CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21698

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

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

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

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/06
See OMB Statement on Page 3.

NDA NUMBER
21-698

NAME OF APPLICANT / NDA HOLDER
Warner-Lambert Company LLC

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

TRADE NAME (OR PROPOSED TRADE NAME)
Zantac 150

ACTIVE INGREDIENT(S)	STRENGTH(S)
Ranitidine	150 mg

DOSAGE FORM
Tablet

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

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

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

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

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent

d. Name of Patent Owner	Address *(of Patent Owner)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) ☞	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☐ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

PSC Media Arts (301) 443-1090 EF

13-0001

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.3 If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3.**		
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☐ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☐ No
2.7 If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☐ No
3.3 If the patent referenced in **3.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?		☐ Yes	☐ No
4.2 Claim Number (*as listed in the patent*)	Does the patent claim referenced in **4.2** claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
4.2a If the answer to **4.2** is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*		

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.	☑ Yes

6. Declaration Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

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

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
Bruce A. Pokras	10/22/03

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☑ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Bruce A. Pokras	
Address 201 Tabor Road	City/State Morris Plains, New Jersey
ZIP Code 07950	Telephone Number (973) 395-5399
FAX Number *(if available)* (973) 385-7330	E-Mail Address *(if available)* bruce.a.pokras@pfizer.com

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book Publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: *http://forms.psc.gov/forms/fdahtm/fdahtm.html.*

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

ITEM 14: PATENT CERTIFICATION (Not Applicable)

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY FOR NDA # __21-698__ SUPPL #__N/A___

Trade Name Zantac 150 Generic Name _ranitidine hydrochloride

Applicant Name Pfizer Consumer Healthcare HFD # 180_

Approval Date If Known _August 31, 2004_____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES /_X__/ NO /___/

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

__505 (b) (1)__

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

YES /_X__/ NO /___/

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

_____

_____

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

_____

_____

d) Did the applicant request exclusivity?

YES /_X_/ NO /___/

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

_____three_____

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

YES /_X__/ NO /___/

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

___no_____

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

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

YES /___/ NO /_X__/

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES /_X__/ NO /___/

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

NDA# 18-703_____ Zantac Tablets_____

NDA# 19-090	Zantac Injection
NDA# 19-593	Zantac Premix IV injection
NDA# 19-675	Zantac Syrup
NDA# 20-095	Zantac Geldose Capsules
NDA# 20-251	Zantac Efferdose
NDA# 20-520	Zantac 75Mg Tablets
NDA# 20-745	Zantac 75 Efferdose Tablets

2. Combination product.

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

YES /___/ NO /_X__/

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

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

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

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

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

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

YES /_X__/ NO /___/

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

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

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

YES /_X__/ NO /___/

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

_____

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

YES /___/ NO /_X__/

(1) If the answer to 2(b) is "yes," do you personally

know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain:

---

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

YES /___/ NO /_X__/

If yes, explain:

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

___RANA3013 and RANA3014 for the treatment of heartburn and RANA3016, RANA3018 and RANA4006 for the prevention of heartburn

---

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	RANA3013	YES /___/	NO /_X__/
Investigation #2	RANA3014	YES /___/	NO /_X__/
Investigation #3	RANA3016	YES /___/	NO /_X__/
Investigation #4	RANA3018	YES /___/	NO /_X__/
Investigation #5	RANA4006	YES /___/	NO /_X__/

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	RANA3013	YES /___/	NO /_X__/
Investigation #2	RANA3014	YES /___/	NO /_X__/
Investigation #3	RANA3016	YES /___/	NO /_X__/
Investigation #4	RANA3018	YES /___/	NO /_X__/
Investigation #5	RANA4006	YES /___/	NO /_X__/

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

_____ _____

_____ _____

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

Investigation #1	RANA3013
Investigation #2	RANA3014
Investigation #3	RANA3016
Investigation #4	RANA3018
Investigation #5	RANA4006

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

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

Investigation #1	!
IND # 43,088__ YES /___/	! NO /_X__/ Explain: Glaxo Welcome is named as the sponsor of the IND, however, Pfizer owns the rights to Zantac 150. (See attached)
Investigation #2	!
IND # 43,088 YES /___/	! NO /_X__/ Explain: Glaxo Welcome is named as the sponsor of the IND, however, Pfizer owns the rights to Zantac 150. (See attached)
Investigation #3	!
IND # 43,088 YES /___/	! NO /_X__/ Explain: Glaxo Welcome is named as the sponsor of the IND, however, Pfizer owns the rights to Zantac 150. (See attached)
Investigation #4	!
IND # 43,088 YES /___/	! NO /_X__/ Explain: Glaxo Welcome is named as the sponsor of the IND, however, Pfizer owns the rights

to Zantac 150. (See attached)

Investigation #5	!
IND # 43,088 YES /___/	! NO /_X__/ Explain: Glaxo Welcome is named as the sponsor of the IND, however, Pfizer owns the rights to Zantac 150. (See attached)

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

Investigation #1	!
YES /_X__/ Explain _____	! NO /___/ Explain _____
See attached letters____	! _____
Investigation #2	!
YES /_X__/ Explain _____	! NO /___/ Explain _____
See attached letters __	! _____
Investigation #3	!
YES /_X__/ Explain _____	! NO /___/ Explain _____
See attached letters __	! _____
Investigation #4	!
YES /_X__/ Explain _____	! NO /___/ Explain _____
See attached letters __	! _____
Investigation #5	!
YES /_X__/ Explain _____	! NO /___/ Explain _____
See attached letters __	! _____

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

considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_X__/

If yes, explain: _____

_____

Signature Diane Moore Date July 28, 2004
Title: Regulatory Project Manager

Signature of Office/ Date
Division Director

Form OGD-011347 Revised 05/10/2004

ITEM 16: DEBARMENT CERTIFICATION

CERTIFICATION UDER SECTION 306(K)(1) OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT (21 U.S.C. 335 a (k))

Pfizer Consumer Healthcare hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this New Drug Application.

NOTE: After the completion of Study RANA3016 (completed October 4, 1994), Dr. Thomas B. Edwards, Albany, New York was listed as a "restricted" investigator. On January 22, 1998 Dr. Edwards signed a FDA document titled "AGREEMENT WITH RESPECT TO USE OF INVESTIGATIONAL NEW DRUGS". The following items were noted:

- Dr. Edwards failed to personally conduct or supervise the clinical investigation and he failed to prepare and maintain adequate records for a study that FDA inspected.
- Dr. Edwards agreed not to conduct more than two clinical studies at a time, to personally conduct and closely supervise the studies, to personally and closely supervise all individuals assisting him and to have a qualified, independent outside auditor conduct on-site audits.
- The agreement did not impact Dr. Edwards' practice of medicine.
- Dr. Edwards' name was added to the list of clinical investigators – who have been disqualified, restricted, or provided assurances.

John R. Jacobs, Vice President
Global Regulatory Affairs

10/22/03
Date

ITEM 20: OTHER:

20.1 PEDIATRIC ASSESSMENT

Pediatric Use Information: Request for full waiver

As required under 314.55, Pfizer Consumer Healthcare is requesting a full waiver for submission of pediatric use information because use of Zantac Tablets in the pediatric population is minimal.

Zantac 75 (Ranitidine hydrochloride) Tablets for OTC use was approved on December 19, 1995 for the treatment of heartburn in patients age 12 and above. Zantac 75 was subsequently approved on June 8, 1998 (Supplement 001) for the prevention of heartburn, in patients age 12 and above, when taken 30 to 60 minutes before eating for or drinking beverages that cause heartburn. Zantac was not studied in the pediatric population since it was not likely to be used in a substantial number of pediatric patients.

The use of Ranitidine has been fully characterized in the pediatric population. Information on the use of Ranitidine in the pediatric population was previously submitted for Zantac Injection by GlaxoSmithKline (GSK; formerly Glaxo-Wellcome) on December 18, 1998 and approved on January 19, 1999. This resulted in receipt of 6 months additional patent exclusivity for all ranitidine products, including Zantac 75.

20.2 REQUEST FOR EXCLUSIVITY

Pfizer Consumer Healthcare is requesting three (3) years of exclusivity pursuant to 21 USC 355 (c) (3) (D) (iii) and 21 CFR 314.108 (b) (4).

The Clinical Studies RANA3013, RANA3014, RANA3016, RANA3018 and RANA4006 included in this New Drug Application (NDA) have not previously been used as the basis for an NDA or Supplemental NDA approval.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # : 21-698 **Supplement Type (e.g. SE5): _____** **Supplement Number:**

Stamp Date: October 31, 2003 **Action Date: August 31, 2004**

HFD-180____ **Trade and generic names/dosage form: Zantac (ranitidine hydrochloride) Tablets, 150 mg**

Applicant: Pfizer Consumer Healthcare **Therapeutic Class: Gastric Secretory Depressants**

Indication(s) previously approved:

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

Number of indications for this application(s): 2

Indication #1: Relieves heartburn associated with acid indigestion and sour stomach

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

x **Yes: Please proceed to Section A.**

☐ **No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed**
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

X **Products in this class for this indication have been studied/labeled for pediatric population. Pediatric patients age 12 to 18 are approved in this application (See page 73 of M.O. review dated 8/13/04.)**

☐ **Disease/condition does not exist in children**

x **Too few children with disease to study in age group less than one month**

☐ **There are safety concerns**

☐ **Other: Prescription Zantac (ranitidine hydrochloride) is approved in pediatric patients ages one month to 18 years for multiple acid-related disorders. There are too few neonates (ages birth to one month) with acid-related disorders; therefore, studies with Zantac in this population are not necessary. This formulation is not advised for small pediatric patients.**

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____	kg_____	mo._____	yr._____	Tanner Stage_____
Max_____	kg_____	mo._____	yr._____	Tanner Stage_____

Reason(s) for partial waiver:

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

☐ **Disease/condition does not exist in children**

☐ **Too few children with disease to study**

☐ **There are safety concerns**

- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

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

Section C: Deferred Studies

Age/weight range being deferred:

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

Reason(s) for deferral:

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

Other:_____

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

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

Section D: Completed Studies

Age/weight range of completed studies:

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

Comments:

Attachment A

Indication #2: Prevents heartburn associated with acid indigestion and sour stomach brought on by certain goods and beverages when taken 30 to 60 minutes before eating food or drinking.

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

x **Yes: Please proceed to Section A.**

☐ **No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed**
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

X` **Products in this class for this indication have been studied/labeled for pediatric population. Pediatric patients age 12 to 18 are approved in this application (See page 73 of M.O. review dated 8/13/04.)**
☐ **Disease/condition does not exist in children**
x **Too few children with disease to study in age group less than one month**
☐ There are safety concerns
☐ **Other: Prescription Zantac (ranitidine hydrochloride) is approved in pediatric patients ages one month to 18 years for multiple acid-related disorders. There are too few neonates (ages birth to one month) with acid-related disorders; therefore, studies with Zantac in this population are not necessary. This formulation is not advised for small pediatric patients.**

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for partial waiver:

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

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

ection C: Deferred Studies

Age/weight range being deferred:

Min _____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for deferral:

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

Other:_____

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

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Comments:

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

This page was completed by:

{See appended electronic signature page}

_____
Diane Moore
Regulatory Project Manager

cc: NDA 21-698
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

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/s/

Diane V. Moore
8/31/04 04:12:07 PM

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-698	NDA	Supplement Number	
Drug: Zantac® (Ranitidine Hydrochloride) Tablets, 150 mg		Applicant: Pfizer Consumer Healthcare (PCH)	
RPM: Diane Moore (DGCDP) RPM: Keith Olin (DOTCDP)		HFD-180	Phone # (301) 827-7476
Application Type: (X) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	8
• Other (e.g., orphan, OTC)	OTC
❖ User Fee Goal Dates	August 31, 2004
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review ( ) CMA Pilot 1 ( ) CMA Pilot 2
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	N/A
• OC clearance for approval	N/A
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	(X) Verified
❖ Patent	
• Information: Verify that form FDA-3542a was submitted.	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted.	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	8/31/04
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!*	( ) Yes, Application #_____ **(X)** No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	4/29/04
General Information	
❖ Actions	
• Proposed action	**(X)** AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only)	**(X)** Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes **(X)** Not applicable
• Indicate what types (if any) of information dissemination are anticipated	**(X)** None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling	5/6/04 and 8/30/04
• Original applicant-proposed labeling	10/31/03
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	DMETS 7/20/04
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	Zantac 75, Pepcid AC, Tagamet HB 200
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	5/6/04
• Reviews	See 7/20/04, 8/12/04 M.O. reviews, 7/6/04 CMC and 6/10/04 B/P reviews; OTC review 8/31/04
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	1/5/04, 1/13/04 (2)
❖ Memoranda and Telecons	2/17/04, 4/5/04, 8/18/04, 8/20/04, 8/27/04, 8/30/04
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	5/8/03
• Pre-NDA meeting (indicate date)	7/17/03
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	1/8/03, 5/8/03, 7/17/03

❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	DGCDP Acting Director 8/31/04 DOTCDP Director 8/31/04
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	OTC 7/20/04 and DGICDP 8/13/04
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	Part of integrated M.O. safety review dated 7/20/04
❖ Risk Management Plan review(s) *(indicate date/location if incorporated in another rev)*	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	8/31/04
❖ Demographic Worksheet *(NME approvals only)*	N/A
❖ Statistical review(s) *(indicate date for each review)*	8/12/04, 8/19/04, 8/27/04
❖ Biopharmaceutical review(s) *(indicate date for each review)*	6/10/04
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	7/6/04
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	7/6/04
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Microbiology (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: November 25, 2003 **(X)** Acceptable **( )** Withhold recommendation
❖ Methods validation	**(X** Completed N/A (see CMC review dated 7/6/04 pages 28-35) **( )** Requested **( )** Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	N/A
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

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/s/

Diane V. Moore
8/31/04 06:07:36 PM

MEMORANDUM OF TELECONFERENCE

MEETING DATE: August 27, 2004

TIME: 12:00 PM- 12:30 PM

LOCATION: Room 6B-45, Parklawn Building

APPLICATION: NDA 21-698

DRUG NAME: Zantac® 150 (ranitidine hydrochloride) tablets

TYPE OF MEETING: Labeling

MEETING CHAIR: Ruyi He, M.D.

MEETING RECORDER: Diane Moore

FDA ATTENDEES:

Division of Gastrointestinal and Coagulation Drug Products (DGCDP)

Joyce Korvick, M.D., M.P.H., Deputy Director
Ruyi He, M.D., Medical Team Leader, Gastrointestinal
Hugo Gallo-Torres, M.D., Ph.D., Gastrointestinal Medical Team Leader
Eric Brodsky, M.D., Medical Officer,
Diane Moore, Regulatory Project Manager

Division of New Drug Chemistry II (DNDC II)

Ramesh Raghavachari, Ph.D., Chemist

Division of Biometrics II (DBII)

Stella Grosser, Ph.D., Biometrics Team Leader
Milton Fan, Ph.D., Biometrics Reviewer

Office of Clinical Pharmacology and Biopharmaceutics (OCPB)

Tien-Mien Chen, Ph.D., Biopharmaceutics Reviewer

Division of Over the Counter Drug Products (DOTCDP)

Charles Ganley, M.D., Director
Curtis Rosebraugh, M.D., Deputy Director
Reynold Tan, Ph.D., Interdisciplinary Scientist
David Hilfiker, Chief, Project Management Staff

Helen Cothran, M.D., Microbiologist
Keith Olin, R.Ph., Project Manager

EXTERNAL CONSTITUENT ATTENDEES:

Pfizer Consumer Healthcare

Sandy Furey, M.D., Ph.D., Senior Director, Clinical Research and Medical Affairs, Rx-to-OTC Switch & GI
Richard D'Souza, Ph.D., Senior Vice President, Pfizer Consumer Healthcare R&D
Robert Kohler, R.Ph., J.D., Senior Director, Global Regulatory Affairs
Don Jantzen, Director, Regulatory Affairs, Oral Care & GI
Dawn Parkin, Senior Manager, Regulatory Affairs, Oral Care & GI
Kon Fung, Ph.D., Senior Director, Statistics & Data Management
Stephanie Buckland, marketing Director, Zantac
John Jacobs, VP Global Regulatory affairs
Sharon Emma, Associate product manager, Zantac

BACKGROUND:

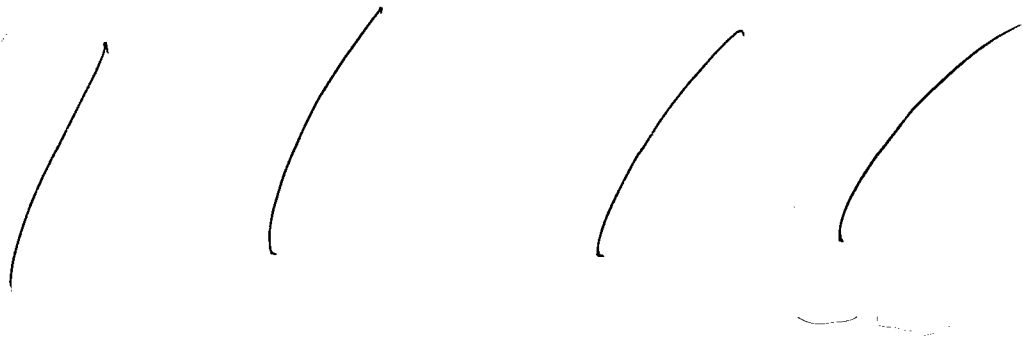
NDA 21-698 for Zantac 150 (ranitidine hydrochloride) tablets was submitted October 31, 2003, for the treatment and prevention of heartburn

The NDA was filed on December 30, 2003. On August 18, 2004, DGCDP sent proposed labeling revisions to Pfizer Consumer Healthcare (Pfizer) via telefacsimilie. On August 20, 2004, representatives from DGCDP and DOTCDP held a teleconference with representatives from Pfizer to discuss the proposed labeling revisions.

MEETING OBJECTIVES:

To continue the discussion of the OTC labeling for Zantac 150.

DISCUSSION POINTS:



A

4 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

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/s/

Diane V. Moore
8/31/04 05:33:28 PM

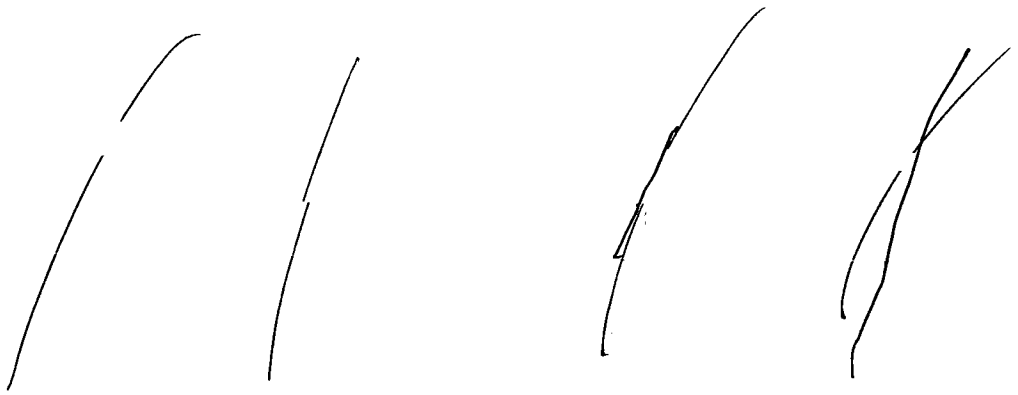
Ruyi He
9/1/04 12:40:45 PM

Division of OTC Drug Products Labeling Review

NDA 21-698/N-000 (BL)

Submission Date:	8/30/2004
Received Date:	8/30/2004
Drug product:	Zantac 150 Tablets
Active ingredient:	Ranitidine Hydrochloride
Pharmacological category:	Acid reducer
Sponsor/Contact:	Don Jantzen, Director, Regulatory Affairs, Oral Care & GI (973)385-4637 Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950
Labeling submitted:	consumer package insert bottle carton bottle label (blister carton blister carton blister backing pouch (1 ct)
Reviewer:	Reynold Tan
Review date:	8/31/04
Project manager:	Keith Olin

Background: The sponsor submitted a minor amendment (NDA 21-698/N-000 (BL)) to their original NDA submission to provide revised draft labeling



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/s/

Reynold Tan
8/31/04 02:50:44 PM
INTERDISCIPLINARY

Helen Cothran
8/31/04 02:57:39 PM
INTERDISCIPLINARY

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Pfizer Consumer Healthcare, Division of Warner-Lambert Company, LLC	August 30, 2004
TELEPHONE NO. *(Include Area Code)* (973) 385-5532	**FACSIMILE** *(FAX)* **Number** *(Include Area Code)* (973) 385-4300
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):* 201 Tabor Road Morris Plains, New Jersey 07950	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

RECEIVED
AUG 31 2004
FDA/CDER

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 21-698

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Ranitidine Hydrochloride	Over-the-Counter (OTC) Zantac 150 (Ranitidine Tablets, 150mg)

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Tablet	150 mg	Oral

(PROPOSED) INDICATION(S) FOR USE:
Over-the-Counter (OTC) treatment and prevention of heartburn

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug _____ Holder of Approved Application _____

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION
Revised Draft Labeling Text, further to August 18, 2004 FDA fax and subsequent August 20, 27 & 30, 2004 FDA/Pfizer telecons

PROPOSED MARKETING STATUS *(check one)* ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

NDA 18-703
)A 20-520

This application contains the following items: *(Check all that apply)*	
☐	1. Index
☒	2. Labeling *(check one)* ☒ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☐	20. OTHER *(Specify)*

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
for John Jacobs	John R. Jacobs, Vice President Global Regulatory Affairs	August 30, 2004

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
201 Tabor Road, Morris Plains, New Jersey 07950	(973) 385-5532

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

DUPLICATE
ORIG AMENDMENT

N-000-BL

Pfizer Consumer Healthcare

August 30, 2004

Via Fax and FedEx

Joyce Korvic, MD, MPH, Acting Director
Division of Gastrointestinal and Coagulation Drug Products; HFD-180
Document Control Room, 8B-45
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: **New Drug Application (NDA) 21-698**
Over-the-Counter (OTC) Zantac 150 (Ranitidine 150 mg Tablets)
Amendment to Pending Application (Draft Labeling)

Subject: **Revised Draft Labeling – Paper**

Dear Dr. Korvic:

Reference is made to the most recent labeling amendment, which was submitted May 6, 2004 and superseded all previously submitted draft labeling. Reference is made to an August 18, 2004 FDA fax which contained revisions to the May 6 Drug Facts, carton front and consumer package insert. Reference is also made to the subsequent Pfizer/FDA teleconferences of August 20, 27 and 30 (12:30 pm and 2:30 pm) in which Zantac 150 labeling revisions were discussed.

In the August 30 2:30 pm teleconference final agreement was reached on the labeling revisions. Enclosed are two versions of this revised labeling: a redline version in which the changes from the May 6 Drug Facts, carton front and consumer package insert are highlighted, and a second version in which these changes have been accepted.

Please contact the undersigned at (973) 385-4637 if you have any questions or require any additional information.

Sincerely,

Pfizer Consumer Healthcare

Don Jantzen
Director, Regulatory Affairs, Oral Care & GI

Enclosures

cc: Diane Moore, HFD-180 (Desk Copy)
Keith Olin, HFD-560 (Desk Copy)

C

27 Page(s) Withheld

_____ Trade Secret / Confidential

✓ Draft Labeling

_____ Deliberative Process

NDA 21-698

Pfizer Consumer Healthcare
Division of Warner-Lambert Company, LLC
Attention: John Jacobs, VP Global Regulatory Affairs
201 Tabor Rd
Morris Plains, NJ 07950

Dear Mr. Jacobs:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac® 150 (ranitidine hydrochloride) tablets.

We also refer to the meeting between representatives of your firm and the FDA on August 20, 2004. The purpose of the meeting was to discuss labeling for Zantac 150.

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

If you have any questions, call me at (301) 827-7476.

Sincerely,

{See appended electronic signature page}

Diane Moore
Regulatory Project Manager
Division of Gastrointestinal and Coagulation
Drug Products (HFD-180)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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/s/

Diane V. Moore
8/31/04 12:44:48 PM

Joyce Korvick
8/31/04 05:12:01 PM

MEMORANDUM OF TELECONFERENCE

MEETING DATE: August 20, 2004

TIME: 10:00 AM- 11:00 AM

LOCATION: Room 6B-45, Parklawn Building

APPLICATION: NDA 21-698

DRUG NAME: Zantac® 150 (ranitidine hydrochloride) tablets

TYPE OF MEETING: Labeling

MEETING CHAIR: Ruyi He, M.D.

MEETING RECORDER: Diane Moore

FDA ATTENDEES:

Division of Gastrointestinal and Coagulation Drug Products (DGCDP)

Joyce Korvick, M.D., M.P.H., Deputy Director
Ruyi He, M.D., Medical Team Leader, Gastrointestinal
Eric Brodsky, M.D., Medical Officer,
Diane Moore, Regulatory Project Manager

Division of New Drug Chemistry II (DNDC II)

Ramesh Raghavachari, Ph.D., Chemist

Division of Biometrics II (DBII)

Milton Fan, Ph.D., Biometrics Reviewer

Office of Clinical Pharmacology and Biopharmaceutics (OCPB)

Tien-Mien Chen, Ph.D., Biopharmaceutics Reviewer

Division of Over the Counter Drug Products (DOTCDP)

Curtis Rosebraugh, M.D., Deputy Director
Reynold Tan, Ph.D., Interdisciplinary Scientist
David Hilfiker, Chief, Project Management Staff
Keith Olin, R.Ph., Project Manager

EXTERNAL CONSTITUENT ATTENDEES:

Pfizer Consumer Healthcare

Sandy Furey, M.D., Ph.D., Senior Director, Clinical Research and Medical Affairs, Rx-to-OTC Switch & GI
Consultant
Richard D'Souza, Ph.D., Senior Vice President, Pfizer Consumer Healthcare R&D
Robert Kohler, R.Ph., J.D., Senior Director, Global Regulatory Affairs
Don Jantzen, Director, Regulatory Affairs, Oral Care & GI
Dawn Parkin, Senior Manager, Regulatory Affairs, Oral Care & GI
Ken Warner, Director, Regulatory Affairs, CMC
Dolores Fliss, Senior Manager, Regulatory Affairs, Submissions
Ger Rikken, M.D., Director, Clinical Research and Medical Affairs, Rx-to-OTC Switch & GI
Kon Fung, Ph.D., Senior Director, Statistics & Data Management
Stephanie Buckland, marketing Director, Zantac

BACKGROUND:

NDA 21-698 for Zantac 150 (ranitidine hydrochloride) tablets was submitted October 31, 2003 for the treatment and prevention of heartburn
The NDA was filed on December 30, 2003. On August 18, 2004, DGCDP sent proposed labeling revisions to Pfizer Consumer Healthcare (Pfizer) via telefacsimilie. On August 19, 2004, Pfizer requested a teleconference with DGCDP and DOTCDP to discuss the proposed labeling revisions.

MEETING OBJECTIVES:

To discuss the proposed revisions to the OTC labeling for Zantac 150.

DISCUSSION POINTS:

10

3 Page(s) Withheld

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_____ Draft Labeling

_____ Deliberative Process

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/s/

Diane V. Moore
8/27/04 10:24:40 AM

Ruyi He
8/27/04 02:53:28 PM

Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

DUPLICATE

Pfizer Consumer Healthcare

RECEIVED
AUG 19 2004
FDR/CDER

August 18, 2004

Robert Justice, M.D., Director
Division of Gastrointestinal and Coagulation Drug Products; HFD-180
Document Control Room, 6B-45
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

N000CC
NEW CORRESP

Re: Submissions made to NDA 21-698 for Zantac 150 mg OTC

Dear Dr. Justice:

As a follow-up to our conversation with Diane Moore (Project Manager, GI Division) on 8/10/04 regarding submissions made to NDA 21-698 for Zantac 150 mg OTC, this letter confirms the following.

- The original NDA was submitted 10/31/03.
- Subsequent submissions except for 3/26/04 were made only in response to requests from the Agency. With the exception of updated stability information, they were reformatted submissions of data contained in the original NDA.
- The submission of 3/26/04 contained a partial response to an information request as well as a four month safety update.
- No new clinical studies are being conducted.
- No additional post-marketing safety data are currently available.
- No new information is to be submitted to support the application.
- We are confirming that the new clinical studies submitted to NDA 21-698 for Zantac 150 mg OTC were conducted under IND 43,088 by Glaxo Wellcome, which had a joint venture with Warner-Lambert Company to commercialize OTC Zantac®. Following the termination of the joint venture, Warner-Lambert (which was subsequently acquired by Pfizer) "purchased all rights" to Zantac 150 mg OTC in the United States from Glaxo Wellcome and purchased (even as to Glaxo Wellcome) rights to these data to support Zantac 150 mg OTC. 21 CFR § 314.108(a) Based on the foregoing, we submit that the new studies are essential to approval of NDA 21-698, in accordance with FFDCA §505(j)(5)(D)(iii) and that they were conducted or sponsored by Pfizer, a predecessor in interest to the IND holder in accordance with FDCA §505(j)(5)(D)(iii) and 21 CFR §

314.108(a). We request that three years of exclusivity be granted this application in accordance with this statute.

If you have any questions contact Robert G. Kohler, Sr., Director Global Regulatory Affairs at 973-385-5419.

Sincerely,

Pfizer Consumer Healthcare

Robert G. Kohler
Sr. Director, Global Regulatory Affairs

cc: Ms. Diane Moore, Project Manager (Division of Gastrointestinal and Coagulation Drug Products)

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

FACSIMILE TRANSMITTAL SHEET

DATE: August 18, 2004

To: Robert G. Kohler	**From:** Diane Moore
Company: Pfizer Consumer Healthcare	Division of Gastrointestinal & Coagulation Drug Products
Fax number: (973) 385-4300	**Fax number:** 301 443-9285
Phone number: (973) 385-5419	**Phone number:** (301) 827-7476

Subject: Zantac 150 labeling

Total no. of pages including cover: 8

Comments:

Document to be mailed: • YES ☑ NO

E

6 Page(s) Withheld

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_____ Deliberative Process

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/s/

Diane V. Moore
8/18/04 05:34:15 PM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Pfizer Consumer Healthcare, Division of Warner-Lambert Company, LLC	08/18/04
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE** *(FAX)* **Number** *(Include Area Code)*
(973) 385-5532	(973) 385-4300
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
201 Tabor Road Morris Plains, New Jersey 07950	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 21-698

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Ranitidine Hydrochloride	Over-the-Counter (OTC) Zantac 150 (Ranitidine Tablets 150 mg)

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*

CODE NAME *(if any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Tablet	150 mg	Oral

(PROPOSED) INDICATION(S) FOR USE:
Over-the-Counter (OTC) treatment and prevention of heartburn

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug _____ Holder of Approved Application _____

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO APENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION
New Drug Application (NDA)

PROPOSED MARKETING STATUS *(check one)* ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)
IND 43,088; NDA 18-703; NDA 20-520; DMF

This application contains the following items: *(Check all that apply)*	
☐	1. Index
☐	2. Labeling *(check one)* ☐ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☐	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☐	20. OTHER *(Specify)*

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
Robert G Kohler for JOHN JACOBS	John R. Jacobs, Vice President Global Regulatory Affairs	08/18/04

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
201 Tabor Road, Morris Plains, New Jersey 07950	(973) 385-5532

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Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

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CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: 4/29/04	**DESIRED COMPLETION DATE:** 8/27/04 **PDUFA DATE:** 8/31/04	**ODS CONSULT #:** 04-0120

TO: Robert Justice, MD
Director, Division of Gastrointestinal and Coagulation Drug Products
HFD-180

THROUGH: Diane Moore
Project Manager
HFD-180

PRODUCT NAME: **Zantac 150™** (Ranitidine Tablets) 150 mg **NDA #: 21-698**	**NDA SPONSOR:** Pfizer Consumer Healthcare

SAFETY EVALUATOR: Felicia Duffy, RN

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name Zantac 150 from a phonetic and/or orthographic perspective. However, DMETS strongly urges the sponsor to exercise prudence in packaging, labeling, and advertising this product in order to prevent confusion between the currently marketed Zantac 75 and Zantac 150. DMETS also recommends an educational campaign to raise the awareness of health care providers and patients of the differences between the over-the-counter and prescription formulations. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

2. DDMAC finds the proprietary name Zantac 150 acceptable from a promotional perspective.

Carol Holquist, RPh
Director, Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 26, 2004

NDA # 21-698

NAME OF DRUG: Zantac 150™
(Ranitidine Tablets)
150 mg

NDA HOLDER: Pfizer Consumer Healthcare

NOTE: This review contains proprietary and confidential information that should not be released to the public.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Gastrointestinal and Coagulation Drug Products (HFD-180), for assessment of the proprietary name, "Zantac 150", regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

Zantac 150 tablets (Ranitidine HCl) was approved in 1983 by prescription only under NDA 18-703. Zantac 150 tablets will switch to over-the-counter (OTC) status with this current NDA submission. However, Zantac effervescent granules and effervescent tablets, also available in 150 mg, will retain their prescription status. Zantac 75 is currently available OTC.

PRODUCT INFORMATION

Zantac 150 (Ranitidine HCl) will be an OTC product indicated for the relief and prevention of heartburn associated with acid indigestion and sour stomach. Zantac 150 will be available in 150 mg tablets. The usual dose is one tablet with a full glass of water one to two times daily.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2], as well as several FDA databases[3] for existing drug names which sound-alike or look-alike to Zantac 150 to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[4]. The Saegis[5] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Zantac 150. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name Zantac 150 acceptable from a promotional perspective.

2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Zantac 150. The products are listed in table 1 (see below), along with the dosage form available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other**
Zantac 150	Ranitidine Tablets: 150 mg	One tablet by mouth one to two times daily.	
Zantac 75 (OTC)	Ranitidine Tablets: 75 mg	One tablet by mouth one to two times daily.	SA/LA
			SA/LA

*Frequently used, not all-inclusive.
**LA (look-alike), SA (sound-alike)
***Name pending approval. Not FOI releasable.**

[1] MICROMEDEX Integrated Index, 2004, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.
[4] WWW location http://www.uspto.gov/tmdb/index.html.
5 Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

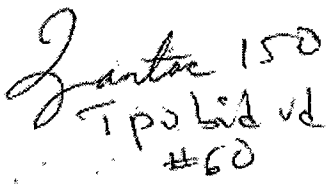
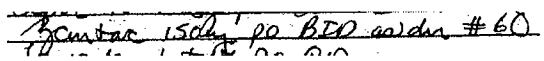
B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Zantac 150 were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Zantac 150 with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 125 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Zantac 150 (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 	Zantac 150 Take one tab by mouth twice a day As directed Dispense 60
Inpatient RX: 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar or look similar to any currently marketed U.S. product. It is noted that none of the study participants included the strength "150" in their response. See appendix A for the complete listing of interpretations from the verbal and written studies.

D. Adverse Event Reporting System (AERS) and DQRS SEARCH

Zantac has been marketed since 1983, thus DMETS searched the FDA Adverse Events Reporting System (AERS) database to determine any post-marketing safety reports of medication errors associated with all Zantac products. The MedDRA Preferred Term (PT), "Medication Error" and tradename "Zantac%" were used to perform the searches. This strategy retrieved one hundred and seven (107) medication errors. Thirty-five (35) of the medication errors pertained to name confusion. The proprietary names that were confused with Zantac are listed in table 2 below. The most prevalent name confusion occurred with Zyrtec which was previously addressed in a separate consult (see ODS consults 01-0014, 01-0014-1, and 01-0014-2).

Table 2: Proprietary Name Confusion Involving Zantac (# of errors in parentheses)

Acyclovir (1)	Cimetidine (1)	Tagamet (1)
Amantadine (1)	Entex (1)	Zenate (1)
Cefotan (1)	Prozac (1)	Zoloft (1)
Ceftin (1)	Rimantadine (3)	Zyrtec (22)

E. SAFETY EVALUATOR RISK ASSESSMENT

1. Sound-Alike and/or Look-Alike Concerns

In reviewing the proprietary name Zantac 150, the names considered having the potential for confusion included — and Zantac 75. Upon further review of the names gathered from EPD, the name — was not reviewed further due to the numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, dosage formulation, and prescriber population.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any currently marketed products. It is noted that all of the respondents left the modifier "150" off of the proprietary name. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size.

a. Zantac 75 and Zantac 150 may look similar when scripted and sound similar when spoken. Zantac 75 is an over-the-counter product indicated for the relief and prevention of heartburn associated with acid indigestion and sour stomach. Zantac 75 is available as 75 mg tablets. The usual dose to relieve heartburn symptoms is one tablet with a glass of water. The usual dose to prevent heartburn symptoms is one tablet 30 to 60 minutes before eating food or drinking beverages that can cause heartburn. Zantac 75 can be taken up to twice daily. Zantac 75 and Zantac 150 look and sound similar because they share the same root name, Zantac. However, both names have different numerical descriptors (75 vs. 150). Both products share overlapping indications for use (heartburn or sour stomach), usual dosage (one tablet), dosing interval (once or twice daily), route of administration (oral), dosage form (tablet), and product availability (OTC). The difference between Zantac 75 and Zantac 150 is the product strength (75 mg vs. 150 mg). It is likely that these products will be stored in close proximity. This has the potential to

cause confusion when one is selecting a product off of the shelf. Additionally, post-marketing experience has shown when a new formulation of an existing drug product is launched, confusion and errors occur. Thus, prominent labeling and sufficient education are a must in order to minimize the confusion. It is imperative that Zantac 150 is distinguishable from Zantac 75. The labeling, packaging, and product appearance of Zantac 150 are crucial features that can aid in the prevention of medication errors with Zantac 75. DMETS believes that the potential for confusion between the two products is likely to occur during the initial product launch, but can be minimized with unique labeling, packaging and an extensive educational campaign.

2. Additional Issues

Zantac 150 is currently available as tablets, effervescent tablets and effervescent granules. The conversion of Zantac 150 from prescription to OTC applies only to the tablet and not the other effervescent formulations. It is possible for a patient to have a script for Zantac 150 where the descriptor "effervescent" is omitted. In this case, the patient will likely be directed to the OTC product. The patient may further discuss with the pharmacist that they should be getting either the effervescent tablets or granules. The pharmacist can then clarify with the health care provider what the intended product is. If the patient receives OTC Zantac 150 tablets for the effervescent granules/effervescent tablets or vice versa, there will be no harm to the patient because the patient will receive the same product in a different formulation. Additionally, we did not have cases such as this reported when both products were prescription, which lessens our concerns with this particular type of confusion.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

DMETS encourages the sponsor to differentiate the labels and labeling of Zantac 150 from the OTC Zantac 75 and prescription Zantac 150 formulations in order to minimize potential selection errors. DMETS also encourages the sponsor to educate health care providers on the differences between the OTC and prescription formulation of Zantac 150.

IV. RECOMMENDATIONS:

A. DMETS has no objections to the use of the proprietary name Zantac 150 from phonetic and/or orthographic perspective. However, DMETS strongly urges the sponsor to exercise prudence in packaging, labeling, and advertising this product in order to prevent confusion between the currently marketed Zantac 75 and Zantac 150. DMETS also recommends an educational campaign to raise the awareness of health care providers and patients of the differences between the over-the-counter and prescription formulations. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.

B. DDMAC finds the proprietary name Zantac 150 acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

Felicia Duffy, RN
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A. Zantac 150 Prescription Study Results

Written Inpatient	**Written Outpatient**	**Verbal**
Zantac	Zantac	Zantac
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/s/

Felicia Duffy
7/20/04 07:51:21 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
7/20/04 09:50:32 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
7/20/04 10:30:10 AM
DRUG SAFETY OFFICE REVIEWER

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-698 Supplement # SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8

Trade Name: Zantac 150
Generic Name: Ranitidine Tablets
Strengths: 150 mg

Applicant: Pfizer

Date of Application: October 31, 2003
Date of Receipt: October 31, 2003
Date clock started after UN: N/A
Date of Filing Meeting: December 9, 2003
Filing Date: February 1, 2004
Action Goal Date (optional): User Fee Goal Date: August 31, 2004

Indication requested: As an over-the-counter (OTC) treatment of heartburn and prevention of heartburn

Type of Original NDA: (b)(1) __X_____ (b)(2) _____
OR
Type of Supplement: (b)(1) _____ (b)(2) _____
NOTE: A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2) application, complete the (b)(2) section at the end of this review.

Therapeutic Classification: S __X_____ P _____
Resubmission after withdrawal? ___no_____ Resubmission after refuse to file? __no_____
Chemical Classification: (1,2,3 etc.) _____
Other (orphan, OTC, etc.) __OTC_____

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

Form 3397 (User Fee Cover Sheet) submitted: YES
User Fee ID # _____4606_____
Clinical data? YES __X_____ NO, Referenced to NDA # _____

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?

NO

If yes, explain: N/A

Does another drug have orphan drug exclusivity for the same indication? NO

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?

N/A

Is the application affected by the Application Integrity Policy (AIP)? NO
If yes, explain.

If yes, has OC/DMPQ been notified of the submission? N/A

- Does the submission contain an accurate comprehensive index? YES
- Was form 356h included with an authorized signature? YES
  If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES
  If no, explain:
- If an electronic NDA, does it follow the Guidance? N/A
  If an electronic NDA, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:
- If in Common Technical Document format, does it follow the guidance? N/A
- Is it an electronic CTD? NO
  If an electronic CTD, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:
- Patent information submitted on form FDA 3542a? YES
- Exclusivity requested? YES, __3_____years
  Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES
  If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

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

- Financial Disclosure forms included with authorized signature? YES
  (Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)

- Field Copy Certification (that it is a true copy of the CMC technical section)? YES

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? YES
  If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

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

- List referenced IND numbers: IND 43,088

- End-of-Phase 2 Meeting(s)? Date(s) _May 8, 2003__ NO
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) _July 17, 2003_____ NO
  If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? YES

- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A

- Has DOTCDP been notified of the OTC switch application? YES

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? N/A

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES
  If no, did applicant submit a complete environmental assessment? N/A
  If EA submitted, consulted to Nancy Sager (HFD-357)? N/A

- Establishment Evaluation Request (EER) submitted to DMPQ? YES
- If a parenteral product, consulted to Microbiology Team (HFD-805)? N/A

If 505(b)(2) application, complete the following section: **N/A**

- Name of listed drug(s) and NDA/ANDA #:
- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").
- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.)

  YES NO
- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9).

  YES NO
- Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9).

  YES NO
- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.

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

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

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

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

  IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

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

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

____ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)
____ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

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

    YES NO
  - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

    YES NO
  - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

    N/A YES NO
  - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?

    N/A YES NO
- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):
  - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

    YES NO
  - A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

    YES NO
  - EITHER
    The number of the applicant's IND under which the studies essential to approval were conducted.

    IND # _____ NO

    OR

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

    N/A YES NO
- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

  YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: December 9, 2003

BACKGROUND:
Zantac® (ranitidine hydrochloride) 150 mg tablets is approved for use by prescription for the following indications:

1. Short term treatment of active duodenal ulcer.
2. Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. Treatment of pathological hypersecretory conditions.
4. Short term treatment of active, benign, gastric ulcer.
5. Maintenance therapy for gastric ulcer patients at reduced dosage after healing of acute ulcers.
6. Treatment of GERD.
7. Treatment of endoscopically diagnosed erosive esophagitis.
8. Maintenance of healing of erosive esophagitis.

The NDA 20-520 for Zantac® (ranitidine hydrochloride) 75 mg tablets was approved on December 19, 1995, for over-the-counter (OTC) use of the drug in the treatment of episodic heartburn. NDA 20-520/S-001 was approved June 8, 1998 for prevention of heartburn.

ATTENDEES:

ASSIGNED REVIEWERS:

Discipline	**Reviewer**
Medical:	Eric Brodsky, M.D.
Secondary Medical:	Ruyi He, M.D.
Statistical:	Milton Fan, Ph.D.
Pharmacology:	N/A
Statistical Pharmacology:	N/A
Chemistry:	Ramesh Raghavachari, Ph.D.
Environmental Assessment (if needed):	N/A
Biopharmaceutical:	Suliman Al-Fayoumi, Ph.D.
Microbiology, sterility:	N/A
Microbiology, clinical (for antimicrobial products only):	N/A
DSI:	Khairy Malek, M.D.
Regulatory Project Management:	Diane Moore
Other Consults:	DMETS, DDMAC, DSRCS, DOTCDP

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

CLINICAL FILE __X____ REFUSE TO FILE _____

- Clinical site inspection needed: NO

- Advisory Committee Meeting needed? NO

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

N/A

CLINICAL MICROBIOLOGY NA

STATISTICS FILE

BIOPHARMACEUTICS FILE

- Biopharm. inspection needed: NO

PHARMACOLOGY NA

- GLP inspection needed: NO

CHEMISTRY FILE

- Establishment(s) ready for inspection? YES
- Microbiology NO

ELECTRONIC SUBMISSION: N/A
Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:

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

__X_____ Filing issues to be communicated by Day 74.

ACTION ITEMS:

Document filing issues/no filing issues conveyed to applicant by Day 74.

_____
Diane Moore
Regulatory Project Manager, HFD-180

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/s/

Diane V. Moore
4/29/04 02:55:35 PM
CSO

MEMORANDUM OF TELECON

DATE: April 1, 2004

APPLICATION NUMBER: NDA 21-698, Zantac (ranitidine) 150 mg

BETWEEN:

Name: Dolores Fliss, Sr. Manager Submissions Regulatory Affairs
Phone: 973-385-6546
Representing: Pfizer Consumer Healthcare

AND

Name: Laura Shay, Regulatory Project Manager
Division of Over-the-Counter Drug Products, HFD-560

SUBJECT: labeling

The purpose of this T-con was to remind the sponsor to revise the Drug Facts label for Zantac 150mg

Laura Shay
Regulatory Project Manager

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/s/

Laura Shay
4/5/04 04:39:12 PM
UNKNOWN

MEMORANDUM OF TELECON

DATE: February 9, 2004

APPLICATION NUMBER: NDA 21-698, Zantac 150 (ranitidine)

BETWEEN:

Name: Robert Kohler, Sr. Director Regulatory Affairs Rx-to-OTC Switch
Dolores Fliss, Sr. Manager Submissions Regulatory Affairs
Regulatory/Clinical Consultant
Phone: 1-877-939-7057
Representing: Pfizer Consumer Health

AND

Name: Laura Shay, Regulatory Project Manager
Andrea Leonard-Segal, MD, Medical Team Leader
Linda Hu, MD, Medical Officer
Division of Over-the-Counter Drug Products, HFD-560

SUBJECT: Clarification of data request by HF-560 listed in the January 13, 2004, Information Request Letter

Provide the following on CD-ROM

- Volume 1 and 58
- synopses and clinical study reports for the 5 clinical studies submitted.
- summaries of epidemiological studies conducted for OTC Zantac 150 mg referred to in Volume 57, P 8--020072., section 8.8.2.3.

Pfizer: No epidemiological studies were ever conducted; this was a typo. The remainder of this request is clear.

Provide the following marketing information

- Tables showing countries where ranitidine 75, 150, 300 mg tablets have been approved, when approved, whether Rx or OTC (distinguish behind the counter vs OTC as in the US), approved indications and labeled duration of use.
- Whether a marketing application was ever withdrawn for safety reasons.
- Numbers of prescriptions by year and dose form, numbers of pills sold by year and dose (US and rest of world). Need OTC and prescription marketing data.

Pfizer: GlaxoSmithKline owns the NDA for overseas marketing of Zantac making it difficult to obtain this information because it is not part of the contract to have rights over marketing information. The most recent annual report for N18-713 would provide information if Zantac has been withdrawn for any reason.

FDA/HFD-560: If possible, obtain this information, otherwise please formally submit to us a statement stating that you were unable to obtain the overseas marketing information and the reason why.
Pfizer: Ok, we will.

Provide the following post-marketing information. Attachments listed on P8-021018, Volume 58.

- For spontaneously reported serious AEs (worldwide 1993-2003) tabulate AEs by body system and sort events by decreasing frequency in the ranitidine population separately for the 75 and 150 mg dosage forms as well as by total daily dose (total of 150 mg/d and 300 mg/d). Serious events and deaths should be tabulated separately. Compare the safety of 75 mg vs 150 mg and analyze whether the higher dose has greater chance of serious AEs. Safety assessments in special populations--liver failure, renal insufficiency, *children ages 12-18*, and the elderly should be done. Provide a detailed assessment of the safety data for ranitidine with regard to hematologic disorders, and with regard to drug interactions.

  FDA/HFD-560 Please compare 75 mg tablets to the 150 mg tablets; We are interested to see if there are any differences. Also tabulate by the total daily dose.
  Pfizer: We will do the best we can, just be aware that the SRS data base reports only by total daily dose. The AERS data base can list out by individual doses, but it only contains the newer data.

- Analyses of Appendix D in Tables 3-11 should be extended to break out dose form and age (the three age categories are OK). For each of the "selected body systems" in those tables, give numbers of reports from SRS and CIOMS vs dose form and age category. {12-18, 18-65, >65}

  Pfizer: Did you mean to list age 18 twice?
  FDA/HFD-560: No, we meant to list the ages as: 12-17, 18-65, >65

- World Health Organization(WHO) report summaries--provide listings by body system of serious adverse events sorted by decreasing frequency in the ranitidine population separately for the 75 and 150 mg dosage forms as well as by total daily dose (total of 150 mg/d and 300 mg/d). Summarize and analyze if higher dose has greater chance of serious AEs.

  Pfizer: Obtaining the WHO information should be no problem; be aware that WHO only reports by total daily dose.

- Provide a tabular summary of the literature references that contain safety information in a form that could be edited. Also supply the articles in pdf form with an index. Sponsor should also provide an analyses of these articles and present the information by body system. Are the serious AEs related to dose?

  Pfizer and FDA/HFD-560 agreed on a tabular summary listed alphabetically by author with book-marking to the articles that will be available as pdf files on a CD-ROM. Pfizer will

look into the capability of "i-copy" to allow for the ability to copy and paste. The issue of copy rights law was discussed as a possibility of making this difficult.

- Data from countries where ranitidine 150 mg is available OTC should also be presented separately. Are there any differences compared to the rest of the data?

  Pfizer: Again stated that Zantac overseas is marketed by GlaxoSmithKline so the problem will exist because they do not have rights over that information. They believe that Australia is the only country that markets the 150 mg dose OTC. Pfizer agreed to verify this information.

Create an Excel table of all serious reports and deaths, 1993-2003, ranitidine :

- one record per case
- fields for each record should include: case ID (in original format, CIOMS or SRS), manufacturer's number, date of event, date of report, age (year and decimal fraction), outcome (those in Table 3 are OK: unknown, recovered, not recovered, recovering, fatal, recovered with sequela), whether the AE was reported by a health care professional (HCP), dose form, total dose per day, duration of use, AE term 1 (primary reaction), AE term 2, AE term 3, AE term 4, suspect drug, secondary suspect drugs, body system corresponding to primary term, concomitant medications, co-morbid conditions, country of origin, narrative summary of the case.

  FDA/HFD-560: If the information available show time-to-onset of the AE.
  Pfizer: I am not sure that it can be done but we will look into it.
  FDA/HFD-560: Re-stated the request to be sure to have a causality field in the table and a field to indicate whether the product was prescription or OTC. The Sponsor will also try to hyperlink each record into a narrative summary of the case.

- any field for which information is unavailable should be left blank. "Concomitant medications" and 'co-morbid conditions' are text listings and should emphasize conditions and medications known to apply at the time of and just prior to the event.

Additional discussion:
Pfizer: Requested if their 4 month safety update that is due on March 1, 2004, could be submitted as part of this safety data request in order to avoid having to do it in duplicate as long as it is in the new format discussed and with up to date information?
FDA/HFD-560: This is acceptable. The GI division has a copy of the case report forms and tabulations; OTC also asked for a copy.
Pfizer: The Sponsor will submit parts of the request earlier as the information becomes available.
Pfizer: The literature analysis and the request from the statistician in HFD-180 may take 4-6 weeks. We can get the literature abstracts to you sooner than that.

Post-Meeting Information:
Pfizer request that HFD-560 find out how they should submit this data. A discussion with the document room yielded this answer: Anything that is submitted in an electric format (CD-ROM) needs to be submitted to the electronic document room. This is to ensure that the information that the reviewing officer is looking at is on record even if there is a hard copy located in the original submission. This process was established in order to ensure consistency in the review process.

Laura Shay
Regulatory Project Manager

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/s/

Laura Shay
2/17/04 11:02:10 AM
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-698

INFORMATION REQUEST LETTER

Pfizer Consumer Healthcare, Inc
Attention: John R. Jacobs
Vice President, Global Regulatory Affairs
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Jacobs:

Please refer to your October 20, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac (ranitidine HCl) Tablets, 150mg OTC.

We are reviewing the Clinical and Statistical 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.

Statistical

1. Provide user guide for statistical reviewer aids including the SAS programs which were used to produce the efficacy results in the report and analysis results.

Clinical (Division of Over-The-Counter Drug Products)

1. Provide the following on CD-ROM.
   - Volumes 1 and 58.
   - Synopses and clinical study reports for the 5 clinical studies submitted.
   - Summaries of epidemiological studies conducted for Over-The-Counter (OTC) Zantac 150 mg referred to in Volume 57, P 8--020072., section 8.8.2.3.

2. Provide the following marketing information.
   - Tables showing countries where ranitidine 75, 150, 300 mg tablets have been approved, when approved, whether Prescription (Rx) or OTC (distinguish behind the counter vs OTC as in the US), approved indications, and labeled duration of use.
   - Whether a marketing application was ever withdrawn for safety reasons.
   - Numbers of prescriptions by year and dose form, numbers of pills sold by year and dose (US and rest of world) for OTC and prescription marketing data.

3. Provide the following post-marketing information. Attachments listed on P8-021018, Volume 58.
   - For spontaneously reported serious adverse events (AEs) (worldwide 1993-2003) tabulate AEs by body system and sort events by decreasing frequency in the ranitidine population separately for the 75 and 150 mg dosage forms as well as by total daily dose (total of 150 mg/d and 300 mg/d). Serious events and deaths should be tabulated separately. Compare the safety of 75 mg vs 150 mg and analyze whether the higher dose has greater chance of serious AEs. Safety assessments in special populations--liver failure, renal insufficiency, *children ages 12-18*, and the elderly should be done. Provide a detailed assessment of the safety data for ranitidine with regard to hematologic disorders, and with regard to drug interactions.
   - Analyses of Appendix D in Tables 3-11 should be extended to break out dose form and age (the three age categories are OK). For each of the "selected body systems" in those tables, give numbers of reports from SRS and CIOMS vs dose form and age category. {12-18, 18-65, >65}.
   - World Health Organization (WHO) report summaries--provide listings by body system of serious adverse events sorted by decreasing frequency in the ranitidine population separately for the 75 and 150 mg dosage forms as well as by total daily dose (total of 150 mg/d and 300 mg/d). Summarize and analyze if higher dose has greater chance of serious AEs.
   - Provide a tabular summary of the literature references that contain safety information in a form that could be edited. Also supply the articles in PDF format with an index. Also, provide an analyses of these articles and present the information by body system. Are the serious AEs related to dose?
   - Data from countries where ranitidine 150 mg is available OTC should also be presented separately. Are there any differences compared to the rest of the data?

4. Create an Excel table of all serious reports and deaths, 1993-2003, ranitidine:
   - one record per case
   - fields for each record should include: case ID (in original format, CIOMS or SRS), manufacturer's number, date of event, date of report, age (year and decimal fraction), outcome (those in Table 3 are OK: unknown, recovered, not recovered, recovering, fatal, recovered with sequela), whether the AE was reported by a health care professional (HCP), dose form, total dose per day, duration of use, AE term 1 (primary reaction), AE term 2, AE term 3, AE term 4, suspect drug, secondary suspect drugs, body system corresponding to primary term, concomitant medications, co-morbid conditions, country of origin, narrative summary of the case
   - any field for which information is unavailable should be left blank. "Concomitant medications" and 'co-morbid conditions' are text listings and should emphasize conditions and medications known to apply at the time of and just prior to the even.

If you have any questions, call Paul E. Levine, Jr., R.Ph., J.D., Regulatory Health Project Manager, at 301-443-8347.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Joyce Korvick
1/13/04 04:21:56 PM
for Dr. Robert Justice

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-698

FILING COMMUNICATION

Pfizer Consumer Healthcare, Inc
Attention: John R. Jacobs
Vice President, Global Regulatory Affairs
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Jacobs:

Please refer to your new drug application (NDA) submitted October 20, 2003, (received, October 21, 2003), under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac (ranitidine HCl) Tablets, 150mg OTC, for the treatment and prevention of heartburn

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act, in accordance with 21 CFR 314.101(a).

In our filing review, we noted that in your application you requested a 24 month expiry dating period and submitted stability test data for the 150 mg tablet in the bottle packaging configuration and the 75 mg tablet in the bottle, listers and pouch packaging configurations. However, your application is submitted for the 150 mg tablet in the (bottle, listers and pouches) container closure systems.

Therefore, we have identified your request for a 24 month expiry dating period as a potential review issue, based upon which we are requesting that you submit stability test data for the 150 mg tablet in listers and pouches within a six month time frame.

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.

If you have any questions, call Paul E. Levine, Jr., R.Ph., J.D., Regulatory Health Project Manager, at (301) 443-8347.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Gastrointestinal & Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Joyce Korvick
1/13/04 03:58:17 PM
for Dr. Robert Justice

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-698

Pfizer Consumer Healthcare, Inc
Attention: John R. Jacobs
Vice President, Global Regulatory Affairs
201 Tabor Road
Morris Plains, NJ 07950

Dear Mr. Jacobs:

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

Name of Drug Product: Zantac (ranitidine HCl) Tablets, 150mg

Review Priority Classification: Standard (S)

Date of Application: October 31, 2003

Date of Receipt: October 31, 2003

Our Reference Number: NDA 21-698

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on December 30, 2003 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be August 31, 2004.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 443-8347.

Sincerely,

{See appended electronic signature page}

Paul E. Levine, Jr., R.Ph., J.D.
Regulatory Health Project Manager
Division of Gastrointestinal
and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

Paul Levine
1/5/04 03:11:50 PM

Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

Pfizer Consumer Healthcare

October 31, 2003

Robert Justice, M.D., Director
Division of Gastrointestinal and Coagulation Drug Products; HFD-180
Document Control Room 6B-45
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

ATTENTION: Document Control Room

Re: New Drug Application (NDA) 21-698; User Fee Number 4606
Over-the-Counter (OTC) Zantac 150 (Ranitidine 150 mg Tablets)

Dear Dr. Justice

Pfizer Consumer Healthcare (PCH), a Division of Warner-Lambert Company, LLC, a Pfizer Company, is submitting a New Drug Application for Over-the-Counter (OTC) Zantac150 (Ranitidine Tablets 150 mg). This NDA provides clinical and statistical data in support of the Over-the-Counter (OTC) use of Zantac 150 (Ranitidine Tablets 150 mg) for the treatment of heartburn and the prevention of heartburn

Reference is made to NDA 20-520 for Over-the-Counter (OTC) Zantac 75® (Ranitidine 75 mg Tablets; approved December 19, 1995 for relief of heartburn), and to Supplement 001 (approved June 8, 1998 for the prevention of heartburn). Additional reference is made to IND 43,088 owned by GlaxoSmithKline (GSK; formerly Glaxo-Wellcome). Ownership of the Zantac 75® NDA was transferred to PCH from GSK on January 1, 1999 along with sole rights to market OTC Zantac 75 in the United States and Canada. Reference is also made to NDA 18-703 maintained by GSK for prescription use of Zantac 150 mg. In October 2000 PCH obtained OTC rights for Zantac 150 mg from GSK. Contained in this NDA is a letter of authorization from GSK allowing PCH to cross-reference NDA 18-703 for this submission.

Additional reference is made to meetings between PCH and FDA on November 7, 2001, May 8, 2003, July 17, 2003 (with a follow-up facsimile received July 28, 2003) and September 11, 2003 during which the following was agreed:

- The NDA will contain data from five clinical trials. Two trials (RANA3013 and RANA3014) supporting the treatment of heartburn and three trials (RANA3016, RANA3018 and RANA4006) supporting the prevention of heartburn.
- Six additional efficacy analyses based on pain relief scores and five additional information requests will be provided for RANA3013 and RANA3014, as described below.
- Statistical data will be submitted electronically on a CD-ROM in SAS transport format.

The efficacy endpoints to be utilized for the Treatment Trials (RANA3013 and RANA3014) are as follows:

The primary efficacy variable for both trials was total pain relief (TOTPAR) from 0 to 2 hours after dosing for the first trial drug-treated heartburn episode, if it was severe or very severe. TOTPAR was calculated as the sum of the relief score at each post-treatment time point. Higher scores indicated more relief.

Based on the telephone discussion between FDA and PCH on July 17, 2003, additional retrospective analyses were performed. The six efficacy endpoints specified by the FDA and analyzed by PCH were as follows:

1. After the first episode of severe or very severe heartburn, the percentage of subjects that achieved complete relief (a 6 on the heartburn pain relief scale) at the two-hour time-point after treatment.
2. After the first episode of severe or very severe heartburn, the percentage of subjects that achieved almost complete or complete relief (a 5 or a 6 on the heartburn pain relief scale) at the two-hour time-point after treatment.
3. After the first episode of severe or very severe heartburn, the time to achieve complete relief (a 6 on the heartburn relief scale) in the subjects that achieved complete relief.
4. After the first episode of severe or very severe heartburn, the time to achieve almost complete or complete relief (a 5 or a 6 on the heartburn relief scale) in the subjects that achieved almost complete or complete relief.
5. The fraction of episodes of severe or very severe heartburn for each subject with complete relief (a 6 on the heartburn relief scale) at the two-hour time point after treatment.
6. The fraction of episodes of severe or very severe heartburn for each subject with almost complete or complete relief (a 5 or a 6 on the heartburn relief scale) at the two-hour time point after treatment.

In the facsimile dated July 28, 2003, FDA requested the following additional information for treatment trials RANA3013 and RANA3014:

1. The average number of all heartburn episodes (of any severity) each subject experienced in each week of the study (including the 1 week run-in phase and the 2 week treatment phase).
2. The average number of severe or very severe heartburn episodes each subject experienced in each week of the study (including the 1 week run-in phase and the 2 week treatment phase).
3. The average number of days in which a study drug and/or Maalox were/was taken in each week of the study period (including the 1 week run-in phase and the 2 week treatment phase). (The maximum number of days in each week in which a drug was taken is 7)
4. The average total number of study doses taken by each subject in each week of the study period (including the 1 week run-in and the 2 week treatment interval). The maximum number of times a study drug was taken by one subject each week is 14.)
5. The average number of days that 2 doses of study drug were taken per subject in each week of the study period (including the 1 week run-in phase and the 2 week treatment phase). The maximum number of days that 2 doses were taken each week is 7.)

PCH is providing summary statistics only, and not statistically comparing the treatment groups for the five items listed above.

A number of secondary efficacy endpoints were collected for the two trials. The ISE focuses on the primary efficacy endpoints, the six efficacy endpoints requested by FDA during the July 17, 2003 telephone discussion, and the following secondary efficacy endpoints:

- TOTPAR for all study drug treated severe or very severe episodes
- Rescue antacid during the first study drug treated episode, if the episode was severe or very severe
- Rescue antacid during all study drug treated severe or very severe episodes
- Duration of relief during the first study drug treated episode, if the episode was severe or very severe
- Duration of relief during all study drug treated severe or very severe episodes

The efficacy endpoints to be utilized for the Prevention Trials (RANA3016, RANA3018 and RANA4006) are as follows:

A primary efficacy endpoint for all three controlled clinical trials supporting the prevention of heartburn was heartburn severity during the Treatment Meal Visit as measured by the Area Under the Curve [AUC (mm•hrs)]. This heartburn severity AUC endpoint has been used previously in trials to support meal-induced heartburn indications. Based on discussions with the FDA at the 18JUL97 meeting held with GlaxoWellcome, three additional clinical efficacy endpoints that provided clinically-meaningful outcome measures were prospectively defined in the trials RANA3016 and RANA3018, and were also included in the Clinical Study Report for RANA4006. For study RANA3018, these three additional endpoints and the Treatment Meal AUC were all primary efficacy endpoints.

The three additional clinical efficacy endpoints were all related to the primary endpoint of heartburn severity AUC and were similar to those used to demonstrate efficacy in meal-induced heartburn prevention trials with other OTC-H_2-receptor antagonists.

The endpoints included:

1. Reduction in heartburn severity AUC by $\geq$40 or 45 mm•hrs from the Run-In Meal Visit to the Treatment Meal Visit
2. Reduction in heartburn severity AUC by $\geq$50% from the Run-In Meal Visit to the Treatment Meal Visit and
3. An average heartburn severity score (Post-Treatment Meal) of <17 mm.

A composite score was calculated from the number of successes on three clinical efficacy endpoints listed above.

A number of secondary efficacy endpoints were collected for all three trials supporting the prevention of heartburn. The ISE focuses on the primary endpoints, the three additional clinical efficacy endpoints, and the following secondary endpoints:

- Percent reduction in heartburn severity AUC from the Run-In Meal Visit to the Treatment Meal Visit
- Treatment Meal peak heartburn severity
- Percent reduction in peak heartburn severity from the Run-In Meal Visit to the Treatment Meal Visit
- Largest number of consecutive time-points without heartburn

NDA Format and Content

This submission contains a **138** Volume Archival Copy (blue jacket)[1], a **1** Volume Chemistry, Manufacturing and Controls (CMC) Review Copy [red jacket], a **56** Volume Clinical Review Copy [light brown jacket] and a **53** Volume Statistical Review Copy [green jacket]. A full duplicate review copy of Item 8: Clinical Section will be provided to The Division of Over-the-Counter (OTC) Drug Products. Pursuant to 21 CFR 314.50, the first volume of the Archival Copy and the first volume of the CMC, Clinical and Statistical Review Copies contain the cover letter, the application FORM FDA 356h (2/03), Item 13: Patent Information, Item 14: Patent Certification, Item 15: Establishment Description, Item 16: Debarment Certification, Item 17: Field Copy Certification, Item 18: User Fee Sheet, Item 19: Financial Disclosure and Item 20: Other: Pediatric Use Information/Request for Exclusivity, Item 1: NDA Index, Item 2: Labeling and Item 3: NDA Summary.

A copy of Item 4: Chemistry, Manufacturing and Controls has been sent to the District Office in Parsippany, NJ. The Methods Validation Package has been included as Volume 2A in the Archival Copy. In addition, three copies have been provided as CMC Review Copies in red jackets.

This New Drug Application (NDA) has been organized according to the Code of Federal Regulations 21 CFR 314.50 and the "Guideline for the Format and Content of the Clinical and Statistical Sections of New Drug Applications". However, the Item numbering of this NDA follows that outlined in the revised FORM FDA 356h (2/03).

The page numbers listed in the Table of Contents refer to the numbers that appear in the lower right corner of every page of this application. The first digit of the page number indicates the Item number and the remaining digits refer to the actual page number, e.g.; page 8-1234 refers to Item 8, page number 1,234.

Pfizer Consumer Healthcare will contact Division personnel shortly after acknowledgement of receipt of the NDA to review the organization of the application and answer any questions.

Electronic Components

The statistical datasets from each of the individual trials and the pooled trials are supplied on a CD-ROM (1 archival copy and 1 desk copy labeled for Mr. Paul Levine). To aid in the review, the CD-ROM is accompanied by a document titled "Zantac 150 (Ranitidine Tablets 150 mg) Database Documentation". This is included in Item 10: Statistical Data and a desk copy is provided for the reviewing statistician.

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[1] The Methods Validation Package is included as Volume 2A . therefore there are actually 139 total volumes.

Labeling

Two copies of Draft Labeling for Zantac 150 (Ranitidine Tablets 150 mg) have been included in this NDA. Item 2 provides the Carton Labeling in the new OTC Drug Facts Format as the March 17, 1999 Final Rule: Over-The-Counter Human Drug - Labeling and the Consumer Package Insert without annotation. Item 3: provides the Labeling and Consumer Package Insert in annotated format. Provided as desk copies (one labeled for Mr. Paul Levine and one labeled for Ms. Laura Shay) are the OTC Drug Facts Carton Labeling and the Consumer Package Insert as MSWORD documents on 3.5" diskettes.

Application Fee

Pursuant to the Prescription Drug User Fee Act, the human drug applications requiring clinical data are subject to an Application Fee. Accordingly, a check for $573,500.00, which represents the full payment of the adjusted FY 2004 Application Fee for this NDA was sent to FDA under separate cover on October 16, 2003. This NDA has been assigned User Fee I.D. Number 4606 by FDA, Central Documents and Records.

Request for Exclusivity

Pfizer Consumer Healthcare is requesting three (3) years of exclusivity pursuant to 21 USC 355 (c) (3)(D)(iii) and 21 CFR 314.108 (b)(4).

Pre-Approval Inspection Readiness

Zantac 150 mg Tablets will be manufactured, packaged and tested by [redacted] Pfizer Consumer Healthcare (PCH) hereby confirms that this facility is ready for an FDA pre-approval inspection relative to this product.

Please be advised that certain information contained in this submission is confidential and should, therefore, be exempt from disclosure under the Freedom of Information Act or otherwise. We request that you notify the undersigned not less than three business days prior to any contemplated disclosure of any or all of this material by FDA.

Please contact Robert Kohler at (973) 385-5419 if you have any questions or require any additional information.

Sincerely,

Pfizer Consumer Healthcare

John R. Jacobs
Vice President, Global Regulatory Affairs

djf

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

See Instructions on Reverse Side Before Completing This Form

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

1. APPLICANT'S NAME AND ADDRESS
Pfizer Consumer Healthcare,
Division of Warner-Lambert Company, LLC
201 Tabor Rd.
Morris Plains, New Jersey 07950

2. TELEPHONE NUMBER *(Include Area Code)*
(973) 385-5532

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER
21-698

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☒ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

3. PRODUCT NAME
Zantac 150 (Ranitidine Tablets 150 mg)

6. USER FEE I.D. NUMBER
4606

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

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

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

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

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
John R. Jacobs	John R. Jacobs Vice President, Global Regulatory Affairs	10/31/2003

FORM FDA 3397 (1/03)

PSC Media Arts (301) 443-1090 EF

18-0002

Memorandum of Meeting Minutes

Meeting Date: July 17, 2003
Meeting Time: 11:00 - 12:00pm
Meeting Location: Conference C, PKLN Bldg., 3rd Floor

Application Number: IND 62,119
Drug Name: Zantac® (ranitidine hydrochloride), 150mg Tablets

Type of Meeting: Industry Meeting, Type C
Meeting Chair: Dr. Hugo Gallo-Torres
Meeting Recorder: Mr. Paul E. Levine, Jr.

List of FDA Attendees

Division of Gastrointestinal and Coagulation Drug Products (HFD-180)

Robert Justice, M.D., M.S., Division Director
Hugo Gallo-Torres, M.D., Ph.D.; Medical Team Leader, Gastrointestinal Drugs
Ruyi He, M.D., Medical Team Leader, Gastrointestinal Drugs
Eric Brodsky, M.D., Medical Reviewer
Liang Zhou, Ph.D. CMC Team Leader
Susan B. Daugherty, RN, BSN, Consumer Safety Officer
Paul E. Levine, Jr., R.Ph, J.D., Regulatory Project Manager

Division of Over the Counter Drug Products (HFD-560)

Charles Ganley, M.D., Director
Curtis Rosebraugh, M.D., Deputy Director
Solbeck Arlene, Interdisciplinary Scientist
Daiva Shetty, M.D., Medical Reviewer
Helen Cothran, B.S., Team Leader
David Hilfiker, M.S., Chief Project Manager Supervisor
Keith Olin, B.S., Regulatory Project Manager
Laura E. Shay, MS, RN, C-ANP, Regulatory Project Manager

External Constituents:

Pfizer Attendees:

Sandy A. Furey, Ph.D., M.D., Sr. Director, Medical/Clinical Development Rx to OTC switches
Alice Hirsch, B.A., M.B.A., Product Manager – New Products Gastrointestinal U.S. Marketing

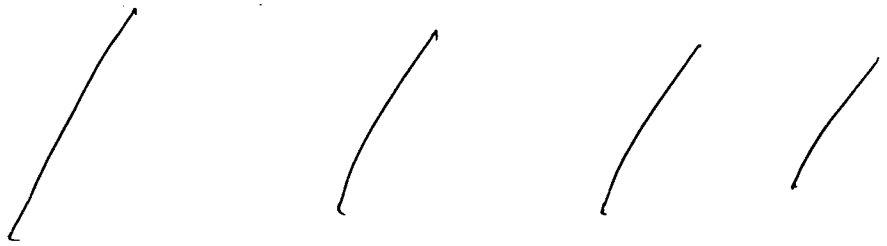
Mike Donnelly, M.D., Medical/Clinical
J. Tony McGuire, M.S., Associate Director, Statistics, Statistics and Data Management
[redacted] Consultant
Dolores Fliss, B.S., M.S., Manager; Regulatory Affairs, Rx to OTC Switches
Robert G. Kohler; R.Ph., J.D., Sr. Director, RX-to-OTC Switches, Global Regulatory Affairs

BACKGROUND:

Zantac®(ranitidine hydrochloride) 150mg Tablets is approved for use by prescription for the following indications:

1. Short term treatment of active duodenal ulcer.
2. Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. Treatment of pathological hypersecretory conditions.
4. Short term treatment of active, benign, gastric ulcer.
5. Maintenance therapy for gastric ulcer patients at reduced dosage after healing of acute ulcers.
6. Treatment of GERD
7. Treatment of endoscopically diagnosed erosive esophagitis.
8. Maintenance of healing of erosive esophagitis.

NDA 20-520 was approved on December 19, 1995, for the over-the-counter (OTC) use of Zantac® (ranitidine hydrochloride) 75mg tablets in the treatment of episodic heartburn.



In December 2000, Pfizer Consumer Healthcare acquired the rights to Zantac® (ranitidine hydrochloride) 150mg Tablets from GlaxoSmithKline (GSK).

On November 07, 2001, the FDA met with representatives of Pfizer to discuss issues related to the development plans for the over-the-counter use of Zantac® 150mg Tablets for the prevention of heartburn.

On March 26, 2003, the sponsor submitted a meeting request to discuss proposed switch of Zantac® 150mg tablets from prescription to OTC use.

MEETING OBJECTIVE:

To provide guidance and answer the sponsor's questions concerning the Pre-NDA development plans for the switch of Zantac® 150mg tablets from prescription to OTC use for the prevention and treatment of heartburn.

DISCUSSION:

The Sponsor provided a history of ranitidine hydrochloride and an overview of the drug development plan for the OTC use of ranitidine 150mg tablets for the prevention and treatment of heartburn (see attached slides).

Response to sponsor's questions:

1. Pfizer Consumer Healthcare (CHC) will submit a New Drug Application (NDA) for Zantac 150 — for over-the-counter (OTC) use in the treatment and prevention of heartburn. Pfizer CHC believes that clinical studies RANA3013, RANA3014, RANA3016, RANA3018, and RANA4006 are adequate to support the efficacy and safety. **Does the Agency concur?**

   FDA Response: No, the Agency does not concur. This question is phrased in a manner that suggests our concurrence with the acceptability of these studies. The application must be formally reviewed before a determination as to whether the studies are adequate to support the efficacy and safety could be made for the population that you are seeking in the label.

   The evaluation of this drug product requires an evaluation of the dose response for a treatment claim and a prevention claim. For each of these indications, there should be some benefit of taking 150mg compared to 75mg.

   There appears to be two studies (3016 and 4006) where the primary endpoints achieve statistical significance — for prevention. The dose response data in the two studies (3013 and 3014) for the treatment claim are less compelling. In these studies, the dose-response data do not clearly establish a differentiation between the 150mg strength and the 75mg strength of Zantac for a treatment claim.

   Additional Discussion: Data supporting a claim for prevention are needed for at least two studies and must be based upon clinically meaningful primary endpoints.

In order to establish a dose response, the sponsor asked if the Agency requires that statistical superiority be demonstrated or is it sufficient to show a statistical trend. The sponsor also requested that the Agency clarify what is meant by clinically meaningful endpoint.

The Agency informed the sponsor that clinically meaningful might include complete relief of heartburn or some acceptable permutation of complete responders. The data should clearly distinguish between complete responders and non-responders. Statistical data showing differentiation between the 150mg and 75mg doses using the clinically meaningful endpoints are needed. This data could be acquired through retrospective analyses if the Agency and sponsor mutually agree upon the type of analyses. The agency has concerns about the retrospective analysis performed by the sponsor for study 3013 and 3014 because there is no way to determine how many other endpoints or analyses were considered but discarded. The Agency recommended that the sponsor have further discussions with the Agency to consider alternative endpoints and analyses that might be acceptable.

The sponsor agreed to submit a meeting request to the GI Division for a discussion with the statisticians and clinicians in order to reach agreement about which retrospective analyses would be acceptable. The request will include the original protocols for study 3013 and 3014, case report forms (CRFs) from these studies, and the method of analysis. Clinical data will not be included in this submission. After the agency has the opportunity to review this information, a determination will be made on the feasibility of identifying clinically meaningful endpoints retrospectively without prejudice (by not accessing the data in making the determination).

2. Pfizer CHC proposes to support Zantac 150 [redacted] by submitting efficacy data to demonstrate that there is a trend showing a greater percentage of responders for the 150 mg vs. the 75 mg dose in the treatment and prevention of heartburn. **Does the Agency concur with this approach?**

   FDA Response: The response rate analysis was based on a retrospective analysis. There is no way to determine whether this was one of many analyses conducted by the sponsor. Consequently, it is difficult to interpret.

Additional Discussion: The sponsor asked if the Agency would consider

3. Pfizer CHC believes that studies RANA3013 and RANA3014 are essential for the approval of Zantac 150 for over-the OTC use in the treatment and prevention of heartburn. **Does the Agency concur?**

   FDA Response: The determination as to whether studies are essential for approval as an OTC product would be made as part of the interdivisional NDA review process once the application is submitted. If it is in reference to the determination of exclusivity, it cannot be answered because the Office of Generic Drugs makes this determination after the review has been completed.

4. Pfizer CHC believes that studies RANA3016, RANA3018, RANA4006, are essential for the approval of Zantac 150 for OTC use in prevention of heartburn **Does Agency concur?**

   FDA Response: See comments to question 3.

5. Treatment and prevention of heartburn by taking an H_2-receptor antagonist is currently an OTC indication (Zantac 75, Tagamet HB, Axid AR and Pepcid). The indications for the Zantac 150 product In addition, there are many examples in the OTC environment for "regular" and "maximum" strength products and consumers have experience in being able to appropriately use and distinguish between these product types. Therefore, Pfizer CHC believes that a regulatory precedent has been established and that a Label Comprehension Study is not required. **Does the Agency concur?**

***FDA Response*:** The currently proposed OTC treatment indication for the 150mg tablet [redacted] Therefore, if this [redacted] is pursued, a label comprehension study might be required to demonstrate that consumers are able to distinguish between the two products.

Additional Discussion: The sponsor asked if this would be a filing issue.

The Agency informed the sponsor that this issue alone would not prevent filing an application, as further discussion could occur post-filing.

6. As noted in Question #4, the indications for Zantac 150 [redacted] Pfizer CHC proposes to provide safety data for Zantac 150 [redacted] based on clinical data, as well as worldwide safety data. In addition, misuse of Zantac 150 [redacted] would not be expected and Pfizer CHC cannot identify a hypothesis to test in an Actual Use setting that resolves any outstanding issues. Therefore, Pfizer CHC believes that an Actual Use Study would not be required. **Does the Agency concur with this approach?**

***FDA Response*:** The Actual Use Study is not required if the label is identical to the 75mg product.

Additional Discussion: The sponsor asked if the Agency would consider [redacted] in the labeled indication as there is evidence that consumers are very familiar with this term.

The Agency informed the sponsor that [redacted] is generally not permitted in the labeling of heartburn relief medication. However, the Agency would consider a proposal from the sponsor with supporting data for use of the term.

7. The Integrated Summary of Safety (ISS) will contain clinical data from five studies (RANA3016, RANA4006, RANA3018, RANA3013 and RANA3014). In addition, Pfizer CHC will incorporate an updated safety assessment of data from:

- Toxic Exposure Surveillance System (TESS),
- American Association of Poison Control Centers (AAPCC),
- World Health Organization (WHO),
- Spontaneous Adverse Event reports,
- Literature review

Does the Agency concur with this approach?

FDA Response: We request that you supply data for serious and non-serious adverse events separately. In addition, we request that you supply data that demonstrate that 150mg dose is safe in children 12-18 years of age.

8. Pfizer CHC has provided (ATTACHMENT x) a proposed format for the statistical tables to be included in the Integrated Summary of Efficacy (ISE) and the Integrated Summary of Safety (ISS)? **Does the agency have any specific comments on these proposed tables?**

   ***FDA Response*:** See response to question 7.

9. Pfizer CHC has provided draft sample format for Case Report Form Tabulations (CRTs; ATTACHMENT x) that will be included in the NDA. **Does the agency have any specific comments on the format of the proposed tabulations?**

   ***FDA Response*:** Currently, submission of data in the traditional or Common Technical Document (CTD) format is acceptable. The project manager from the GI Division will inform you which format is required for future submissions.

10. Does the Agency have any specific comments regarding the proposed Drug Facts Labeling?

    ***FDA Response*:** Generally, your OTC labeling for Zantac should include all relevant warnings related to or associated with the use of the drug. Additional comments are attached.

CONCLUSION:

1. The sponsor agreed to submit a meeting request to the GI Division for a discussion with the statisticians in order to reach agreement about which retrospective analyses and endpoints would be acceptable. The request will include the sponsor's proposed protocol, case report forms (CRFs) from the relevant studies, and the method of analysis. Clinical data will not be included in this submission.
2. The project manager from the GI Division will inform sponsor if the CTD format is required for future submissions.
3. The minutes would reflect additional post-meeting labeling comments - (see below text)

F

2 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

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

/s/

Paul Levine
12/9/03 12:45:53 PM

MEMORANDUM OF TELECONFERENCE MEETING

Meeting Date: January 8, 2003

Time : 1 PM
Location: S205, 9201 Corporate Blvd
Rockville, MD

Application: Zantac 150mg

Type of Meeting: Sponsor feedback Concerning Meeting Request

Meeting Chair: Charles Ganley, M.D., Division Director, HFD-560

Meeting Recorder: Daniel P. Keravich, R.Ph, M.S., MBA.

TELECONFERENCE PARTICIPANTS

Pfizer
Bob Kohler, Senior Director, Regulatory Affairs

Agency Participants
Charles Ganley, M.D., Division Director, HFD-560
Dan Keravich, RPh., M.S., M.B.A., Regulatory Project Manager, HFD-560

BACKGROUND

The sponsor had submitted a meeting request on November 21, 2002 requesting a teleconference to receive guidance on the possibility of not submitting a label comprehension study with an OTC switch application for Zantac 150mg OTC. The sponsor wanted to submit the study after receiving feedback by the division on the appropriate label.

OBJECTIVES:

- To provide sponsors with feedback concerning his meeting request on label comprehension studies
- To provide the sponsor with additional feedback on several potential indications for Zantac 150mg in the OTC setting

Before the Agency could address the sponsor's questions on label comprehension, the sponsor was first questioned about what indications were being identified for the NDA submission. The sponsor was planning

Since our last meeting with the sponsor, we have provided an alternative option to other sponsors. Higher doses of H2 blockers may be acceptable for the same claim as the lower dose of the H2 blocker. The sponsor may not have to show a significant difference between the doses but would have to provide data to support a dose response using clinically interpretable endpoints (clinically significant dose response using a trend analysis for example). The details of such an analysis, and acceptable endpoints, need to be worked out with our statisticians and would be a worthwhile discussion for the sponsor.

The sponsor decided that they would rethink the contents of their application internally based on this new information, and would re-propose a meeting request, request a Pre IND meeting for Zantac 150mg.

The telecon ended amiably.

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

/s/

Daniel Keravich
1/15/03 12:25:23 PM
CSO

Charles Ganley
1/27/03 11:53:53 AM
MEDICAL OFFICER

June 14, 2002

GlaxoSmithKline

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Victor Raczkowski, M.D., Acting Director
Division of Gastrointestinal and Coagulation Drug Products
Center for Drug Evaluation and Research
Attn: Document Control Room
Office of Drug Evaluation III
Food and Drug Administration
HFD-180, 6B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 18-703; ZANTAC® 150/300 (ranitidine hydrochloride) Tablets, USP
General Correspondence: Other

Dear Dr. Raczkowski:

We wish to inform you that by this reference letter, we authorize **Pfizer Inc., Warner-Lambert Company, Pfizer Consumer Group and Pfizer Consumer Healthcare** (individually and collectively, **"Pfizer"**) of 201 Tabor Road, Morris Plains, New Jersey, to make reference to the below enumerated sections of NDA #18-703 in connection with Pfizer's NDA submission for Ranitidine 150 mg RX to OTC Switch for heartburn prevention:

- Item 4: Chemistry, Manufacturing and Controls Section (to include both drug substance and drug product information)
- Item 5: Nonclinical Pharmacology and Toxicology Section
- Item 6: Human Pharmacokinetics and Bioavailability Section
- Item 8: Clinical Section (specifically the Clinical Pharmacology Study Information)
- All reports of post-marketing adverse drug experiences submitted to FDA pursuant to 21 C.F.R. Section 314.80 (or any analogous successor regulation), irrespective of the timing of submission.

It is expressly acknowledged and understood that the information contained within the referenced NDA remains confidential and according to this reference letter is to be used exclusively for your review of relevant applications submitted by Pfizer.

Please feel free to contact me at (919) 483-3640 if you have any questions regarding this matter.

Sincerely,

Craig A Metz

Craig A. Metz, Ph.D.
Vice President
Regulatory Affairs

3.3 Foreign Marketing History

Pfizer Consumer Healthcare (PCH) obtained over-the-counter (OTC) marketing rights for Zantac 150 (Ranitidine Tablets 150 mg) in the United States and Canada from GlaxoSmithKline (GSK) [formerly GlaxoWellcome] in October 2000. To date, this product has not been approved for OTC use in Canada. GSK maintains rights to OTC Zantac 150 for the rest of the world and all rights to prescription Zantac 150.

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Zantac® 150 (ranitidine) Tablets
Pfizer Consumer Healthcare

Safety Update Review

The safety updates submitted on March 26, 2004 (received March 30, 2004), April 28, 2004 (received April 29, 2004), May 13, 2004 (received May 14, 2004) and June 30, 2004 (received July 1, 2004) were reviewed as part of the integrated safety review for the original NDA submission (see OTC Medical Officer review by Dr. Linda Hu dated July 20, 2004). The March 26, 2004, submission contained a four month safety update. The April 28, 2004, submission contained complete literature data referenced in the October 31, 2003, submission. The May 13 and June 30, 2004, submissions were resubmissions of data submitted in the original NDA in revised formats. In the August 18, 2004 submission, the sponsor notes that no new clinical studies are being conducted and that no additional post-marketing safety data are currently available.

Deane Mogo
8/18/04

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Abuse Liability review(s)

This product does not require an abuse liability review.

Diane Moore 7/29/04

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DSI Audit of Clinical Studies

No clinical studies were audited in accordance with the recommendation by Dr. Eric Brodsky, Medical Officer.

Diane Moore 7/29/04

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Statistical Review(s) of Carcinogenicity Studies

Carcinogenicity studies were reviewed with the original NDA submission.

Diane Moore 7/29/04

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Environmental Assessment

A categorical exclusion is claimed for this NDA in accordance with 21 CFR part 25.31 (b), as amended in the 29-Jul-1997 Federal Register. The proposed categorical exclusion for the environmental assessment is acceptable per Chemistry and Manufacturing review by Dr. Ramesh Raghavachari dated July 6, 2004 (see page 47).

Diane Moore 7/29/04

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Micro (validation of sterilization) Review(s) and Memoranda

This is not a sterile product. No microbiology review is required.

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EER

There were no manufacturing changes - no EER is required.

Diane Moore 7/29/04

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Microbiology Review

A microbiology review is not required for tablets.

Diane Moore 7/29/04

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Methods Validation

Methods were not changed from previously approved methodology for Zantac products. Method validation is not required for this application.

Deane Moore 7/29/04

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Statistics review(s) and memoranda regarding dissolution and/or stability

No statistical review of drug stability is needed for this application.

Deane Moore 7/29/04

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Pharmacology/Toxicology review(s) and Memoranda

No pharmacology information was submitted to this NDA. The dose and duration of this drug product is within the limits of the prescription product. A Pharmacology review is not required for this application

Diane Moore 7/29/04

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Memo from DSI regarding GLP inspection (if any)

No GLP inspection was needed from DSI for this drug product.

Diane Moore 7/29/04

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CAC/ECAC Report

No CAC/ECAC report was needed for this NDA.

Diane Moore
7/29/04

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Risk Management Plan review

This is not a new molecular entity. No risk management plan is required.

Diane Moore 8/13/04

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Group Leader's Memo

No Group Leader's memo will be prepared; the Group Team Leader concurs with the medical review (see M.O. review by Eric Brodsky, M.D. dated August 13, 2004).

Diane Moore 8/31/04

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Federal Register Notices

This application was not the subject of any Federal Register Notices.

Diane Moore 7/29/04

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Advisory Committee Meeting Minutes

This application was not the subject of an Advisory Committee Meeting.

Diane Moore 7/29/04

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Post-marketing Commitments

There were no post-marketing commitments made for this drug product.

Deane Moore 7/28/04

NDA 21-698
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Labeling Reviews

See individual discipline reviews for labeling comments.

Deane Moore 7/29/04

NDA 21-698
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Foreign Labeling

The sponsor does not distribute this drug product outside the U.S.A. There is no foreign labeling for this product.

Diane Moore
1/28/04

NDA 21-698
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Advertising Material

No advertising material has been submitted for this application. Advertising material is requested in the approval letter.

Diane Moore
8/31/04

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Public Communications

No public communications are required for this application.

Diane Moore 7/29/04

NDA 21-698
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Application Integrity Policy

The Application Integrity Policy (AIP) has not been invoked for this NDA or this NDA sponsor.

Diane Moore 7/28/04