Surveillance and Epidemiology
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	5/12/09
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<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 (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>9/29/09</u> If PeRC review not necessary, explain: _____ • Pediatric Page (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<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 (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 12/4/09

❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)	E-MAIL 12/3, 12/4, 12/15 and 12/16/2009 LETTERS 4/1, 5/27, 8/3, 8/4, 9/8, 9/24, 10/26, 11/2, 12/16/2009 and 1/8/10 T-CON 11/19/09
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Pre-Approval Safety Conference (<i>indicate date of mtg; approvals only</i>)	Not applicable
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> Not applicable
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilot programs) (<i>indicates dates</i>)	none
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/19/10
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/19/10
PMR/PMC Development Templates (<i>indicate total number</i>)	<input type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	1/19/10
• Clinical review(s) (<i>indicate date for each review</i>)	Filing Review
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	Page 12 of MO review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable

⁵ Filing reviews should be filed with the discipline reviews.

❖ Risk Management	
<ul style="list-style-type: none"> REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) REMS Memo (<i>indicate date</i>) Risk management 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>) 	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None Filing 5/6/09 NDA Review 10/23/09
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None Filing 6/3/09 NDA Review 1/6/10/ & 1/15/10
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	<input type="checkbox"/> None 1/14/10
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
<ul style="list-style-type: none"> ADP/T Review(s) (<i>indicate date for each review</i>) Supervisory Review(s) (<i>indicate date for each review</i>) Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None
	<input checked="" type="checkbox"/> None
	<input type="checkbox"/> None Filing 5/6/09 NDA Review 11/18/10
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
<ul style="list-style-type: none"> ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>) Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None
	<input checked="" type="checkbox"/> None

<ul style="list-style-type: none"> • Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>) 	<input type="checkbox"/> None filing 5/7/09 NDA Review 1/4/10 Biopharm 10/7/09
<ul style="list-style-type: none"> ❖ Microbiology Reviews <ul style="list-style-type: none"> <input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (<i>indicate date of each review</i>) 	<input type="checkbox"/> Not needed 10/1/09 and 12/23/09
<ul style="list-style-type: none"> ❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>) 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> ❖ Environmental Assessment (check one) (original and supplemental applications) 	
<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>) 	1/4/10 Page 141 of CMC review
<ul style="list-style-type: none"> <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) 	
<ul style="list-style-type: none"> <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) 	
<ul style="list-style-type: none"> ❖ Facilities Review/Inspection 	
<ul style="list-style-type: none"> <input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) 	Date completed: 1/4/10 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> <input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) 	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> ❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>) 	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

OLGA SALIS
01/19/2010

David, Jeannie C

From: David, Jeannie C
Sent: Wednesday, December 16, 2009 4:50 PM
To: 'lan.x.nguyen@gsk.com'
Cc: Salis, Olga
Subject: RE: NDA 22460 - Request for a Courtesy Copy the FDA's Information Request - December 2009

Dear Ms. Nguyen,

We thank you for your consideration. The Agency no longer sees a need for a teleconference. The proposal to submit the updated validation data in the annual report is acceptable.

Please submit your amendment with a revised specification table for Dutasteride and Tamsulosin Combination Capsules (DTC) to reflect our agreements on 1) the dissolution method and acceptance criteria and 2) the microbial limit tests and criteria, and update all affected sections of the NDA. Please also include a statement of GSK's commitment to submit the aforementioned updated validation data in the annual report.

We would like to request that the amendment be provided by December 24, 2009, if feasible. We also would appreciate an electronic courtesy copy, in order to facilitate our review.

Thank you,

Jeannie

Jeannie David, M.S.
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drug Quality Assessment
10903 New Hampshire Avenue
Building 22, Mail Room 1491
Silver Spring, MD 20993
Phone: (301) 796-4247
Fax: (301) 796-9877

jeannie.david@fda.hhs.gov

From: lan.x.nguyen@gsk.com [mailto:lan.x.nguyen@gsk.com]
Sent: Tuesday, December 15, 2009 3:33 PM
To: David, Jeannie C
Cc: Salis, Olga
Subject: RE: NDA 22460 - Request for a Courtesy Copy the FDA's Information Request - December 2009

Dear Ms. David,

GSK acknowledge the receipt of FDA's meeting request which was sent by email on December 15, 2009 related to our New Drug Application (NDA) 22-460 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 0.4 mg Dutasteride and 0.5 mg Tamsulosin Hydrochloride Capsules.

Reference is made to the teleconference held between representatives of FDA and GSK on November 19, 2009 and the additional development information that GSK submitted on November 24, 2009. GSK thanks the Agency for reviewing the

12/16/2009

additional development data.

GSK agrees to the changes recommended by the Agency in the attached email. We will amend our NDA by January 7, 2010 to update the method and acceptance criteria for Dutasteride and Tamsulosin Combination Capsules (DTC) as indicated in the FDA's attached document. GSK is in the process of re-validating the DTC dissolution method for Tamsulosin HCl release with the 50rpm paddle speed. The validation will be completed before the release testing of commercial batches. All commercial batches will be tested against the updated specification using the updated method. GSK is requesting the Agency's permission to submit the updated validation data in the annual report.

In light of the above agreement, please let us know if there is still a need for a meeting on December 17, 2009.

Reference is also made to GSK agreement made on December 03, 2009 of adding the microbiological tests to the DTC specification. We will amend our NDA to reflect this change by January 07, 2009.

GSK appreciates to know if there may be other CMC questions from the Agency before the action date of January 20, 2010. Please be aware that GSK has a year-end shutdown from December 25, 2009 to January 3, 2010. For urgent matters, please do not hesitate to call me on my cellular phone at 919 607-0222 during the shutdown period.

Best Regards,

Lan Nguyen

Global Pre-Approval
CMC Regulatory Affairs
GlaxoSmithKline
P.O.Box 13398
5.5347.5C
Research Triangle Park, NC 27709
Phone: (919) 483-4625
Fax: (919) 483-5381
Email: lan.x.nguyen@gsk.com

"David, Jeannie C" <Jeannie.David@fda.hhs.gov>

15-Dec-2009 11:19

To lan.x.nguyen@gsk.com

cc

Subject RE: NDA 22460 - Request for a Courtesy Copy the FDA's Information Request - December 2009

Dear Ms. Nguyen,

Please refer to GSK's New Drug Application (NDA) 22-460 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 0.4 mg dutasteride and 0.5 mg tamsulosin hydrochloride Capsules. Please also refer to the teleconference held between representatives of your firm and the FDA on November 18, 2009. We request a teleconference to discuss issues as follow up to the November 18, 2009, teleconference, related to the Biopharmaceutics sections of NDA 22-460. For your convenience, the topics for discussion are provided below:

1. *The data submitted to NDA 22-460 on November 24, 2009 regarding the dissolution method and specification for the dutasteride component of your DCT product support your proposed dissolution acceptance criterion of Q = (b) (4) % in 60 minutes.*
2. *We have reviewed the bioequivalence studies conducted with DTC Batch 705002-91294 and the similar DTC product Batch 710001-102133 as well as the dissolution profiles data for these batches. Your proposed lower limit of the specification for the tamsulosin hydrochloride component of (b) (4) % at 3 hours is supported given that the mean dissolution profile for bath 710001-102133 was (b) (4) %. However, your proposed upper limit of (b) (4) % at 3 hours is NOT justified based on a mean dissolution profile of (b) (4) % for batch 705002-91294. We recommend that the upper bound be set as (b) (4) %.*
3. *In summary, the following method and acceptance criteria for Dutasteride and Tamsulosin Hydrochloride Capsules*

12/16/2009

have been agreed upon or recommended by the Agency:

We request a half-hour (1/2 hr) teleconference within the following timeframes:

- Thursday, December 17, within 11:00 AM - 1:00 PM
- Thursday, December 17, within 3:00 PM - 4:00 PM

Please provide a call in number for the teleconference.

Thank you,

Jeannie
Jeannie David, M.S.
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drug Quality Assessment
10903 New Hampshire Avenue
Building 22, Mail Room 1491
Silver Spring, MD 20993
Phone: (301) 796-4247
Fax: (301) 796-9877
jeannie.david@fda.hhs.gov

From: lan.x.nguyen@gsk.com [<mailto:lan.x.nguyen@gsk.com>]
Sent: Tuesday, November 17, 2009 2:03 PM
To: David, Jeannie C
Cc: Salis, Olga
Subject: NDA 22460 - Request for a Courtesy Copy the FDA's Information Request - November 2009

Dear Ms. David,

Thank you so much for your notification by telephone this afternoon regarding the FDA's information and meeting requests.

I appreciate if you could send me the courtesy copy of the information request by email.

GSK will be able to meet with the FDA reviewers this Thursday at 4pm.

We look forward to meeting with the agency to discuss any concerns that the Agency may have.

Best Regards,

Lan Nguyen

CMC Pre-Approval
Global Regulatory Affairs
GlaxoSmithKline
P.O.Box 13398
5.5347.5C
Research Triangle Park, NC 27709
Phone: (919) 483-4625
Fax: (919) 483-5381
Email: lan.x.nguyen@gsk.com

12/16/2009

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

JEANNIE C DAVID
12/16/2009

MEMORANDUM OF TELECON

DATE: November 19, 2009

APPLICATION NUMBER: NDA 22-460 dutasteride and tamsulosin capsules

BETWEEN:

Name: Meg Thompson, Manager, Pharmaceutical Development
John McCune, Director, Pharmaceutical Development
Michael Fossler, Director, Clinical Pharmacology
Susan Holmes, Director, Global Pre-Approval, CMC Regulatory Affairs
Lan Nguyen, Asst Director, Global Pre-Approval, CMC Regulatory Affairs

Phone: Call-in number provided by GSK
Lan Nguyen, office: (919) 483-4625

Representing: GlaxoSmithKline

AND

Name: *Office of New Drug Quality Assessment*
Sandra Suarez, Ph.D., Biopharmaceutics Reviewer
Patrick Marroum, Ph.D., Biopharmaceutics Reviewer
Yichun Sun, Ph.D., Chemistry Reviewer
Donna Christner, Ph.D., Pharmaceutical Assessment Lead
Jeannie David, M.S., Regulatory Health Project Manager

SUBJECT: Biopharmaceutics requests

Background:

GSK submitted an original NDA 22-460 on March 20, 2009. GSK submitted a Response to Information Request amendment on October 2, 2009, to address an FDA Information Request letter dated September 24, 2009, requesting dissolution information for the dutasteride and tamsulosin components of the drug product.

The following 2 points were conveyed to Lan Nguyen, GSK, from Jeannie David, Regulatory Project Manager in FDA/ONDQA, by email on November 18, 2009, in preparation for discussion for the November 19, 2009, teleconference:

1. On October 2, 2009, you provided requested information regarding the dissolution method development for the tamsulosin component of the combination product. These data included the evaluation of the effect of dissolution media, pH, and paddle speed. It was shown that there was no difference in the dissolution profile as a function of paddle speed (e.g. (b) (4) rpm); therefore, we recommend that you use the lower paddle speed (e.g 50 rpm) instead.

Based on the mean tamsulosin hydrochloride dissolution profiles from combination capsules batches used on BE Studies (Batch 705002), primary stability testing (Batches 94705001 and 705004-91294) and at registration (Batch 806001), the following acceptance criteria for the dissolution test of the tamsulosin component are recommended:

Drug Name	Dosage Form	USP Apparatus	Speed (rpms)	Medium	Volume (mL)	Acceptance Criteria
Flodart (tamsulosin component)	Capsule (tamsulosin part: ER pellets)	II (Paddle)	50	Acid Stage (0-2 hrs): 0.1 N HCl Buffer stage: Add 250 mL of 0.2 M Sodium Phosphate Tribasic, Dodecahydrate pH 6.8	750 1000	Acid Stage: Not greater than (b) (4) % dissolved in 2 hours Buffer Stage: Timepoint Acceptance Criteria 3 hrs: (b) (4) % 6 hrs: (b) (4) %

2. Based on the data provided the following acceptance criterion for the dissolution test of the dutasteride component is recommended:

Drug Name	Dosage Form	USP Apparatus	Speed (rpm)	Medium	Volume (mL)	Acceptance Criterion
Flodart (dutasteride component)	Capsule (soft gelatin)	II (Paddle)	75	Tier I (non-enzymatic): 900 mL of 1% w/v cetyltrimethylammonium bromide (CTAB) in 0.1 N HCl Tier II (enzymatic) 900 mL of 1% w/v CTAB in 0.1 N HCl with 0.16% w/v pepsin	900	Q = (b) (4) % in 45 minutes

Discussion:

Regarding Point 1 for the dissolution test of the tamsulosin component, where the FDA had recommended a lower paddle speed of 50 rpm, GSK stated that although they have limited data at this speed, **GSK agrees to the change.**

Regarding Point 1 for the dissolution test of the tamsulosin component, where the FDA had recommended a buffer stage timepoint acceptance criterion of 6 hrs: (b) (4) %, (b) (4) %, (b) (4) %, **GSK stated that they will accept this change.**

Regarding Point 1 for the dissolution test of the tamsulosin component, where the FDA had recommended a buffer stage timepoint acceptance criterion of 3 hrs: (b) (4) %, GSK requested clarification of the FDA's concerns. The FDA stated that as recommended under the Guidance, they had considered the mean +/- 10% tolerance based on the data provided. GSK replied that they had taken the mean dissolution from the 3 hour timepoint and used the mean of (b) (4) % weight gain for the enteric coat for the top of the specification, and used the mean of (b) (4) % weight gain for the enteric coat for the bottom of the specification. The sponsor added that the (b) (4) % weight gain formulation was shown to be bioequivalent to Flomax. **FDA stated that we would go back and**

review if the data would support reconsideration of our recommendation. FDA stated that they would get back to GSK on this.

At present, the FDA will accept all data collected at a paddle speed of (b) (4) rpm, but that from this point on, GSK should use 50 rpm for release and stability testing.

Regarding Point 2 for the dissolution test of the dutasteride (DTC) component, where the FDA had recommended $Q = \frac{(b)}{(4)}\%$ in 45 minutes, GSK requested clarification of the FDA's concerns. The FDA stated that our recommendation was based on the dissolution data provided. Based on the *in vitro* performance, and the applicability of the bioequivalence data that crosslinked the capsules to Avodart only, FDA stated that the specification must be the same as for Avodart. FDA also added that from long standing policy, the timepoint selected is that at which $\frac{(b)}{(4)}\%$ dissolution occurs, which in this case is at 45 minutes, so the 60 minutes is not justified. GSK replied that the addition

(b) (4)

specification. **FDA requested that GSK submit the data showing how the** (b) (4)
(b) (4), and the FDA will review if the data support reconsideration to $Q = \frac{(b)}{(4)}\%$ in 60 minutes.

The call ended.

Jeannie David
Regulatory Project Manager
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Concurrence:

P. Marroum 12/11/09 verbal from S. Suarez

S. Suarez 12/7/09

Y. Sun 12/4/09

D. Christner 12/4/09

Post-teleconference related activities:

11/24/2009 Quality/Response to Information Request submitted to NDA 22-460 EDR

12/07/2009 Suarez, Sandra - REV-QUALITY-03(General Review)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

JEANNIE C DAVID

12/15/2009

Concurrence on minutes from biopharm and chemistry team

David, Jeannie C

From: David, Jeannie C
Sent: Friday, December 04, 2009 1:26 PM
To: 'lan.x.nguyen@gsk.com'
Cc: Salis, Olga
Subject: Re: NDA 22-460 FDA Request for Teleconference - December 2009

Dear Ms. Nguyen,

In light of GSK's agreement to the proposed specification, the Agency no longer sees a need for a teleconference. Please provide your response as a formal submission to the NDA, including updates to the DP specification table and all affected sections of the NDA.

Thank you,

Jeannie

Jeannie David, M.S.
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drug Quality Assessment
10903 New Hampshire Avenue
Building 22, Mail Room 1491
Silver Spring, MD 20993
Phone: (301) 796-4247
Fax: (301) 796-9877

jeannie.david@fda.hhs.gov

From: lan.x.nguyen@gsk.com [mailto:lan.x.nguyen@gsk.com]
Sent: Thursday, December 03, 2009 3:39 PM
To: David, Jeannie C
Cc: Salis, Olga
Subject: Re: NDA 22-460 FDA Request for Teleconference - December 2009

Dear Ms. David,

GSK considered the agency's request related to the drug product microbiological attributes. We agree with the Agency's proposal to add the microbial limit tests and criteria to the regulatory specification for Dutasteride and Tamsulosin Combination Capsules. The specification criteria will be "the product meets the requirements of USP <1111>, <61> and <62> if tested". If the Division agrees, GSK will submit a response to the Division of Reproductive and Urologic Products in Maryland to confirm GSK agreement in this regard.

Best Regards,

Lan Nguyen

Global Pre-Approval
CMC Regulatory Affairs
GlaxoSmithKline

12/4/2009

P.O.Box 13398
5.5347.5C
Research Triangle Park, NC 27709
Phone: (919) 483-4625
Fax: (919) 483-5381
Email: lan.x.nguyen@gsk.com

"David, Jeannie C" <Jeannie.David@fda.hhs.gov>

03-Dec-2009 10:39

To lan.x.nguyen@gsk.com

cc "Salis, Olga" <OLGA.SALIS@fda.hhs.gov>

Subject NDA 22-460 FDA Request for Teleconference - December 2009

Dear Ms. Nguyen,

Please refer to GSK's New Drug Application (NDA) 22-460 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 0.4 mg dutasteride and 0.5 mg tamsulosin hydrochloride Capsules. As discussed, we are reviewing the Chemistry, Manufacturing and Controls sections of GSK's submission and request a teleconference to discuss an issue related to the Drug Product Microbiological Attributes. For your convenience, the topic for discussion is provided below:

The batch release criteria should identify the specific manufacturing process tests and criteria used to assess the finished product as microbiologically suitable for release. In that regard, the product specification should state that "the product meets the requirements of USP <1111>, <61> and <62> if tested" in your batch release criteria.

We request a half-hour (1/2 hr) teleconference within the following timeframes:

- Monday, December 7, after 2:00 PM
- Tuesday, December 8, after 2:00 PM

We would appreciate if you could provide a call in number for the teleconference as well. Thank you for your assistance.

Regards,

Jeannie

Jeannie David, M.S.
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drug Quality Assessment
10903 New Hampshire Avenue
Building 22, Mail Room 1491
Silver Spring, MD 20993
Phone: (301) 796-4247
Fax: (301) 796-9877

jeannie.david@fda.hhs.gov

From: lan.x.nguyen@gsk.com [mailto:lan.x.nguyen@gsk.com]
Sent: Tuesday, November 17, 2009 2:03 PM
To: David, Jeannie C

12/4/2009

Cc: Salis, Olga

Subject: NDA 22460 - Request for a Courtesy Copy the FDA's Information Request - November 2009

Dear Ms. David,

Thank you so much for your notification by telephone this afternoon regarding the FDA's information and meeting requests.

I appreciate if you could send me the courtesy copy of the information request by email.

GSK will be able to meet with the FDA reviewers this Thursday at 4pm.

We look forward to meeting with the agency to discuss any concerns that the Agency may have.

Best Regards,

Lan Nguyen

CMC Pre-Approval
Global Regulatory Affairs
GlaxoSmithKline
P.O.Box 13398
5.5347.5C
Research Triangle Park, NC 27709
Phone: (919) 483-4625
Fax: (919) 483-5381
Email: lan.x.nguyen@gsk.com

12/4/2009

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

JEANNIE C DAVID
12/04/2009
concurrence from Quality Micro and Quality Review



NDA 22-460

INFORMATION REQUEST

SmithKline Beecham Corp. d/b/a GlaxoSmithKline
Attention: Sherman N. Alfors
Director, U.S. Regulatory Affairs
5 Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Alfors:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 0.4 mg dutasteride and 0.5 mg tamsulosin hydrochloride Capsules.

We are reviewing the Chemistry, Manufacturing and Controls sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Your response would be appreciated by November 13, 2009:

1. Provide a certificate of analysis of the primary reference standard used to evaluate tamsulosin hydrochloride in DTC.
2. Provide detailed information on the preparation, and a certificate of analysis for the working reference standard used to evaluate tamsulosin hydrochloride in DTC.
3. The proposed holding times for the dutasteride and tamsulosin hydrochloride intermediates are not supported by the stability data provided. The holding time is granted (b) (4) for the dutasteride and tamsulosin hydrochloride intermediates.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Olga Salis, Regulatory Project Manager in the Division of Reproductive and Urologic Products (Olga.Salis@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

MOO JHONG RHEE
11/02/2009
Chief, Branch III

Salis, Olga

From: Salis, Olga
Sent: Monday, November 16, 2009 3:42 PM
To: Kaul, Suresh
Cc: Nguyen, Christine
Subject: FW: NDA 22-460 Flodart

Importance: High

We got the waiver (see e-mail below)

Thanks,
Olga

From: Greeley, George
Sent: Monday, September 28, 2009 1:34 PM
To: Salis, Olga
Cc: Stowe, Ginneh D.
Subject: NDA 22-460 Flodart
Importance: High

Hi Olga,

The Flodart (dutasteride and tamsulosin) full waiver was reviewed by the PeRC PREA Subcommittee on September 23, 2009.

The Division recommended a full waiver because studies would be impossible or highly impracticable and because disease/condition does not exist in children.

The PeRC agreed with the Division to grant a full waiver for this product.

Thank you.

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

 Please consider the environment before printing this e-mail.



NDA 22-460

INFORMATION REQUEST

SmithKline Beecham Corp. d/b/a GlaxoSmithKline
Attention: Sherman N. Alfors
Director, U.S. Regulatory Affairs
5 Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Alfors:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 0.4 mg dutasteride and 0.5 mg tamsulosin hydrochloride Capsules.

We are reviewing the Chemistry, Manufacturing and Controls sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Your response would be appreciated by October 2, 2009:

1. Provide measures taken to prevent overestimation of the amount of dutasteride dissolved in the dissolution medium due to formation of MDC droplets during the dissolution test of dutasteride and tamsulosin hydrochloride capsules.
2. The dissolution information for the dutasteride component of your proposed dutasteride and tamsulosin combination product, is insufficient. Please provide the following information for the dutasteride component of the proposed dutasteride and tamsulosin combination product:
 - Dissolution profiles considering the following time points: 5, 10, 15, 30, 45, and 60 minutes (refer to "Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms").
 - pH dissolution profile
 - Data, if available, supporting consistent bioavailability of dutasteride from the proposed dutasteride and tamsulosin combination product formulation, in the presence of the gelatin capsules crosslinking effect.
2. Provide dissolution method development report and validation for the tamsulosin component of your proposed dutasteride and tamsulosin combination product. The

dissolution method development report should include (but not be limited to) the following information:

- The pH solubility profile of the drug substance
- Dissolution profiles generated at different agitation speeds.
- Dissolution profiles generated in at least three dissolution media.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Olga Salis, Regulatory Project Manager in the Division of Reproductive and Urologic Products (Olga.Salis@fda.hhs.gov).

If you have any questions with regard to this information request letter, contact Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE
NDA-22460	ORIG-1	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLIN E	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

MOO JHONG RHEE
09/24/2009
Chief, Branch III



NDA 22460

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

SmithKline Beecham Corporation
d/b/a GlaxoSmithKline
5 Moore Drive
Research Triangle Park, NC 27709

ATTENTION: Sherman N. Alfors
Director, US Regulatory Affairs

Dear Mr. Alfors:

Please refer to your New Drug Application (NDA) dated March 20, 2009, received March 20, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dutasteride and Tamsulosin Hydrochloride Capsules 0.4 mg/0.5 mg.

We also refer to your June 16, 2009, correspondence, received June 16, 2009, requesting review of your proposed proprietary name, Flodart. We have completed our review of the proposed proprietary name, Flodart, and have concluded that this name is unacceptable for the following reasons.

[Redacted block] (b) (4)

Flodart

Flodart

Flodart

[Redacted block] (b) (4)

We note that you have proposed an alternate proprietary name in your submission dated June 16, 2009. In order to initiate the review of the alternate proprietary name, ^{(b) (4)}, submit a new complete request for proprietary name review. The review of this alternate name will not be initiated until the new submission is received.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Olga Salis, at (301) 796-0837.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22460	ORIG-1	GLAXOSMITHKLIN E INC	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

CAROL A HOLQUIST
09/08/2009



INFORMATION REQUEST LETTER

NDA 22-460

GlaxoSmithKline
Attention: Sherman Alfors
US Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709-3398

Dear Mr. Alfors:

Please refer to your new drug application (NDA) dated March 20, 2009, received March 20, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for dutasteride and tamsulosin capsules.

We are reviewing the Drug Product section, Microbiological Attributes and Quality Overall Summary subsections, of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

The product specification should continue to include the following wording:
“meets the requirements of USP <1111>, <61> and <62> if tested.”

The batch release criteria should identify the specific manufacturing process tests and criteria used to assess the finished product as microbiologically suitable for release. For example, these tests and criteria should include the following:

- Microbial limits data for critical raw materials
- Microbiological environmental monitoring data for critical processing steps, and
- In-process control parameters (e.g., heat, drying, washing) that may affect product quality microbiology

If you have any questions, call Olga Salis, Regulatory Project Manager, at (301) 796-0837

Sincerely,

{See appended electronic signature page}

George Benson, M.D.
Deputy Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

GEORGE S BENSON
08/04/2009



NDA 22-460

**PROPRIETARY NAME REQUEST
WITHDRAWN**

Smith Kline Beechan Corp
d/b/a GlaxoSmithKline
One Franklin Plaza
200 North 16th Street
Philadelphia, PA 19102

ATTENTION: Sherman N. Alfors
Director, US Regulatory Affairs

Dear Mr. Alfors:

Please refer to your New Drug Application (NDA) 22-460 dated March 20, 2009, received March 20, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dutasteride and Tamsulosin Hydrochloride Capsules 0.4 mg/0.5 mg capsules.

We acknowledge receipt of your June 30, 2009, correspondence received on June 30, 2009, notifying us that you are withdrawing your May 12, 2009, request for a review of the proposed proprietary name Flodart. This proposed proprietary name request is considered withdrawn as of June 30, 2009.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Maria Wasilik, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager Olga Salis, at (301) 796-0837.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22460	ORIG 1	GLAXO	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE
NDA 22460	ORIG 1	GLAXO	DUTASTERIDE/ TAMSULOSIN HYDROCHLORIDE

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/s/

LAURIE A KELLEY
07/29/2009

CAROL A HOLQUIST
08/03/2009

GSK has requested to delete the microbial limits testing for future “Flodart” commercial batches.

Upon review of Drug Product sections m.3.2.P.2 (5) Microbiological Attributes and m.2.3.P (5.6) Quality Overall Summary, it is determined that the product specification for Flodart should include the following information.

Comment:

“The product specification should continue to include “meets the requirements of USP <1111>, <61> and <62> if tested.” However, the batch release criteria should identify the specific manufacturing process tests and criteria used to assess the finished product as microbiologically suitable for release. These tests and criteria should include, for example:

- Microbial limits data for critical raw materials,
- Microbiological environmental monitoring data for critical processing steps, and
- In-process control parameters (e.g., heat, drying, washing) that may affect product quality microbiology.”

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/s/

VINAYAK B PAWAR
07/27/2009



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-460

GlaxoSmithKline
Attention: Sherman Alfors
US Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709-3398

Dear Mr. Alfors:

Please refer to your new drug application (NDA) dated March 20, 2009, received March 20, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (dutasteride and tamsulosin) Capsules.

We also refer to your submissions dated April 1, May 5, and May 12, 2009.

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 **Standard**. Therefore, the user fee goal date is January 20, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by December 30, 2009.

During our filing review of your application, we identified the following potential review issues and/or have the following information requests:

Clinical

1. Provide the version of MedDRA coding dictionary used to code the adverse events.

2. Provide the mapping of investigator verbatim terms to the MedDRA Preferred Terms and from the MedDRA Preferred Terms to the investigator verbatim terms.
3. Provide the correct titles for Listing 8 and Table 8 in Module 5.3.5.1.22. Currently, Listing 8 is titled “Summary of Non-Fatal Serious AEs and Study Drug Discontinued” and Table 8 is titled “Summary of Non-Fatal Serious AEs (Post-Randomization) and Study Drug Permanently Discontinued.” Listing 8 and Table 8 appear to be a listing and summary, respectively, of all non-fatal SAEs from post-randomization to December 8, 2008, whether or not these SAEs led to permanent drug discontinuation.
4. Clarify if there is any difference between adverse event listings/tables in Module 5.3.5.1.22 that are labeled “Post-Randomization” versus “Cumulative”; both of these terms appear to describe the time period from post-randomization to December 8, 2008.

Chemistry

1. Provide updated data on the supportive batches manufactured using the aged intermediates prior to month 6 of the review cycle to provide additional evidence that the expiration dating period can begin from the date of encapsulation.
2. State what holding time you are requesting for each intermediate prior to encapsulation of the DTC.
3. Be aware that the request to [REDACTED] (b) (4) and [REDACTED] (b) (4) for future commercial batches has been noted and is under review. The microbial limits testing question has been consulted to the Microbiology group for evaluation.

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.

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.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Olga Salis, Regulatory Project Manager, at (301) 796-0837.

Sincerely,

{See appended electronic signature page}

George Benson, M.D.
Deputy Director
Division of Reproductive and Urologic
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

George Benson
5/27/2009 02:51:32 PM

**45 Day NDA Meeting Checklist
Pharmacology/Toxicology**

NDA Number: 22460
Drug Name: FLODART
Sponsor: GlaxoSmithKline

Date: 4 May 2009
Reviewer: Laurie McLeod-Flynn

Date CDER Received: 20 March 09
Filing Date: 19 May 2009
User Fee Date: 20 January 2010
Expected Date of Draft Review: September 2009

On initial overview of the Pharm/Tox portion of the NDA application

	ITEM	YES / NO	COMMENTS
1)	On its face, is the Pharm/Tox section of the NDA organized in a manner to allow substantive review to begin?	x	
2)	Is the Pharm/Tox section of the NDA indexed and paginated in a manner to allow substantive review to begin?	x	
3)	On its face, is the Pharm/Tox section of the NDA legible so that substantive review can begin? Has the data been presented in an appropriate manner?	x	
4)	Are all necessary and appropriate studies for this agent, including special studies/data requested by the Division during pre-submission communications/discussions, completed and submitted in this NDA?	x	No P/T studies were requested for this combination of 2 previously approved products. The P/T section consists of 3 pharmacology studies and labeling. The new formulation will also be reviewed, along with any new impurities which may exceed the qualification limits.
5)	If the formulation to be marketed is not identical to the formulation used in the toxicology studies (including the impurity profiles), has the Sponsor clearly defined the differences and submitted reviewable supportive data?	x	

6)	Does the route of administration used in animal studies appear to be the same as the intended human exposure? If not, has the sponsor submitted supportive data and/or an adequate scientific rationale to justify the alternative route?	x	
7)	Has the sponsor submitted a statement(s) that all the pivotal Pharm/Tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?	x	
8)	Has the sponsor submitted a statement(s) that the Pharm/Tox studies have been performed using acceptable, state-of-the-art protocols which also reflect agency animal welfare concerns?	x	
9)	Has the proposed draft labeling been submitted? Are the appropriate sections for the product included and generally in accordance with 21 CFR 201.57? Is information available to express human dose multiples in either mg/m ² or comparative serum/plasma AUC levels?	x x x	
10)	From a Pharm/Tox perspective, is this NDA fileable? If not, please state in item #11 below why it is not.	x	
11)	Reasons for refusal to file:	NA	

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/s/

Laurie McLeod
5/12/2009 09:46:11 AM
PHARMACOLOGIST

Lynnda Reid
5/12/2009 01:41:28 PM
PHARMACOLOGIST

REQUEST FOR CONSULTATION

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

FROM (Name, Office/Division, and Phone Number of Requestor): Olga Salis
Division of Reproductive and Urologic Products

301-467-5085

DATE 5/7/09	IND NO.	NDA NO. 22-460	TYPE OF DOCUMENT new NDA (b2)	DATE OF DOCUMENT 3/20/09
NAME OF DRUG Flodart (dutasteride and tamsulosin)		PRIORITY CONSIDERATION S	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE 7/30/09

NAME OF FIRM: GSK

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG SAFETY

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

V. SCIENTIFIC INVESTIGATIONS

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

COMMENTS / SPECIAL INSTRUCTIONS:

This is an electronic NDA that can be viewed in EDR under 22-460.

The subject of this application is FLODART, a dutasteride (0.5 mg) and tamsulosin hydrochloride (0.4 mg) combination capsule, which is intended to treat symptomatic benign prostatic hyperplasia (BPH). This indication is consistent with the currently approved indication for dutasteride (AVODART) co-administered with tamsulosin (NDA 21- 319 S-014 approved last year).

The Dosage form is a hard gelatin capsule which contains a soft gelatin capsule containing dutasteride API and enteric-coated pellets of tamsulosin API.

(b) (4)

Please evaluate if their request is acceptable.

As always feel free to call me if you have any questions.

**Olga Salis
PM DRUP**

SIGNATURE OF REQUESTOR

METHOD OF DELIVERY (Check one)

DFS

EMAIL

MAIL

HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Olga Salis
5/7/2009 10:58:26 AM

REQUEST FOR CONSULTATION

TO (Office/Division): Division of Drug Marketing, Advertising and Communications (DDMAC) HFD-42, BLD WO 51 Room 3251
Attn: Janice Maniwang
cc: Jialynn Wang

FROM (Name, Office/Division, and Phone Number of Requestor): Olga Salis, Project Manager, Division of Reproductive and Urologic Drug Products, HFD-580
301-796-0837

DATE 4/7/09	IND NO.	NDA NO. 22-460	TYPE OF DOCUMENT NDA	DATE OF DOCUMENT 3/20/09
NAME OF DRUG Flodart (dutasteride and tamsulosin)		PRIORITY CONSIDERATION S	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE 7/30/09

NAME OF FIRM: GSK

REASON FOR REQUEST

I. GENERAL

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

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

III. BIOPHARMACEUTICS

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

IV. DRUG SAFETY

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

V. SCIENTIFIC INVESTIGATIONS

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

COMMENTS / SPECIAL INSTRUCTIONS:

Dear Janice,

This is an all electronic submission that can be viewed by going to edr under NDA 22-460. Please launch the GS Review tool to view the submission. The PI can be found under 1.14.1.

Background Information:

The subject of this application is FLODART, a dutasteride (0.5 mg) and tamsulosin hydrochloride (0.4 mg) combination capsule, which is intended to treat symptomatic benign prostatic hyperplasia (BPH). This indication is consistent with the currently

approved indication for dutasteride (AVODART) co-administered with tamsulosin (NDA 21- 319 S-014 approved last year).

As monotherapy, dutasteride (a 5 α -reductase inhibitor [5ARI]) is indicated for the treatment of symptomatic BPH in men with an enlarged prostate to improve symptoms, and reduce the risks of AUR and need for BPH-related surgery. Tamsulosin is indicated for the treatment of the signs and symptoms of BPH. Dutasteride, as AVODART, has been marketed in the US since 2003 and tamsulosin, as FLOMAX, since 1997. FLOMAX will facilitate the early introduction of dutasteride into BPH therapy, while ensuring rapid symptom improvement provided by the alpha blocker tamsulosin.

This is a b2 NDA. Please keep in mind that Flomax is under patent until October 27, 2009 and belongs to BI, the NDA number for Flomax is 20-579. GSK has no right to the name or likeness of Flomax. GSK owns Avodart. We can not contact BI with any comments in regards to this combination NDA because GSK has not informed them they have submitted this NDA. The PDUFA goal date is January 20, 2010 if BI does not get an extension to patent.

As always feel free to call me if you have any questions.

Olga Salis
PM DRUP

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Olga Salis

4/7/2009 10:24:12 AM

REQUEST FOR CONSULTATION

TO (Office/Division):

CDER OSE CONSULTS

FROM (Name, Office/Division, and Phone Number of Requestor): Olga Salis,
Project Manager, Division of Reproductive and Urologic
Drug Products, HFD-580
301-796-0837

DATE 4/7/09	IND NO.	NDA NO. 22-460	TYPE OF DOCUMENT NDA	DATE OF DOCUMENT 3/20/09
NAME OF DRUG Flodart (dutasteride and tamsulosin)		PRIORITY CONSIDERATION S	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE 7/30/09

NAME OF FIRM: GSK

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG SAFETY

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

V. SCIENTIFIC INVESTIGATIONS

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

COMMENTS / SPECIAL INSTRUCTIONS:

Dear Cheryl,

This is an all electronic submission that can be viewed by going to edr under NDA 22-460. Please launch the GS Review tool to view the submission. All the labeling is found under Module 1.14.1. We are requesting the review of the PI, PPI, Tradename, and carton and container labeling.

Background Information:

The subject of this application is FLODART, a dutasteride (0.5 mg) and tamsulosin hydrochloride (0.4 mg) combination capsule, which is intended to treat symptomatic benign prostatic hyperplasia (BPH). This indication is consistent with the currently approved indication for dutasteride (AVODART) co-administered with tamsulosin (NDA 21- 319 S-014 approved

last year).

As monotherapy, dutasteride (a 5 α -reductase inhibitor [5ARI]) is indicated for the treatment of symptomatic BPH in men with an enlarged prostate to improve symptoms, and reduce the risks of AUR and need for BPH-related surgery. Tamsulosin is indicated for the treatment of the signs and symptoms of BPH. Dutasteride, as AVODART, has been marketed in the US since 2003 and tamsulosin, as FLOMAX, since 1997. FLOMAX will facilitate the early introduction of dutasteride into BPH therapy, while ensuring rapid symptom improvement provided by the alpha blocker tamsulosin.

This is a b2 NDA. Please keep in mind that Flomax is under patent until October 27, 2009 and belongs to BI, the NDA number for Flomax is 20-579. GSK has no right to the name or likeness of Flomax. GSK owns Avodart. We can not contact BI with any comments in regards to this combination NDA because GSK has not informed them they have submitted this NDA. The PDUFA goal date is January 20, 2010 if BI does not get an extension to the patent.

As always feel free to call me if you have any questions.

Olga Salis
PM DRUP

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Olga Salis
4/7/2009 10:36:38 AM



NDA 22-460

NDA ACKNOWLEDGMENT

GlaxoSmithKline
Attention: Sherman Alfors
US Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709-3398

Dear Mr. Alfors:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: (dutasteride and tamsulosin) Capsules.

Date of Application: March 20, 2009

Date of Receipt: March 20, 2009

Our Reference Number: NDA 22-460

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 May 19, 2009 in accordance with 21 CFR 314.101(a).

The NDA number provided above should 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:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic 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, call me at, (301) 796-0837.

Sincerely,

{See appended electronic signature page}

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

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/s/

Olga Salis
4/1/2009 11:09:46 AM