DMETS Response: This method of "checking" is not common practice, especially in the retail setting. Also, if the sponsor is referring to the recent approved barcoding rule, many institutions are in the process of implementing this kind of practice, but are yet to be compliant. In the retail setting, the pharmacist would more likely "scan" the prescription label at the final "checking" stage to review the accuracy of the filled medication with the ordered medication on the prescription.

d. ***Sponsor's Comment:*** *If there ever was written confusion over the brand name ([redacted] vs. Tenormin) the tablet size, tablet strength, dosing, number of tablets, and number of refills are too different to allow a mix-up.*

DMETS Response: See comment under New Information Summary (B.1.b. and B.1.d).

3. Medical Risks of a Mix-up

a. ***Sponsor's Comment:*** *This is atenolol, a cardioselective beta-blocker for treating angina, hypertension, and arrhythmia. In general, populations prescribed this drug will be older than those prescribed [redacted] will primarily be used in younger, healthier patients.*

DMETS Response: Tenormin is indicated in the treatment of hypertension, angina pectoris, and acute myocardial infarction. It would be misleading to assume that this product would primarily be used exclusively in an "older" population, as the aforementioned disease states can be present in any age group. A potential for overlap in patient population exists for Tenormin and [redacted]

d. ***Sponsor's Comment:*** *Short-term administration of atenolol by mistake is not likely to cause significant medical concerns.*

DMETS Response: Adverse effects resulting from an inadvertent administration of atenolol may not always "cause significant medical concerns", however, the possibility still exists that an adverse event may occur. The predominant symptoms reported following Tenormin overdose are lethargy, disorder of respiratory drive, wheezing, sinus pause and bradycardia. Additionally, common effects associated with overdosage of any beta-adrenergic blocking agent and which might also be expected in Tenormin overdose are congestive heart failure, hypotension, bronchospasm and/or hypoglycemia. All drug misadventures are serious in nature and should be prevented if possible.

e. ***Sponsor's Comment:*** *It is highly unlikely that a pharmacist will dispense four 50 mg atenolol tablets for one-time consumption since this is such an unusual dose. This mis-interpretation of the trade name would generate a call to the physician.*

DMETS Response: DMETS agrees that dispensing four 50 mg atenolol tablets may be "unusual", but in some cases (e.g. titration/cost), prescribers write/call in prescriptions asking for lower strengths, with the intention of adjusting the dose as needed. The Tenormin package insert lists 200 mg as an acceptable dose in

certain indications. Therefore, it would not necessarily generate a "call to the physician", since this dose (Tenormin 200 mg or Tenormin 50 mg – 4 tablets) would fall within an acceptable dosage range.

d. ***Sponsor's Comment:*** *In the event that an acute dose of [redacted] is dispensed to a first time user of Tenormin, there is little likelihood of serious complications and most likely the patient will question a why only a few tablets have been dispensed for their chronic condition.*

DMETS Comment: See comment under Medical Risks of Mix-up (B.3.b.).

e. ***Sponsor's Comment:*** *It is unlikely that a patient already established on Tenormin therapy would be inadvertently switched to [redacted] in the case of a pharmacy mix-up given the pharmacy computer systems. However, should it happen, the size, shape, color, and markings of the [redacted] tablet will be very different from the Tenormin tablet. The patient will detect an inappropriate change.*

DMETS Response: DMETS agrees that some patients are aware of their medication regimen and would recognize changes in their medications. However, not all patients are astute, and many may continue to take the medication undetected. In some instances, patients assume they are receiving an generic version or an alternate generic version of their prescribed medication, and do not question the "change" in drug appearance. All drug misadventures, whether or not a serious outcome results, are serious in nature and should be prevented if possible.

C. The sponsor submitted container label and carton and insert labeling for the [redacted] tablet. DMETS reviewed the [redacted] container label and carton and insert labeling during the September 9, 2003 proprietary name review and made recommendations that may minimize potential user error. The labels and labeling have not been revised since the completion of that review, thus DMETS refers the sponsor to our original comments.

V. RECOMMENDATIONS:

A. DMETS does not recommend the use of the proprietary name, [redacted] The sponsor has failed to submit persuasive evidence for DMETS to reverse its initial decision on the acceptability of the proprietary name [redacted] However, DMETS has no objections to the use of the proprietary name Tindamax. This decision 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 names, [redacted] and Tindamax, 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.

Jinhee L. Jahng, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina R. Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

____1____ page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

A-18

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/s/

Jinhee Jahng
4/26/04 11:35:30 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
4/26/04 11:39:03 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
4/26/04 11:53:13 AM
DRUG SAFETY OFFICE REVIEWER

Jerry Phillips
4/27/04 07:53:54 AM
MEDICAL OFFICER

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

FACSIMILE TRANSMITTAL SHEET

DATE: December 17, 2003

To: John E. Presutti President	**From:** Christina H. Chi, Ph.D. Regulatory Project Manager
Company: Presutti Laboratories, Inc.	Division of Special Pathogen and Immunologic Drug Products (HFD-590)
Fax number: (847) 359-7878	**Fax number:** (301) 827-2325
Phone number: (847) 359-7800	**Phone number:** (301) 827-2127

Subject: Comments and recommendations regarding the proposed propriety names [redacted] (NDAs 21-618, 21-681 and 21-682)

Total no. of pages including cover: 8

Document to be mailed: ☐ YES ☑ NO

NDA 21-618
NDA 21-681
NDA 21-682

Dear Mr. Presutti:

Please refer to NDAs 21-618, 21-681, and 21-682 for tinidazole tablets. We have completed our preliminary review of your proposed propriety names , [redacted] , and have the following comments.

The Division of Special Pathogen and Immunologic Drug Products and the Division of Medical Errors and Technical Support (DMETS) do not recommend the use of the proposed proprietary names, [redacted]

1. In reviewing the proprietary name [redacted], the primary concerns related to look-alike, sound-alike confusion with Trimox and Tenormin.

   a. Trimox and [redacted] may look-alike when scripted. Trimox is a penicillin antimicrobial agent available in capsule or suspension form and is typically given twice or thrice daily. Trimox and [redacted] can look similar when scripted (see below) as demonstrated in the DMETS prescription analysis studies. Although [redacted] letters versus Trimox's six, the prefix [redacted] looks similar to "Tri-" as do the suffixes [redacted]. In addition, Trimox, when used to eradicate *H. pylori*, has a recommended dose of 1 gram twice daily, which is similar to [redacted] twice daily dosing regimen. Because both drugs are indicated for treatment of organisms, it would not be unreasonable for the prescriptions to be confused with one another, given the commonalities they share. Equally alarming are the other similarities both Trimox and [redacted] share, such as dosage form (capsule) and dosage strength (250 mg and 500 mg). A patient inadvertently receiving Trimox instead of [redacted] is at risk of receiving sub-optimal therapy to eradicate microorganisms that [redacted] is specifically indicated for and also may be subject to pancytopenia, diarrhea, abdominal cramps, pseudomembranous colitis, interstitial nephritis, cutaneous reactions, urticaria, and hypersensitivity reactions. Any interruption in therapy is undesirable and should be prevented if possible. DMETS believes that a likelihood for a dispensing error with Trimox and [redacted] exists.

[redacted] Trimox
500 mg. 500 mg.
ii po bid ii po bid

b. Tenormin and [redacted] were found to have look-alike similarities. Tenormin is a long-acting, cardioselective beta-adrenergic blocking agent without membrane stabilizing or intrinsic sympathomimetic activities. Tenormin has eight letters whereas [redacted] has seven, however, the "-or-" in Tenormin can resemble an "a" when scripted (see below), increasing the likelihood for confusion between the two names. This similarity is compounded by the overlapping characteristics of "-enorm-" in Tenormin with the ' [redacted] Also, the suffix ' [redacted] resemble [redacted] if the letters are not precisely scripted to illustrate each upstroke and downstroke. One respondent from the DMETS prescription analysis studies interpreted [redacted] as Tenormin, and two respondents remarked that [redacted] has the potential to be confused with Tenormin. Tenormin is available as a 25 mg, 50 mg, and 100 mg tablet; [redacted] is available as a 250 mg and 500 mg tablet. Although Tenormin's strength is 1/10 of [redacted] postmarketing experience has shown medication errors occurring as a result of a numerical similarity in strengths (25 mg vs. 250 mg, 50 mg vs. 500 mg). Also, Tenormin can be given twice daily, like [redacted] Inadvertent administration of Tenormin instead of [redacted] may cause bradycardia, cold extremities, fatigue, nausea, skin rash and bronchospasm; retroperitoneal fibrosis has also been reported. In addition, the patient is at risk of receiving suboptimal therapy to eradicate microorganisms. On the contrary, inadvertent administration of [redacted] may subject the patient to severe allergic reactions, headaches and gastrointestinal effects such as bitter eructation, nausea, vomiting, and anorexia. [redacted] can potentiate the effects of anticoagulating drugs. Any interruption in therapy is undesirable and should be prevented if possible. Their dosage strengths vary, but Tenormin and [redacted] share enough characteristics to increase the likelihood for a potential dispensing mishap.

Tenormin [redacted]

2. In reviewing the proprietary name [redacted] the primary concerns related to look-alike, sound-alike confusion with Danazol, Timolol, Tioconazole (established name), Virazole, Tapazole, and Terazol.

a. Danazol and [redacted] have the potential for sound-alike confusion. Danazol is a synthetic steroid analog that has strong antigonadotropic properties. It has been used extensively for the treatment of endometriosis and has also been used for fibrocystic breast disease, breast cancer, hemophilia, idiopathic thrombocytopenic purpura, and hereditary angioedema. Both Danazol and [redacted] have three syllables and share similar sounds ("D-" vs. "T-" and [redacted] '). Danazol is available as a 50 mg, 100 mg, and 200 mg capsule and is typically dosed twice daily. Danazol and [redacted] share a common route of administration (oral) and dosage schedule (twice daily) which may further aid in causing confusion between the two drug names. Likewise, a verbal order for Danazol 50 mg may be easily confused with [redacted] 500 mg and vice versa. Postmarketing experience has shown medication errors occurring as a result of a numerical similarity in strengths (50 mg vs. 500 mg). Overlapping characteristics

of Danazol and [redacted] are significant and the opportunities for errors are likely in any situation where the prescriber communication is unclear to the practitioners interpreting the medication order. This commonly occurs when the prescription is ambiguous or incomplete. An example of when such an error can occur includes a verbal prescription for "Danazol 50 mg bid" may be misinterpreted as [redacted] 500 mg bid" or vice versa. Use of Danazol is contraindicated in pregnancy due to the possibility of androgenic effects on the female fetus. Thromboembolisms, thrombotic and thrombophlebitic events, including life-threatening or fatal strokes have been reported with the use of Danazol. Danazol is associated with several cases of benign intracranial hypertension. Likewise, a patient inadvertently given Danazol instead of [redacted] is at risk of receiving suboptimal therapy to eradicate microorganisms. [redacted] may cause severe allergic reactions, headaches and gastrointestinal effects such as bitter eructation, nausea, vomiting, and anorexia. [redacted] can potentiate the effects of anticoagulating drugs. Any interruption in therapy is undesirable and should be prevented if possible. DMETS believes there is potential for confusion to exist between Danazol and [redacted]

b. Timolol and [redacted] have sound-alike similarities. Timolol is a nonselective beta-adrenergic blocking agent. It is an effective drug for the treatment of elevated intraocular pressure and has also been used in the treatment of hypertension, angina, and for the reduction of mortality following myocardial infarct. Timolol and [redacted] have three syllables and begin ("Tim-" vs. [redacted]") and end ([redacted]) with similar sounding letter combinations. The two names also share rhyming characteristics. Timolol is available as a 5 mg, 10 mg, and 25 mg tablet; [redacted] is available as a 250 mg and 500 mg tablet. Although Timolol's strength is 1/10 of [redacted] postmarketing experience has shown mediation errors occurring as a result of a numerical similarity in strengths (25 mg vs. 250 mg). Also, Timolol and [redacted] can both be given as a single dose per day. Inadvertent administration of Timolol instead of [redacted] can result in bradycardia, arrhythmia, hypotension, dizziness, headache, depression and hallucinations. Their dosage strengths vary, but Timolol and [redacted] share enough characteristics to increase the likelihood for a potential dispensing mishap.

c. Virazole and [redacted] have look-alike characteristics. Virazole is a synthetic nucleoside with antiviral activity, which is available as a sterile, lyophilized powder to be reconstituted for aerosol administration. Virazole is indicated for the treatment of hospitalized infants and young children with severe lower respiratory tract infections due to respiratory syncytial virus (RSV). Virazole and [redacted] have [redacted] letters and share the same letter combination except for the prefixes "Vir-"and [redacted] These names when scripted share similar upstroke characteristics creating the potential for confusion and misinterpretation (see page 4). Virazole is indicated for use in hospitalized infants and young children whereas [redacted] is indicated for use in the adult and pediatric (> 3 years of age) patient population.

Although the drug products differ in dosage form (powder for reconstitution vs. tablet), strength, and dosage schedule, post-marketing experience has demonstrated that errors do occur between drugs that share no commonalities other than a similar name especially when the prescription is ambiguously written. Confusion and error can occur when an inpatient prescription order for "D/C Virazole" is misinterpreted as [redacted] or vice versa, causing the discontinuation of wrong medication if the patient is prescribed both medications simultaneously. The consequences of discontinuing the wrong medication may leave the patient's disease state untreated. DMETS believes the potential for a dispensing mishap exists given the orthographic similarities the two names share.

[redacted]

Virazole

[redacted]

VIRAZOLE

d. Tapazole and [redacted] look similar when written and sound similar when pronounced. Tapazole is an antithyroid drug used for the treatment of hyperthyroidism. It can also be used as long-term therapy to produce remissions or in preparation for radioactive iodine therapy or thyroidectomy. Tapazole and [redacted] contain the same letter combination except for the two letters ([redacted]) and each name has eight letters with similar upstroke characteristics creating the potential for confusion and misinterpretation (see page 5). In addition, the names have the potential to sound-alike because each share three syllables, rhyming characteristics, and [redacted] sounds. Tapazole and [redacted] share the same route of administration (oral) and dosage schedule. One may argue that confusion between Tapazole and [redacted] is minimized because of the variance in strengths between the two products. Tapazole is available as a 5 mg and 10 mg tablet; [redacted] is available as a 250 mg and 500 mg tablet. A verbal discontinuation order transcribed onto a medical chart could be misinterpreted if two names with sound-alike properties coexist on the patient's medication profile. In this scenario, confusion is further heightened since the strength oftentimes is not specified. The person transcribing the order or the person reading the order could mistake Tapazole for [redacted] or vice versa. The potential for confusion is likely given the similarity in dosage form, dosing regimen, route of administration, and name. A dispensing error could lead to temporary, if not permanent harm to the patient. Tapazole has been associated with the inhibition of myelopoiesis (agranulocytosis, granulocytopenia, and thrombocytopenia), aplastic anemia, drug fever, a lupus-like syndrome, insulin autoimmune syndrome (which can result in hypoglycemic coma), hepatitis (jaundice may persist for several weeks after discontinuation of the drug), periarteritis, hypoprothrombinemia, and nephritis. Tapazole is contraindicated in

nursing mothers because the drug is excreted in milk. A patient unaware of a "mix-up" may not know what signs/symptoms to report to their provider and in turn, may be subject to an adverse event.

Tapazole

TAPAZOLE

We have also completed a preliminary review of the container labels, carton and insert labeling of [redacted] focused on safety issues relating to possible medication errors. We have identified the following areas of possible improvement which might minimize potential user error.

a. CONTAINER LABEL

i. Include the dosage form in the established name. For example: Tinidazole Tablets.

ii. Include the statement: "Each tablet contains xxx mg of tinidazole" on the side panel.

iii. We note that you propose to market this product in bottles containing 20 and 40 tablets. We consider these bottles unit of use containers. Please ensure that the containers have a Child Resistant Closure (CRC) cap in order to be compliant with the Poison Prevention Act.

b. CARTON LABELING

See Container Label Comments.

We are providing the above information via telephone facsimile for your convenience. Please feel free to contact me at (301) 827-2127 if you have any questions regarding the contents of this transmission.

Sincerely yours,

{See appended electronic signature page}

Christina H. Chi, Ph.D.
Regulatory Project Manager
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Ellen Molinaro
12/17/03 02:13:05 PM
CSO
for Christina H. Chi, Ph.D. (NDA 21-681, NDA 21-681, and NDA 21-682)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-618
NDA 21-681
NDA 21-682

Presutti Laboratories, Inc.
Attention: John Presutti, President
1607 N. Douglas Avenue
Arlington Heights, IL 60004

Dear Mr. Presutti:

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: [redacted]™ (tinidazole) tablets, 250 and 500 mg

Please note, as Christina Chi of this Division explained to you by telephone, separate NDA numbers as listed below have been assigned to each of the proposed indications for our administrative purposes.

Please note the following information for NDAs 21-618, 21-681, and 21-682:

Our Reference Number	Indication
NDA 21-618	Trichomoniasis
NDA 21-681	Giardiasis
NDA 21-682	Amebiasis

Review Priority Classification: Standard

Date of Applications: July 16, 2003

Date of Receipt: July 17, 2003

Under 21 CFR 314.102(c), you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the ultimate approvability of the application. Alternatively, you may choose to receive a report by telephone.

Please cite the NDA numbers listed above at the top of the first page of any communications concerning these applications. Address all communications concerning these NDAs as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Special Pathogen and Immunologic Drug Products, HFD-590
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Special Pathogen and Immunologic Drug Products, HFD-590
Attention: Document Room
9201 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions, call Christina H. Chi, Ph.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Ellen F. Molinaro, R.Ph.
Chief, Project Management Staff
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Ellen Molinaro
9/29/03 05:01:10 PM
NDA 21-618, NDA 21-681, and NDA 21-682

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING REVIEW LETTER

NDA 21-618
NDA 21-681
NDA 21-682

Presutti Laboratories, Inc.
Attention: John Presutti, President
1607 N. Douglas Avenue
Arlington Heights, IL 60004

Dear Mr. Presutti:

Please refer to your July 16, 2003 new drug applications (NDAs) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for [redacted] (tinidazole) tablets, 250 and 500 mg.

We also refer to your submissions dated September 15 and 29, 2003.

We have completed our filing review and have determined that your applications are sufficiently complete to permit a substantive review. Therefore, these applications have been filed under section 505(b) of the Act on September 15, 2003, in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the applications and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Christina H. Chi, Ph.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Ellen F. Molinaro, R. Ph.
Chief, Project Manager Staff
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Ellen Molinaro
9/29/03 05:07:00 PM
NDA 21-618, NDA 21-681, and NDA 21-682

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-618 for Trichomoniasis Supplement # N/A SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8
NDA # 21-681 for Giardiasis
NDA # 21-682 for Amebiasis
(Note: NDA 21-618 is administratively split into 3 NDAs according to the indications).

Trade Name: [redacted]
Generic Name: Tinidazole
Strengths: 500 mg and 250 mg tablets

Applicant: **Presutti Laboratories**

Date of Application: July 16, 2003
Date of Receipt: July 17, 2003
Date clock started after UN:
Date of Filing Meeting: August 28, 2003
Filing Date: September 15, 2003
Action Goal Date (optional): April 12, 2003 **User Fee Goal Date: May 17, 2004**

Indication(s) requested: **Trichomoniasis, Giardiasis, Amebiasis**

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

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

Therapeutic Classification: **S___ X__** P _____
Resubmission after a withdrawal? _____ Resubmission after a refuse to file? _____
Chemical Classification: (1,2,3 etc.) __1_____
Other (orphan, OTC, etc.) **Orphan for giardiasis (letter 4/18/2002) and amebiasis (letter 8/20/2003)**

User Fee Status: Paid _____ or **Waived** ___x___ (e.g., small business, public health, government)
Small business (letter 3/19/2003).

Form 3397 (User Fee Cover Sheet) submitted: YES NO
User Fee ID # none

Clinical data? **YES __X__(literature)** 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: Tinidazole has never been approved in the US.

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

Alinia Oral suspension (nitazoxanide) was granted orphan designation on 2/14/02 for the treatment of intestinal giardiasis((see the list of Orphan Drug Designations and Approvals at http://www.fda.gov/orphan/designat/list.htm. It was approved on November 22, 2002 for diarrhea caused by Cryptosporidium parvum and Giardia lamblia in pediatric patients only. It has 7 years of **Orphan drug exclusivity.**

(On 10/23/01 [redacted] was also designated as an Orphan Drug for intestinal amebiasis but is not approved yet for the indication of amebiasis).

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

YES NO

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

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

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

- **Exclusivity** requested? **YES** NO
  Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
  Additional comments: NME status gives **5 years of exclusivity for the product.**
  If this application is approved for **giardiasis indication**, it will receive **Orphan drug exclusivity for 7 years for giardiasis only (2 yrs in addition to the 5 yrs from being an NME). This will also be true for amebiasis.**

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

  NOTE: Debarment Certification must have correct wording, e.g.: "I, the undersigned, hereby certify that _____ Co. did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with the studies listed in Appendix ____." Applicant may not use wording such as "To the best of my knowledge . . ."

- Financial Disclosure information included with authorized signature? **YES** NO
  (Forms 3454 and/or 3455 must be used and must be signed by the APPLICANT.)
  Form 3454, signed by Mr. Presutti on 7/9/03, can be found in the original submission, vol. 1.8, p. 9-524

- Field Copy Certification (that it is a true copy of the CMC technical section)? **YES** NO
  Field Copy Certification can be found in the original submission, vol. 1.4, p. 7-1008/1014)

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? **YES** NO
  Note: If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
  Action goal date: April 12, 2004

- Drug name/Applicant name correct in COMIS? **YES** NO
  (If not, have the Document Room make the corrections).

- List referenced IND numbers: **pre-IND ——— → IND 62,292**

- End-of-Phase 2 Meeting(s)? Date(s) **N/A** **NO**
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) **May 27, 2003** NO
  If yes, distribute minutes before filing meeting.

Project Management

- Package insert consulted to DDMAC? **Not yet; DDMAC representative requested that they be included only during the labeling or the last 3 months of the review period.** YES NO

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

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

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

If Rx-to-OTC Switch application:

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

- Has DOTCDP been notified of the OTC switch application? [N/A] YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? [N/A] YES NO

Chemistry:

- Did applicant request categorical exclusion for environmental assessment? [YES] NO

  If no, did applicant submit a complete environmental assessment? YES NO

  If EA submitted, consulted to Nancy Sager (HFD-357)? [YES] NO

- Establishment Evaluation Request (EER) submitted to DMPQ? [YES] NO

- If parenteral product, consulted to Microbiology Team (HFD-805)? [N/A] **(tablet)** YES NO

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

- Name of listed drug(s) and NDA/ANDA #: **The application is based on literature; there is no approved product in the US. The comparator drug is Fasigyn, which is marketed in Europe since mid 1970's.**

- 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"). N/A.

- 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.) N/A 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). N/A 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). N/A 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.

  _x__ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Patent # 3376311 to Kenneth Butler on 4/2/1968 and assigned to Pfizer).

  ____ 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?

    N/A 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).

    N/A YES NO

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

    YES NO

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

    YES, IND 62,292 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?

    YES NO

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

  YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: **August 28, 2003**

BACKGROUND: Tinidazole tablet has been marketed in Europe and other continents since 1970's for a number of indications, such as trichomoniasis, giardiasis, amebiasis, BV, and lyme disease. No sponsor has submit any application for the marketing approval in the U.S.A.

ATTENDEES: Renata Albrecht, Steve Gitterman, Leonard Sacks, Regina Alivisatos (t.con), Maureen Tierney (t.con); Carl Kraus, Norman Schmuff, Dorota Matecka, Stephen Hundley, Shuka Bala, Kalavati Suvarna, Gerlie De Los Reyes, Karen Higgins, LaRee Tracy, Ellen Molinaro, Christina Chi, Jeffrey Fritsch, Karen Storms.

ASSIGNED REVIEWERS:

Discipline	Reviewer
Medical: For trichomoniasis (NDA 21-618):	Regina Alivisatos, M.D.
For giardiasis & amebiasis (NDAs 21-681 & 21-682):	Maureen Tierney, M.D.
Safety assessment of NDAs 21-618, 21-681 & 21-682:	Carl Kraus, M.D.
Secondary Medical:	Leonard Sacks, M.D.
Statistical:	LaRee Tracy
Pharmacology:	Stephen Hundley, Ph.D.
Statistical Pharmacology:	N/A
Chemist:	Dorota Matecka, Ph.D.
Environmental Assessment (if needed):	Nancy Sager
Biopharmaceutical:	Gerlie De Los Reyes, Ph.D.
Microbiology, sterility:	N/A (the product is in tablet form)
Microbiology, clinical (for antimicrobial products only):	Kalavati Suvarna, Ph.D.
DSI:	Karen Storms
Regulatory Project Manager:	Christina Chi, Ph.D.
Other Consults: DMETS for Trade name:	Sammy Beam
DDMAC:	Shannon Benedetto

Per reviewers, are all parts in English or English translation? [YES] (Except a reference by Cervantes) NO

CLINICAL: Trichomoniasis FILE [YES] REFUSE TO FILE _____
(Two references, by Fantini and Otturi, are missing)

Giardiasis FILE [YES] REFUSE TO FILE _____

Amebiasis FILE [YES] REFUSE TO FILE _____

Safety (Data) Profile FILE [YES] REFUSE TO FILE _____

- Clinical site inspection needed: YES [NO]
- Advisory Committee Meeting needed? YES, date if known _____ [NO]

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A YES NO

(CLINICAL) MICROBIOLOGY: FILE __YES__ REFUSE TO FILE ____

STATISTICS: FILE __YES__ REFUSE TO FILE ____

BIOPHARMACEUTICS: FILE __YES__ REFUSE TO FILE ____

- Biopharm. inspection needed: YES NO

PHARMACOLOGY: FILE __YES__ REFUSE TO FILE ____

- GLP inspection needed: YES NO

CHEMISTRY: FILE __YES__ REFUSE TO FILE ____

- Establishment(s) ready for inspection? YES Inspection requested (in Poland) YES NO
- Microbiology YES NO

ELECTRONIC SUBMISSION: N/A Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:

The application is unsuitable for filing (explain & list; filing issues to be communicated by Day 74). N/A
The application, on its face, appears to be well organized and indexed. YES
The application appears to be suitable for filing. YES
No filing issues have been identified. YES

CONCLUSION: The application is filable.

ACTION ITEMS:

1. Request the English translation of the Spanish reference paper by Cervantes to be sent by September 14, 2003.

2. Request that the two missing references, a paper by Fantini and a paper by Otturi (and their respective English translation) to be sent by September 14, 2003.

3. Issue filing letter stating that no filing issues was identified to applicant within 74 days.

Concurrence:

(Christina H. Chi, Ph.D.)

Regulatory Project Manager, HFD-590

(Ellen Molinaro, R.Ph,)

Chief, Project Management Staff, HFD-590

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Office of Orphan Products Development *(HF-35)*
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

August 20, 2003

Presutti Laboratories, Inc.
1607 N. Douglas Avenue
Arlington Heights, IL 60004

Attention: John E. Presutti
President

Re: Designation Request # 03-1736

Dear Mr Presutti:

Reference is made to your request for orphan-drug designation dated June 19, 2003, of tinidazole for the treatment of amebiasis. Reference is also made to our acknowledgement letter dated July 28, 2003.

Pursuant to section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 360bb), your request for orphan-drug designation of tinidazole for the treatment of amebiasis is granted.

Please note that if the above product receives marketing approval for an indication broader than what is designated, it may not be entitled to exclusive marketing rights under section 527 (21 U.S.C. § 360cc). Therefore, prior to final marketing approval, we request that you compare the product's designated orphan indication with the proposed marketing indication, and submit additional information to amend the orphan-drug designation if warranted.

Please submit to the Office of Orphan Products Development a brief progress report of drug development within 14 months after this date and annually thereafter until marketing approval (*see* 21 C.F.R. § 316.30). Finally, please notify this Office within 30 days of a marketing application submission for the product's designated use.

If you need further assistance in the clinical development of your product, please feel free to contact John J. McCormick, MD, at (301) 827-3666. Please refer to this letter as official notification and congratulations on obtaining your orphan-drug designation.

Sincerely yours,

/S/

Marlene E. Haffner, MD, MPH
Rear Admiral, United States Public Health Service
Director, Office of Orphan Products Development

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and echnical Support (DMETS), HFD-420
. KLN Rm. 6-34

FROM: Christina H. Chi, Ph.D. Reg. Health Project Manager
Division of Special Pathogen and Immunologic Drug Products, HFD-590
Rm. N-303, 9201 Corporate Blvd., Rockville, MD, 20850

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 28, 2003	62,292	21-618	Proposed Trade Name	July 11, 2003

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
[redacted]	Standard	4021100 Antimicrobials	November 1, 2003

NAME OF FIRM: Presutti Laboratories

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE–NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*. Trade name review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ ND OF PHASE II MEETING ☐ NTROLLED STUDIES ☐ OTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:

The NDA is split into 3 NDAs (according to the indications) for administrative purposes: NDA 21-618 ([redacted] for trichomoniasis), NDA 21-681 ([redacted] for giardiasis), and NDA 21-682 ([redacted] for amebiasis).

6 jackets with the information of the name, draft package insert, container, carton labels, etc, is being sent to your office in a separate envelope through inter-office courier. Please call Christina Chi at 7-2166 if you have not receive it by august 5, 2003. Thanks.

PDUFA DATE:
ATTACHMENTS: Draft Package Insert, Container and Carton Labels
CC:
hival NDA 21-618 ([redacted] for trichomoniasis), NDA 21-681 ([redacted] for giardiasis), and NDA 21-682 ([redacted] for amebiasis).
-590Division File
D-591/CChi
HFD-590/Chem Reviewer/ D. Matecka and HFD-590/Team Leaders/LSacks

SIGNATURE OF REQUESTER Christina H. Chi, Ph.D. /S/	METHOD OF DELIVERY (Check one) ☐ MAIL ☒ HAND
SIGNATURE OF RECEIVER /S/	SIGNATURE OF DELIVERER /S/

8 page(s) of revised draft labeling has been redacted from this portion of the review.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910
Expiration Date: February 29, 2

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 t 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 rat can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Presutti Laboratories, Inc.
1607 N. Douglas Avenue
Arlington Heights, IL 60004

2. TELEPHONE NUMBER *(Include Area Code)*

(847) 359-7800

3. PRODUCT NAME

[redacted] 'tinidazole) tablets

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

N021618

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).

6. USER FEE I.D. NUMBER

Exemption Letter Follows

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 FOR THIS APPLICATION? ☑ YES ☐ NO

(See item 8, reverse side if answered YES)

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

Department of Health and Human Services
Food and Drug Administration
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
[signature]	President	07/16/2003

FORM FDA 3397 (1/03)

PSC Media Arts (301) 443-1090 EP

U-1

Presutti
Presutti Laboratories, Inc.
1207 N. Douglas Avenue
Arlington Heights, IL 60004

Tel: 847-359-7800
Fax: 847-359-7878
presind@aol.com

July 16, 2003

Renata Albrecht, MD
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation
Food and Drug Administration
9201 Corporate Boulevard, HFD-590
Rockville, MD 20850

Re: Submission of NDA 21-618: Tinidazole (IND # 62292)

Dear Dr. Albrecht,

Enclosed please find 5 copies plus the original of NDA 21-618. Desk copies for various reviewers have also been forwarded separately. This NDA requests approval of tinidazole 500mg and 250mg tablets for the treatment of trichomoniasis [redacted], giardiasis [redacted] and amebiasis (both intestinal and amebic liver abscess)

As you are aware, Presutti Laboratories is a very small, privately funded start-up pharmaceutical company. Tinidazole is our first NDA submission. We have been working closely with the Agency for the past 3 1/2 years to bring tinidazole to the U.S. market. As a small business filing its first NDA, we have requested and received a waiver from the NDA user application fee (section 736(d)(1)(D)). Tinidazole has been granted Orphan Drug Designation for the treatment of giardiasis. In addition, we have recently filed an application to have tinidazole designated as an Orphan Drug for the treatment of amebiasis. Presutti Laboratories was awarded a grant from the FDA's Office of Orphan Products Development to facilitate U.S. development of tinidazole.

This NDA is considered a 505(b)(2) submission since it relies extensively on published literature in the public domain to support the approval. Since tinidazole is a new molecular entity (NME) in the U.S., we are requesting 5 years of exclusivity per existing legislation.

For each of the desired indications, we believe that tinidazole offers significant medical benefits to U.S. patients. Metronidazole, in the case of trichomoniasis, is currently the only effective option available to U.S. physicians, and for other disease states, is the only practical therapeutic available to U.S. physicians. Tinidazole has been shown to be useful in cases of [redacted] trichomoniasis and giardiasis

7 page(s) of revised draft labeling has been redacted from this portion of the review.

A-70

20 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAR 19 2003

John E. Presutti
President
Presutti Laboratories, Inc.
1607 N. Douglas Avenue
Arlington Heights, IL 60004

RE: Presutti Laboratories, Inc., Small Business Waiver Request 2003.040 for Tinidazole, NDA 21-618

Dear Mr. Presutti:

This responds to your January 27, 2003, letter requesting a waiver of the human drug application fee for new drug application (NDA) 21-618 for tinidazole under the small business waiver provision, section 736(d)(1)(D)[1] of the Federal Food, Drug, and Cosmetic Act (the Act) (Waiver Request 2003.040). For the reasons described below, the Food and Drug Administration (FDA) grants the request from Presutti Laboratories, Inc. (Presutti), for a small business waiver of the application fee for NDA 21-618 for tinidazole.

According to your waiver request, Presutti is a small business with fewer than 500 employees, including employees of your affiliates. You note that NDA 21-618, tinidazole is for treatment of trichomoniasis, and giardiasis. This is your first application submitted to FDA for review. You also note that you do not have any affiliates.

Under section 736(d)(3)(B) of the Act,[2] a waiver of the application fee shall be granted to a small business for the first human drug application that a small business or its affiliate[3] submits to the FDA for review. The small business waiver provision entitles a small business to a waiver when the business meets the following criteria: (1) the business must employ fewer than 500 persons, including employees of its affiliates, and (2) the marketing application must be the first human drug application, within the meaning of the Act, that a company or its affiliate submits to FDA.

FDA's decision to grant Presutti's request for a small business waiver for NDA 21-618 for tinidazole is based on the following findings. First, the Small Business Administration (SBA) determined and stated in its letter dated March 3, 2003, that Presutti has fewer than 500 employees. SBA also determined that Presutti does not have any affiliates.

---

[1] 21 U S.C. 379h(d)(1)(D).
[2] 21 U.S.C. 379h(d)(3)(B).
[3] "The term 'affiliate' means a business entity that has a relationship with a second business entity if, directly or indirectly — (A) one business entity controls, or has the power to control, the other business entity; or (B) a third party controls, or has the power to control, both of the business entities" (21 U.S.C. 379g(9)).

Second, according to FDA records, the marketing application for tinidazole, NDA 21-618, is the first human drug application, within the meaning of the Act, to be submitted to FDA by Presutti or its affiliates. Consequently, your request for a small business waiver of the application fee for NDA 21-618 is granted, provided that FDA receives the marketing application for tinidazole no later than March 3, 2004, 1 year after the effective date of the size determination made by SBA. Please include a copy of this letter with your application.

If FDA refuses to file the application or Presutti withdraws the application before it is filed by FDA, a reevaluation of the waiver may be required should the company resubmit its marketing application. If this situation occurs, Presutti should contact this office approximately 90 days before it expects to resubmit its marketing application to determine whether it continues to qualify for a waiver.

We have notified the FDA Office of Financial Management (OFM) of this waiver decision and have asked them to waive the application fee for NDA 21-618.

FDA plans to disclose to the public information about its actions granting or denying waivers and reductions. This disclosure will be consistent with the laws and regulations governing the disclosure of confidential commercial or financial information.

If any billing questions arise concerning the marketing application or if you have any questions about this small business waiver, please contact Beverly Friedman, Michael Jones, or Tawni Schwemer at 301-594-2041.

Sincerely,

/S/

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research

U-3

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Office of Orphan Products Development *(HF-35)*
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

April 18, 2002

Presutti Laboratories, Inc.
1607 North Douglas Avenue
Arlington Heights, IL 60004

Attention: John E. Presutti
President

Re: Designation Request # 02-1554

Dear Mr Presutti:

Reference is made to your request for orphan-drug designation dated January 31, 2002, of tinidazole for the treatment of giardiasis Please also refer to our acknowledgment letter dated March 4, 2002.

We have completed the review of this request and have determined that tinidazole qualifies for orphan-drug designation for the treatment of giardiasis. Please note that it is tinidazole and not its formulation that has received orphan-drug designation

Please be advised that if tinidazole is approved for an indication broader than the orphan-drug designation, your product might not be entitled to exclusive marketing rights pursuant to Section 527 of the FFDCA (21 U.S C. 360cc). Therefore, prior to final marketing approval, we request that you compare the designated orphan indication with the proposed marketing indication, and to submit additional data to amend the orphan-drug designation prior to marketing approval if warranted.

Finally, please notify this Office within 30 days of submission of a marketing application for the use of tinidazole as designated Also an annual progress report must be submitted within 14 months after the designation date and annually thereafter until a marketing application is approved (21 CFR 316 30). If you need further assistance in the development of your product for marketing, please feel free to contact Henry Startzman, MD, at (301) 827-3666

Please refer to this letter as official notification and congratulations on obtaining your orphan-drug designation.

Sincerely yours,

/S/

Marlene E. Haffner, MD, MPH
Rear Admiral, United States Public Health Service
Director, Office of Orphan Products Development