# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER: 20-114/S006

## ADMINISTRATIVE DOCUMENTS

**PATENT CERTIFICATION**

The undersigned declares that Patent No. 5,164,194, which expires on November 1, 2010, covers the formulation, composition, and/or method of use of Astelin (azelastine HCl) Nasal Spray, 137 mcg. This product is currently approved under Section 505 of the Federal Food, Drug and Cosmetic Act (NDA 20-114).

George R. Hemsworth, Ph.D.
Director, Regulatory Affairs
Carter-Wallace, Inc.
Cranbury, New Jersey

APPEARS THIS WAY
ON ORIGINAL

# PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

| | | | |
|---|---|---|---|
| **NDA Number:** | 020114 | **Trade Name:** | ASTELIN NASAL SPRAY |
| **Supplement Number:** | 006 | **Generic Name:** | AZELASTINE HYDROCHLORIDE |
| **Supplement Type:** | SE5 | **Dosage Form:** | |
| **Regulatory Action:** | OP | **COMIS Indication:** | ALLERGIC RHINITIS |
| **Action Date:** | 11/15/99 | | |

**Indication # 1** Seasonal Allergic Rhinitis in children 5 years and older, and Vasomotor Rhinitis in children 12 years and older.
Label Adequacy: Adequate for SOME pediatric age groups
Forumulation Needed: NO NEW FORMULATION is needed
Comments (if any): Approval based on revised labeling.

| Lower Range | Upper Range | Status | Date |
|---|---|---|---|
| 5 years | Adult | Deferred | 9/14/02 |

This page was last edited on 9/15/00

/S/ 9.15.00

Signature - Date

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

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

# USER FEE COVER SHEET

*See Instructions on Reverse Side Before Completing This Form*

1. APPLICANT'S NAME AND ADDRESS

Wallace Laboratories,
Division of Carter-Wallace, Inc.
P.O. Box 1001/Half Acre Road
Cranbury, NJ 08512

Contact: George R. Hemsworth, Ph.D.
Director, Regulatory Affairs

2. TELEPHONE NUMBER *(Include Area Code)*

(609 ) 655-6357

3. PRODUCT NAME

Astelin® Nasal Spray, 137 mcg

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? — 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).

5. USER FEE I.D. NUMBER

3821

6. LICENSE NUMBER / NDA NUMBER

N020114

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 A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) 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)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☒ YES ☐ NO *(See reverse side if answered YES)*

***A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.***



| SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE | TITLE | DATE |
|---|---|---|
| [signature] | Director, Regulatory Affairs | November 10, 1999 |

# DEBARMENT CERTIFICATION

Carter-Wallace, Inc. for its Wallace Laboratories Division has made a diligent effort to ensure that no person barred under Section 306 (a) or 306 (b) of the Federal, Food, Drug and Cosmetic Act has provided or will provide any services in connection with this application. All employees of Carter-Wallace, Inc. connected with this application will be required to certify to Carter-Wallace, Inc. that he or she has not been debarred. All persons not employed by Carter-Wallace, Inc. who provide services in connection with this application will be required to certify to Carter-Wallace, Inc. in connection with this application that no person employed by them has been debarred under Section 306 (a) or 306 (b) of the Federal, Food, Drug and Cosmetic Act and that no debarred person will in the future be employed by them. Relying in part on these certifications, Carter-Wallace, Inc. certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 (a) or 306 (b) of the Federal, Food, Drug and Cosmetic Act in connection with this application.

CARTER-WALLACE, INC.

By: _____
George R. Hemsworth, Ph.D.
Director
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Date: November 10, 1999

certif

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

# CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

*TO BE COMPLETED BY APPLICANT*

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

*Please mark the applicable checkbox.*

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

| Clinical Investigators | | |
|---|---|---|
| | See Attached List | |
| | | |
| | | |

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

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

| NAME | TITLE |
|---|---|
| Jay R. Brennan | V.P. Finance & Business Development |
| FIRM/ORGANIZATION: Wallace Laboratories, Division of Carter-Wallace, Inc. | |
| SIGNATURE: J R Brennan | DATE: 11-4-99 |

**Paperwork Reduction Act Statement**

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

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

WITHHOLD 1 PAGE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Draft

Food and Drug Administration
Rockville MD 20857

William E. Berger, M.D.
26732 Crown Valley Parkway
Suite 361
Mission Viejo, CA 92691

MAY 30 2000

Dear Dr. Berger:

Between March 28 - 29, 2000, Mr. Randall N. Johnson, representing the Food and Drug Administration (FDA) inspected your conduct as the investigator of record of a clinical study (protocol #346) of the investigational drug Astelin® (azelastine hydrochloride) Nasal Spray that you conducted for Wallace Laboratories. This inspection is part of FDA's Bioresearch Monitoring Program. This program includes inspections to determine the validity of clinical drug studies that may provide the basis for drug marketing approval and to assure that the rights and welfare of the human subjects who participated in those studies have been protected.

From our evaluation of the inspection report prepared by Mr. Johnson and your oral responses to the inspectional observations, we conclude that you did not adhere to all pertinent Federal regulations and/or good clinical investigational practices governing the conduct of clinical investigations and the protection of human subjects. In particular, we note your lack of documentation for the final disposition of unused study drug at the close of the study.

Please ensure that corrective actions will be taken to prevent similar problems in your current and future studies.

We appreciate the cooperation shown Investigator Johnson during the inspection. Should you have any questions or concerns regarding this letter or the inspection, please contact me by letter at the address given below.

Sincerely,

/S/

for

David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Medical Policy (HFD-45)
Center for Drug Evaluation and Research
7520 Standish Place, Suite 103
Rockville, MD 20855

DEPARTMENT OF HEALTH & HUMAN SERVICES

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Food and Drug Administration
Rockville MD 20857

00 JUN 12 PM 1:57

JUN 9 2000

Jonathan Matz, M.D.
Atlantic Asthma & Allergy
7939 Honeygo Blvd, #219
Baltimore, Maryland 21236

Dear Dr. Matz:

Between March 20 and 28, 2000, Ms. Barbara A. Burke, representing the Food and Drug Administration (FDA) inspected your conduct as the investigator of record of a clinical study (protocol #375) of the investigational drug Astelin® (azelastine hydrochloride) Nasal Spray that you conducted for Wallace Laboratories. This inspection is part of FDA's Bioresearch Monitoring Program. This program includes inspections to determine the validity of clinical drug studies that may provide the basis for drug marketing approval and to assure that the rights and welfare of the human subjects who participated in those studies have been protected.

At the close of the inspection, Ms. Burke presented her inspectional observations (Form FDA 483) and discussed these observations with you. From our evaluation of the inspection report, your oral responses to the inspectional observations and your unsigned letter dated April 10, 2000, we conclude that you did not adhere to all pertinent federal regulations and/or good clinical investigational practices governing the conduct of clinical investigations and the protection of human subjects. In particular, we note that you failed to: (1) maintain adequate Drug Dispensing Records; (2) exclude one subject (#35) due to use of a prohibited medication; (3) adequately and accurately report the dates of adverse events for five subjects (#21, 24, 28, 313, and 322); and (4) document the concomitant medications for two subjects (#5 and 26).

Please ensure that corrective actions will be taken to prevent similar problems in your current and future studies.

We appreciate the cooperation shown Investigator Burke during the inspection. Should you have any questions or concerns regarding this letter or the inspection, please contact me by letter at the address given below.

Sincerely yours,

/S/

for

David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Medical Policy (HFD-45)
Center for Drug Evaluation and Research
7520 Standish Place, Suite 103
Rockville, MD 20855

## Division Director's Memorandum

| | |
|---|---|
| Date: | Thursday, September 14, 2000 |
| NDA: | 20-114, SE1-006 |
| Sponsor: | Carter-Wallace Laboratories |
| Proprietary Name: | Astelin (azelastine HCL) Nasal Spray |

Introduction: This is a supplemental NDA for Astelin Nasal Spray, an antihistamine nasal spray previously approved for the treatment of seasonal allergic rhinitis in adults and children down to age 5. This application is for the vasomotor rhinitis indication for Astelin down in patients ages 12 and above. Dr. Lee's primary medical review and Dr. Chowdhury's secondary review offer very fine discussions of the data and I concur with their findings.

CMC: No new issues, as there are no changes proposed to the marketed, approved product.

Pharmacology/toxicology: No new issues, given the indication and population sought.

Labeling: The labeling needed some modification from that proposed by the sponsor, particularly to achieve better clarity about the indication sought, the appropriate dose and the related safety information. The sponsor has submitted appropriate labeling except for some necessary restructuring of the Dosage and Administration section. They have agreed to changes proposed by Dr. Lee and this will be stated in the approval letter.

Conclusions: This supplement will be approved.

/S/

Robert J. Meyer, MD
Director,
Division of Pulmonary and Allergy Drug Products.

APPEARS THIS WAY
ON ORIGINAL

# CATEGORICAL EXCLUSION FROM PREPARATION OF AN ENVIRONMENTAL ASSESSMENT

Wallace Laboratories states that the Astelin (azelastine HCl) Nasal Spray, 137 mcg Vasomotor Rhinitis Supplement qualifies for a categorical exclusion from the preparation of an environmental assessment. The applicable categorical exclusion is cited as 21 CFR 25.31 (b). To the best of our knowledge there are no extraordinary circumstances that exist with regards to the Astelin Nasal Spray Vasomotor Rhinitis Supplement.



vmrexc