IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

WINSTON LABORATORIES, INC., a Delaware corporation,	)	
Plaintiff,	)	
v.	)	**Case Number: 09 CV**
KATHLEEN SEBELIUS, as Secretary and Senior Officer of United States Department of Health and Human Services; and MARGARET HAMBURG, M.D., as Commissioner and Senior Officer of United States Food and Drug Administration,	)	**Judge**
Defendants.	)	

EXHIBITS TO COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Exhibit A

WINSTON
Laboratories

May 21, 2008

100 Fairway Drive
Suite 134
Vernon Hills, Illinois 60061

P: 847.362.8200
F: 847.362.8394

www.winstonlabs.com

Beverly Friedman
Food and Drug Administration
10903 New Hampshire Ave, Building 51, Room 6222
Silver Spring, MD 20993-0002

RE: Request for Waiver of New Drug Application User Fee

On behalf of Winston Laboratories, Inc., I request a waiver of the new drug application fee for the following product proposed to be filed with the FDA on July 30, 2008:

Civanex (civamide (zucapsaicin)) Cream 0.075%

Enclosed are a formal request and a certification statement from Winston Laboratories, Inc. regarding the number of persons employed by the company.

I will be the main contact for this request for fee waiver. My contact information is:

Scott B. Phillips, M.D.
Senior Vice President, Scientific Affairs
Winston Laboratories, Inc.
100 North Fairway Drive, Suite 134
Vernon Hills, IL 60061

Phone: 847-362-8200
Fax: 847-362-8394
scott@winstonlabs.com

Please contact me if you have any questions or require any additional information.

Sincerely,

Scott B. Phillips, M.D.
Senior Vice President, Scientific Affairs
Winston Laboratories, Inc.

Request for Small Business Waiver of First Human Drug Application Fee

A. Name and address of the entity, including the company name, and the name and telephone number of the contact person for the fee waiver or reduction request.

Sponsor:

Scott B. Phillips, M.D.
Senior Vice President, Scientific Affairs
Winston Laboratories, Inc.
100 North Fairway Drive, Suite 134
Vernon Hills, IL 60061 USA

Phone: 847-362-8200
Fax: 847-362-8394
www.winstonlabs.com

B. Identification of the specific fee for which a waiver, refund, or reduction is requested.

Fee Type:	Application
Request:	Waiver
Basis for Waiver:	Small business
Product:	Civanex (civamide (zucapsaicin)) Cream 0.075%

C. The application or supplement number for which the waiver, refund, or reduction is requested, the date the application was submitted, and whether the application requires clinical data for approval.

Application Number:	To be determined
Date of Application:	Proposed: July 30, 2008
Date of Receipt by Agency:	Proposed: July 31, 2008
Clinical Data Required for Approval:	Yes

D. The statutory provision under which the waiver or reduction is requested.

The Agency will waive the application fee for the first human drug application that a small business or its affiliate submits for review under section 736 (d)(1)(D) of the FD&C Act.

E. Information and analyses demonstrating that the criteria for the waiver of fees are met:

Company name:

Winston Laboratories, Inc.
100 North Fairway Drive,
Suite 134
Vernon Hills, IL 60061 USA

Phone: 847-362-8200
Fax: 847-362-8394
www.winstonlabs.com

Number of Affiliates as defined as 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 of control, the other business entity; or (B) a third party controls, or has the power to control, both entities as defined in section 735(9) of the FD&C Act:	1
Number of Employees as of May 21, 2008:	11
Previous Human Drug Applications submitted for Review:	0

F. Date on which payment was or will be made to FDA of the fee for which a waiver or reduction is requested:

No payment will be made under this waiver. Without the waiver, payment is due July 31, 2008.

Small Business PDUFA User Fee Waiver Certification

I hereby certify that Winston Laboratories, Inc.:

- Employs a total of 11 individuals as of May 21, 2008,
- Does not have a prescription drug product introduced or delivered for introduction into interstate commerce, and does not expect to introduce a prescription product within the next twelve months and
- Expects to be prepared to submit an application to the agency within 90 days of this request

5/21/08

Date

Scott B. Phillips, M.D.
Senior Vice President, Scientific Affairs
Winston Laboratories, Inc.
100 North Fairway Drive, Suite 134
Vernon Hills, IL 60061

Phone: 847-362-8200
Fax: 847-362-8394
www.winstonlabs.com

FedEx Shipment Receipt

Address Information

Ship to:	**Ship from:**
Beverly Friedman	Kelly Wilson
Food and Drug Administration	Winston Laboratories
10903 NEW HAMPSHIRE BLDG 51	100 Fairway Drive
AVE.	Suite 134
SILVER SPRING, MD 20993-0002	Vernon Hills, IL 60061
US	US
8473628200	8473628200

Shipping Information

Tracking number: 790019548725
Ship date: 05/21/2008
Estimated shipping charges: 16.98

Package Information

Service type: Standard Overnight
Package type: FedEx Envelope
Number of packages: 1
Total weight: 0.5LBS
Declared value: 0.00USD
Special Services:
Pickup/Drop-off: Give to scheduled courier at my location

Billing Information

Bill transportation to: Sender
Your reference: Request
P.O. no.:
Invoice no.:
Department no.:

Thank you for shipping online with Fedex ShipManager at fedex.com.

Please Note

Exhibit B

U.S. SMALL BUSINESS ADMINISTRATION
Office of Government Contracting, Area IV
500 West Madison Street, Suite 1240
Chicago, IL 60661-2511

Determination 4-2008-55

(renumbered from Size Determination 4-2008-43)

Date:	August 13, 2008
Size Determination of:	Winston Laboratories, Inc.
Address:	100 Fairway Drive, Suite 134 Vernon Hills, IL 60061
Requested by:	Food and Drug Administration
Size Standard:	500 employees (maximum)

Introduction:
On June 26, 2008, the SBA's Office of Government Contracting in Chicago (hereafter, "Area IV") received a request from the Food and Drug Administration for an employee count of Winston Pharmaceuticals, Inc. (hereafter, "Winston") which has requested a waiver of the fee owed to the FDA for reviewing a new drug application. The size determination will be performed in accordance with 13 CFR Part 121.

Evidence:
On July 11, 2008, Winston submitted a completed Form 355 and other information as requested. The company subsequently responded to additional inquiries from Area IV by providing answers to specific questions as well as additional documents.

Is Winston affiliated with any other companies?:
Winston has three wholly owned subsidiaries: Winston Pharmaceuticals, Inc.; Winston Laboratories Limited; and Rodlen Laboratories, Inc. Based upon the terms of §121.103(c)(1), all are affiliates of Winston.

Winston is a privately owned corporation with two principal shareholders. Section 121.103(c)(1) provides that any person owning 50% or more of a concern's voting stock controls that concern. Joel Bernstein and his immediate family[1] own approximately 61% of Winston. Thus, the Bernsteins control Winston and their outside positions and interests must be examined to determine whether they control any other entities which might be affiliates of Winston.

Does the Bernstein family control any other entities?
Dr. Bernstein and his wife own a majority interest in Elorac, Inc. and in Gideon Pharmaceuticals, Inc. They thus control or have the power to control each entity and both are affiliated with Winston.

[1] Section 121.103(f) provides that immediate family members are presumed to share an identity of economic interest justifying the aggregating of their separate holdings.

Getting Ready Corp.

In November 2007, Winston executed a Merger Agreement and Plan of Reorganization with Getting Ready Corp. Winston provided a copy of the agreement to Area IV. Under §121.103(d)(1), "...SBA considers...agreements to merge (including agreements in principle) to have a present effect on the power to control a concern. SBA treats such...agreements as though the rights granted have been exercised." A review of Articles VII ("Conditions Precedent to the Closing") and VIII ("Termination") of the Merger Agreement discloses only ordinary and expected provisions, such as receipt of any required government approvals, stockholder approval, absence of adverse material changes, receipt of required lockup agreements, and so forth. None of the conditions precedent set forth are "incapable of fulfillment, speculative, conjectural, or unenforceable under state or Federal law"; nor does anything in the file suggests that the "probability of the transaction...occurring...[is] extremely remote." §121.103(d)(3). Therefore, the Merger Agreement must be given present effect and Getting Ready Corp. must be considered an affiliate of Winston.

Is Frost Gamma Investments Trust affiliated with Winston?

Frost Gamma Investments Trust (hereafter, "FGIT"), owns the only other large block of shares (28%) in Winston. Although the Bernstein family controls Winston by virtue of owning more than 60% of its stock, the question arises whether FGIT is nevertheless affiliated with Winston because of the merger with Getting Ready Corporation. FGIT is the largest single shareholder in Getting Ready Corp. before the merger (controlling approximately one-third of its outstanding shares,[2]).

The merger involves additional capitalization, a substantial portion of which will be provided by Philip Frost (and other individuals).[3] Frost (and the other investors) will receive preferred stock for their investment; that stock carries the right to be converted into common shares. When those shares are converted, Dr. Frost will own something less than 24% of the surviving entity.[4] The Bernstein family (including Bernstein's wife and children) will own approximately 46% of the surviving entity. Thus, although Bernstein and Frost will both own minority blocks, those holdings will not be "equal or approximately equal in size." As a result, the Bernstein family—and neither Dr. Frost nor FGIT—will control the surviving entity.

Ivax Corporation

The FDA identified one additional entity which it suggested might also be an affiliate of Winston: Ivax Corporation. That entity no longer exists; it was acquired by Teva Pharmaceu-

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[2] The next largest block of shares is under 10%. This information can be found in the Getting Ready Corporation, Schedule 14C, page 59. That document may be found at the Securities and Exchange website on the internet at http://www.sec.gov/Archives/edgar/data/1302554/000095014408005443/g14161prer14c.htm.

[3] Getting Ready Corporation, Schedule 14C, page 3, under "Additional Capitalization."

[4] See Merger Agreement, §4.6 and Press Release. http://www.secinfo.com/dsVsf.uAcf.c.htm#1stPage. The precise number is impossible to determine because not all of the monies involved in the additional capitalization have yet been contributed. The figure relied upon was supplied by David Starr, Chief Financial Officer of Winston, in an e-mail to Area IV on August 12, 2008.

tical Industries Ltd of Jerusalem, Israel, in January 2006. No affiliation is possible with a non-existent firm. The only ties SBA has been able to discover between Ivax Corporation and Winston relate to the merger between Winston and Getting Ready Corporation. Those ties are (i) Philip Frost was the former chairman and CEO of IVAX Corporation and (ii) two former officers of IVAX Corporation will be members of the Board of Directors of the surviving company. In both instances, the tie is too remote to comprise a basis for a finding of affiliation. The only ties involve former executives of a now-defunct firm. There is no present connection between the individuals and IVAX because IVAX does not exist.

Is Winston small?:

The rule for measuring employees is set forth in §121.106:

> "(a) In determining a concern's number of employees, SBA counts all individuals employed on a full-time, part-time, or other basis....
> (b) Where the size standard is number of employees, the method for determining a concern's size includes the following principles:
>> (1) The average number of employees of the concern is used (including the employees of its domestic and foreign affiliates) based upon numbers of employees for each of the pay periods for the preceding completed 12 calendar months.

Employee data for Winston Laboratories, Inc., as calculated in accordance with §121.106, indicates that the it has fewer than 500 employees, considered alone. Even after adding the number of employees for all of its affiliates (Winston Pharmaceuticals, Inc.; Winston Laboratories Limited; Rodlen Laboratories, Inc.; Elorac, Inc.; Gideon Pharmaceuticals, Inc.; and Getting Ready Corp.), the total number of Winston's employees does not exceed 500.

Conclusion:

Based on the evidence above, Winston Laboratories, Inc. is a small business concern.

Robert P. Murphy
Area Director
for Government Contracting

Exhibit C

U.S. SMALL BUSINESS ADMINISTRATION
Office of Government Contracting, Area IV
500 West Madison Street, Suite 1240
Chicago, IL 60661-2511

RECEI[illegible]

Via certified mail #7005 0390 0001 4822 4966

August 13, 2008

Winston Laboratories, Inc.
100 Fairway Drive, Suite 134
Vernon Hills, IL 60061
Attention: David Starr

Subject:	Size Determination Case No.:	4-2008-55 (formerly numbered -43)
	Requested by:	Food and Drug Administration
	Size Standard:	500 employees

Dear Mr. Starr,
The Small Business Administration has made a formal size determination that Winston Laboratories, Inc. has fewer than 500 employees. A copy of the determination is enclosed.

Any person adversely affected by this decision may appeal to SBA's Office of Hearings and Appeals (OHA).

An appeal petition must be filed with OHA at the following address:

Office of Hearings and Appeals
U.S. Small Business Administration
409 Third Street, S.W.
Washington, DC 20416

An appeal petition must include the following information:

- the Area Office which issued the size determination;
- the solicitation or contract number, if applicable;
- name, address, telephone, and facsimile number of the contracting officer, if applicable;
- the date of receipt of the size determination;
- a full and specific statement as to why the size determination is alleged to be in error, together with argument supporting such allegations; and
- the name, address, telephone, facsimile number and signature of the petitioner or its attorney.

The OHA regulations (13 CFR Part 134) may be found at on the internet at the SBA website http://www.sba.gov/services/contractingopportunities/sizestandardstopics/part121sects/index.html . Please read them carefully for very specific filing instructions.

If additional information or assistance is needed, please contact David Gordon by phone at (312) 353-7674, by fax at (202) 481-1842, or by e-mail at david.gordon@sba.gov.

Sincerely,

Robert P. Murphy
Area Director
for Government Contracting

Enclosures

cc: Beverly Friedman, Food and Drug Administration

Exhibit D

Department of Health and Human Services Public Health Service
Food and Drug Administration
Rockville, MD 20857

DEC 1 2008

Scott B. Phillips, MD
Senior Vice President, Scientific Affairs
Winston Laboratories, Inc.
100 North Fairway Drive, Suite 134
Vernon Hills, IL 60061

RE: Winston Laboratories, Inc., Small Business Waiver Request 2008.062 for a New Drug Application, NDA 22-403 for Civanex (civamide (zucapsaicin)) Cream 0.075%

Dear Dr. Phillips;

This responds to your May 21, 2008, letter requesting a waiver of an application user fee under the small business waiver provision, section 736(d)(1)(D)[1] of the Federal Food, Drug, and Cosmetic Act (the Act) (Waiver Request 2008.062). You request a waiver of the fiscal year (FY) 2008[2] human drug application fee for new drug application (NDA) 22-403 for Civanex (civamide (zucapsaicin)) cream 0.075%. For the reasons described below, the Food and Drug Administration (FDA) denies the Winston Laboratories, Inc. (Winston) request for a small business waiver of the application fee for NDA 22-403 for Civanex (civamide (zucapsaicin)) Cream 0.075%.

I. Winston's Waiver Request

According to your waiver request, Winston employs a total of 11 individuals. You certify that Winston does not have a prescription drug product introduced or delivered for introduction into interstate commerce, and does not expect to introduce a prescription product within the next twelve months. You also anticipated filing a market application for Civanex (civamide (zucapsaicin)) Cream 0.075% within 90 days of your small business waiver request. In your September 8, 2008, response to an inquiry from Beverly Friedman of my staff, you state that there is no relationship between Northbrook Testing Company, Inc., and Winston.

II. Criteria for Small Business Waivers

Under section 736(d)(4) of the Act,[3] a waiver of the application fee is granted to a small business for the first human drug application that it or its affiliate[4] 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:

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[1] 21 U.S.C. 379h(d)(1)(D).
[2] FY 2008 = October 1, 2007, through September 30, 2008.
[3] 21 U.S.C. 379h(d)(4).
[4] "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(11)).

(1) The business must employ fewer than 500 persons, including employees of its affiliates.
(2) The business does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce.
(3) 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.

III. Evaluation of Winston's Request

The Small Business Administration (SBA) determined and stated in its letter dated August 13, 2008, that Winston is a small business with the following affiliates: Winston Pharmaceuticals, Inc.; Winston Laboratories, Limited; Rodlen Laboratories, Inc.; Elorac, Inc.; Gideon Pharmaceuticals, Inc.; Getting Ready Corp; and Joel Bernstein, M.D., and his immediate family. SBA also confirmed that Winston and its affiliates have fewer than 500 employees.

Based on the SBA determination that Winston and affiliates have fewer than 500 employees, Winston meets the first criterion for a small business waiver.

The SBA does not consider those firms that are no longer in existence in determining affiliates. However, for purposes of determining whether to grant a small business waiver, FDA considers all affiliates, even those that are no longer in existence. According to FDA records, the marketing application for NDA 22-403, Civanex Cream 0.075%, is not the first human drug application, within the meaning of the Act, to be submitted to FDA by Winston or its affiliates.

It is recorded in the public record that Dr. Bernstein founded both GenDerm Corporation (GenDerm) and Winston. According to letters submitted to FDA by GenDerm, Dr. Bernstein was the Chairman of Genderm. Because of Dr. Bernstein's relationship with GenDerm, FDA considers GenDerm to be an affiliate of Winston. According to FDA records, GenDerm previously submitted a human drug application, NDA 20-318, Carbamide Peroxide Solution, for review and approval.

In addition, Winston's NDA 19-060, Papulex (nicotinamide), was originally submitted to FDA by Northbrook Testing Co., Inc. (Northbrook). Dr. Bernstein signed the application cover letter and 356H form as the President of Northbrook. Ownership of the application was subsequently transferred to GenDerm and then to Winston. According to the State of Illinois Controller's Office, Dr. Bernstein was the president of Northbrook.[5]

Because Winston and its affiliates have previously submitted NDAs for review by FDA, the application for NDA 22-403, Civanex Cream 0.075%, is not the first human drug application submitted by Winston or its affiliates to the FDA. Consequently, Winston does not meet the third criterion for a small business waiver, and your request for a small business waiver of the application fee is denied. Because Winston does not meet the third criterion for a small business

[5] Northbrook was later renamed Jaye-Boern Laboratories, Inc. (Jaye-Boern). In the public record, Dr. Bernstein is the founder of Jaye-Boern.

waiver, FDA has not determined whether Winston or its affiliates have a human drug product introduced or delivered for introduction into interstate commerce.

IV. Reconsideration

You may request reconsideration of this denial of your waiver request. Any request for reconsideration should be made within 15 days of receipt of this letter and should state Winston's reasons for believing that this decision was in error. You should also address the relationships (1) between GenDerm, Northbrook, Jaye-Boern, and Dr. Bernstein and Winston and (2) between Bioglan Pharma and Winston. Additional information to support your position should be included. A request for reconsideration should be sent to this office, at the following address:

Associate Director for Policy
Attention: User Fee Waiver Office (Michael Jones)
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Building 51, Room 6216
Silver Spring, MD 20993-0002

Fax: 301-847-8711

V. Disclosure of Public Information

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

If you have any questions about this matter, please contact Beverly Friedman or Michael Jones at 301-796-3602.

Sincerely,

Jane A. Axelrad

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

Exhibit E

WIN O
Laboratories

100 Fairway Drive, Suite 134
Vernon Hills, Illinois 60061
Tel: 847-362-8200
Fax: 847-362-8394

December 9, 2008

Associate Director for Policy
Attention: User Fee Waiver Office (Michael Jones)
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Building 51, Room 6216
Silver Spring, MD 20993-0002

RE: Winston Laboratories, Inc., Small Business Waiver Request 2008.062 for a New Drug Application, NDA 22-403 for Civanex (civamide (zucapsaicin) Cream 0.075%

To Whom It May Concern:

Winston Laboratories, Inc., ("Winston") received a letter from FDA dated December 1, 2008 in response to our May 21, 2008 letter requesting a waiver of an application user fee for NDA 22-403 for Civanex Cream under the small business waiver provision of the Federal Food, Drug and Cosmetic Act. In a letter dated August 13, 2008 from the Small Business Administration ("SBA"), which was provided to FDA in August, the SBA determined and stated that Winston is a small business. You then proceeded to deny Winston the requested waiver on the basis that Northbrook Testing Company, Inc. ("Northbrook") and GenDerm Corporation ("GenDerm") were Winston Affiliates. In your letter you define affiliate as follows:

> "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(11))."

Winston has consulted the following five (5) attorneys with respect to your interpretation of whether Winston could be considered an affiliate of these other entities:

Peter Barton Hutt, Esquire, Covington & Burling
Michael J. Feldman, Esquire, Seyfarth Shaw LLP
William McErlean, Esquire, Barnes & Thornburg LLP
Robert A. Yolles, Esquire, Retired, Co-Chair of Jones Day's Corporate Practice
Charles M. Modlin, Esquire, Seyfarth Shaw LLP

Associate Director for Policy
December 9, 2008

All of the above parties expressed the unequivocal opinion that Winston is not an affiliate of Northbrook or GenDerm.

Northbrook was dissolved in 1984, 14 years before Winston was originally incorporated. Incidentally, Northbrook was dissolved 9 years before user fees were initiated by FDA under PDUFA. GenDerm submitted an NDA in November 1992 which received a refuse to file from FDA in December 1992. This again was before user fees for NDAs were imposed under PDUFA. GenDerm was sold to Medicis on December 3, 1997 and no shareholder of Winston, including myself, has owned a single share of GenDerm since its December 1997 sale. Furthermore, I was not a controlling shareholder in GenDerm. I owned 27% of GenDerm while the venture capitalists who controlled the Board of Directors owned over 50%. As to Bioglan Pharma, Bioglan Pharma purchased an equity stake of less than 20% of Winston in December 1999, which Winston repurchased in 2007.

All of the lawyers cited above said that under any definition of affiliate they have ever seen, including the definition of affiliate referenced in your letter (21U.S.C. 379g(11)), Winston cannot be considered an affiliate of Northbrook or GenDerm.

Winston herein requests reconsideration of this decision, and trusts that Winston will promptly receive its waiver so that it can proceed to file its NDA.

Thank you for your prompt attention this matter.

Sincerely,

Joel E. Bernstein, M.D.
Chief Executive Officer

JEB:ceg

cc: Peter Barton Hutt, Esquire
Robert A. Yolles, Esquire
Michael Feldman, Esquire
Scott B. Phillips, M.D.
David A. Henninger
Jane A. Axelrad (via fax: 301-847-8440)

Exhibit F

Department of Health and Human Services Public Health Service
Food and Drug Administration
Rockville, MD 20857

FEB 2 2009

Joel E. Bernstein, MD
Chief Executive Officer
Winston Laboratories, Inc.
100 North Fairway Drive, Suite 134
Vernon Hills, IL 60061

RE: Winston Laboratories, Inc., Small Business Waiver Reconsideration Request 2009.030 for a New Drug Application, NDA 22-403 for Civanex (civamide (zucapsaicin)) Cream 0.075%

Dear Dr. Bernstein;

This responds to your December 9, 2008, letter requesting reconsideration of the Food and Drug Administration's (FDA's) December 1, 2008, decision to deny Winston Laboratories, Inc.'s (Winston's) request for a small business waiver for a new drug application (NDA) 22-403 for Civanex (civamide (zucapsaicin)) cream 0.075% (Waiver Request 2009.030). Winston's waiver request was submitted under the small business waiver provision, section 736(d)(1)(D)[1] of the Federal Food, Drug, and Cosmetic Act (the Act).[2]

For the reasons described below, the Food and Drug Administration (FDA) denies the Winston Laboratories, Inc. (Winston) reconsideration request for a small business waiver of the application fee for NDA 22-403 for Civanex (civamide (zucapsaicin)) Cream 0.075%.

I. Winston's Waiver Reconsideration Request

According to your waiver reconsideration request, Winston consulted five attorneys whether Winston could be considered an affiliate of Northbrook Testing Company, Inc. (Northbrook) and GenDerm Corporation (GenDerm). You claim that they said Winston cannot be considered an

[1] 21 U.S.C. 379h(d)(1)(D).
[2] Application fees were implemented under the Prescription Drug User Fee Act of 1992 (PDUFA) signed in November 1992, however the fees were assessed retroactive to September 1, 1992. The small business waiver provision of the Act was enacted with the Food and Drug Administration Modernization Act of 1997 and further amended with the Prescription Drug User Fee Amendments of 2002 and 2007.

affiliate of Northbrook or GenDerm under 21 U.S.C 379g(11)[3] or any other definition of affiliate they have ever seen.

You state that Northbrook was dissolved in 1984, 14 years before Winston was originally incorporated and 9 years before user fees were initiated by FDA under the Prescription Drug User Fee Act (PDUFA). You also state that GenDerm submitted an NDA in November 1992 that FDA refused to file in December 1992, also before user fees for NDAs were imposed under PDUFA. You also note that GenDerm was sold to Medicis on December 3, 1997, and no shareholder of Winston, including yourself, has owned a single share of GenDerm since the sale. You also state that you were not a controlling shareholder in GenDerm, owning only 27% of GenDerm while the venture capitalists who controlled the Board of Directors owned over 50%.

In response to the FDA request for additional information about the relationship between Winston and Bioglan Pharma (Bioglan), you stated that Bioglan purchased an equity stake of less than 20% of Winston in December 1999 which Winston repurchased in 2007.

II. Criteria for Small Business Waivers

Under section 736(d)(4) of the Act,[4] a waiver of the application fee is granted to a small business for the first human drug application that it or its affiliate 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.
(2) The business does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce.
(3) 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.

III. Evaluation of Winston's Reconsideration Request

As noted in the December 1, 2008, waiver decision letter, Winston meets the first criterion for a small business waiver, based on the SBA determination that Winston and affiliates have fewer than 500 employees.

FDA has also determined that Winston and its affiliates do not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce. This meets the second criterion for a small business waiver.

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[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(11)).
[4] 21 U.S.C. 379h(d)(4).

However, Winston does not meet the third criterion for a small business waiver. NDA 22-403 for Civanex is not the first human drug application, within the meaning of the Act, that Winston or its affiliates have submitted to FDA.

The Small Business Administration (SBA) determined and stated in its letter dated August 13, 2008, that Winston is a small business with the following affiliates: Winston Pharmaceuticals, Inc.; Winston Laboratories, Limited; Rodlen Laboratories, Inc.; Elorac, Inc.; Gideon Pharmaceuticals, Inc.; Getting Ready Corp; and Joel Bernstein, M.D., and his immediate family.

Although you noted that Northbrook was dissolved in 1984, 14 years before Winston was originally incorporated and was dissolved 9 years before user fees were initiated under PDUFA, you did not dispute nor did you provide evidence to the contrary that Dr. Joel Bernstein was an affiliate of Northbrook. There is no requirement in the definition of affiliate that all relevant parties be in existence at the same time.

As noted in our previous letter, NDA 19-690, Papulex (nicotinamide), was originally submitted to FDA by Northbrook and Dr. Bernstein signed the application cover letter and 356H form as President of Northbrook. In addition, according to the State of Illinois Controller's Officer, Dr. Bernstein was the president of Northbrook.[5] Nothing in your letter refutes the fact that Dr. Bernstein is an affiliate of Winston and that Dr. Bernstein submitted a human drug application. In addition, because Dr. Bernstein controlled both Winston and Northbrook, under the definition of affiliate in PDUFA,[6] Northbrook is an affiliate of Winston. Because Winston or its affiliate has submitted a human drug application, Winston does not meet the third criterion for a small business waiver. The fact that Northbrook was dissolved in 1984 does not negate the fact that an affiliate of Winston submitted an NDA to FDA. FDA, therefore, confirms its previous decision and your small business waiver request is denied.

In addition, you noted that GenDerm submitted an NDA in November 1992 which received a refuse to file action from FDA in December 1992. You further stated that this was before user fees for NDAs were imposed under PDUFA. You also note that GenDerm was sold to Medicis on December 3, 1997. You also state that no shareholder of Winston, including yourself, has owned a single share of GenDerm since its December 1997 sale. You also state that you were not a controlling shareholder in GenDerm and that you owned 27% of GenDerm while the venture capitalists who controlled the Board of Directors owned over 50%.

As noted in our previous letter, it is recorded in the public record that Dr. Joel Bernstein founded both GenDerm Corporation and Winston. According to letters submitted to FDA by GenDerm, Dr. Bernstein was the Chairman of GenDerm. In addition, it is a matter of public record that Dr.

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[5] Northbrook was later renamed Jaye-Boern Laboratories, Inc. (Jaye-Boern). In the public record, Dr. Bernstein is the founder of Jaye-Boern.

[6] "The term 'affiliate' means a business entity that has a relationship with a second business entity if, directly or indirectly . . . a third party [in this case, Dr. Bernstein] controls, or has the power to control, both of the business entities" (21 U.S.C. 379g(11)).

Joel Bernstein was the founder, Chairman and Chief Executive Officer of the privately held company, GenDerm. Although you note that venture capitalists controlled the Board of Directors, you provided no evidence that at the time of submission of NDA 20-318, Carbamide Peroxide Solution, Dr. Joel Bernstein did not control, or did not have the power to control, GenDerm.[7] Because Dr. Joel Bernstein had the power to control both Winston and GenDerm, GenDerm is considered an affiliate of Winston for purposes of the Act. GenDerm submitted a human drug application (i.e., NDA 20-318, Carbamide Peroxide Solution), and thus Winston does not meet the third criterion for a small business waiver. The fact that Dr. Bernstein ceased to be involved in GenDerm upon its sale in 1997 does not negate the fact that when controlled by Dr. Bernstein, GenDerm submitted an NDA to FDA. Nor is there any language in the Act to indicate that the third criterion for a small business waiver turns on whether the marketing application was filed after the enactment of PDUFA. FDA, therefore, confirms its previous decision and your small business wavier request is denied.

We thank you for providing the information on Winston's relationship with Bioglan Pharma. We have reviewed the information and have no further questions or comments at this time.

IV. Appeal of FDA's Waiver Reconsideration Decision

Winston may appeal this denial of its small business waiver reconsideration request for the application fee. Any appeal should be made within 15 days of receipt of this letter. The appeal should contain a copy of the initial resolution, a copy of this reconsideration decision, and a statement of the reasons you believe the decisions are in error. The appeal should contain specific references to information or analyses already submitted to FDA that support your position. No new information should be submitted in an appeal. The appeal should be sent to the following address.

Deputy Commissioner for International and Special Programs
User Fee Appeals Officer, HF-3
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

FAX: 301-443-3100

If you appeal the decision, please send a copy of your submission to me as well (FAX: 301-847-8711).

[7] We note that even if we agreed with your argument that Dr. Bernstein did not control GenDerm, you make no such argument about Northbrook.

V. Disclosure of Public Information

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

If you have any questions about this matter, please contact Beverly Friedman or Michael Jones at 301-796-3602.

Sincerely,

Jane A. Axelrad

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

Exhibit G

Colleen Giovenco

From: Conlon, Marianne [mconlon@cov.com] on behalf of Hutt, Peter [phutt@cov.com]
Sent: Wednesday, April 08, 2009 3:32 PM
To: Murray.lumpkin@fda.hhs.gov
Cc: Senger, Jeffrey
Subject: User Fee Appeal
Attachments: David Gordon email.pdf; SBA.pdf

Dr. Lumpkin:

As the attached emails relate, on March 31 we submitted an appeal of a CDER decision denying a user fee waiver for Winston Laboratories to Acting FDA Chief Counsel Senger. In an email dated April 6 Mr. Senger informed us that the appeal must be directed to your Office. We are therefore forwarding all of the relevant documents to our attention.

We request an immediate decision on this matter. It has been pending for almost a year. If we do not hear within 30 days we will regard the CDER decision as final agency action for purposes of judicial review under the Administrative Procedure Act.

Sincerely yours,

Peter Barton Hutt

Covington & Burling LLP
1201 Pennsylvania Avenue, N.W.
Washington, DC 20004
(202) 662-5522 - Phone
(202) 778-5522 - Fax
phutt@cov.com - Email
www.cov.com - Web

From: Senger, Jeffrey [mailto:Jeffrey.Senger@fda.hhs.gov]
Sent: Monday, April 06, 2009 6:06 PM
To: Hutt, Peter
Subject: RE: Legal Review of CDER Legal Decisiion Under the Prescription Drug User Fee Act

Mr. Hutt:

I have received your email of March 31 requesting that I intervene in FDA's review process for your client Winston Laboratories' small business waiver request. As explained in FDA's February 2 letter to Winston, the agency has a procedure for private parties to seek appeal of a decision with which they disagree. The decision Winston wishes to appeal was made by the Center for Drug Evaluation and Research. In order to appeal that decision, Winston should submit a copy of the initial resolution, a copy of the reconsideration decision, and a statement of the reasons it believes the decision was in error. The appeal should contain specific references to information or analyses already submitted to FDA that support your client's position, and it should not contain any new information. The appeal should be sent to the following address:

Deputy Commissioner for International and Special Programs
User Fee Appeals Officer, HF-3
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Sincerely yours,
Jeffrey Senger
Acting Chief Counsel
Food & Drug Administration

From: Vida, Beth [mailto:bvida@cov.com] **On Behalf Of** Hutt, Peter
Sent: Tuesday, March 31, 2009 2:27 PM
To: Senger, Jeffrey
Cc: Hutt, Peter
Subject: Legal Review of CDER Legal Decisiion Under the Prescription Drug User Fee Act

Mr. Senger:

We are writing to obtain your legal review of a legal decision made by the Center for Drug Evaluation and Research (CDER) under the Prescription Drug User Fee Act. CDER has denied Winston Laboratories a small business waiver from a user fee for a new drug application (NDA) on the ground that two companies no longer in busines are "affiliates" of Winston.

This matter has been pending for almost a year. The matter is very simple. Because it is solely a legal issue and you are the highest ranking FDA legal official, we are requesting a response within 30 days. If there is no response within 30 days, or the response is negative, we will regard this as final agency action for purposes of judicial review under the Administrative Procedure Act.

Winston Laboratories is a small pharmaceutical company that has been ready to file an NDA for approximately the past eight months. On May 21, 2008, Winston requested a waiver of an application user fee for NDA 22-403 and on August 13, 2008, Winston received a formal determination by the Small Business Administration (SBA) that it qualifies as a small business because Winston (including all affiliates) has fewer than 500 employees (copy attached). The actual number of employees is fewer than 20. The SBA letter was provided to FDA in August 2008.

Winston heard nothing further from FDA until the CDER User Fee Waiver Office informed the Company on December 1, 2008, that the requested waiver was denied on the grounds that Northbrook Testing Company and GenDerm Corporation are affiliates (copy attached). Winston replied on December 9, 2008, stating that Northbrook was dissolved in 1984 and GenDerm was sold in 1997 and thus could not be regarded as affiliates (copy attached). FDA responded on February 2, 2009 with a denial letter that was essentially a repetition of its December 1, 2008 letter (copy attached). Every legal source consulted by the Company, including the SBA (*see* David Gordon's attached email), agrees that under the definition of affiliate in 21 U.S.C. 379g(11) neither Northbrook nor GenDerm could be regarded as an affiliate of Winston.

Although Winston's fee waiver request was based solely on the criterion "the applicant involved is a small business submitting its first human drug application to the Secretary for review" (21 U.S.C. 379h(d)(1)(D)), which appeared straightforward and unimpeachable, Winston also qualifies for the waiver under the statutory criterion in 21 U.S.C. 379h(d)(1)(B) which states that "the assessment of the fee would present a significant barrier to innovation because of limited resources available to such person or other circumstances." Winston currently has a total of approximately $2.5M in cash and investments, a burn rate of $400,000 per month, and no income. Consequently, Winston cannot afford to pay a user fee of over $1 million and remain in business.

This is a very serious matter for a small company like Winston. The Company does not have sufficient assets to allow it to pay the large user fee and then hope to get it refunded later.

The NDA -- which was ready for filing in August 2008 -- has been held up for eight months because of FDA inaction on an extremely simple administrative matter. FDA's failure to accept the SBA determination could put Winston out of business if not reversed immediately.

We are requesting that you inquire into this matter and resolve it within 30 days.

Sincerely yours,
Peter Barton Hutt

Exhibit H

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

June 18, 2009

Pefer Barton Hutt, Esq.
Covington & Burling LLP
1201 Pennsylvania Avenue, N.W.
Washington, DC 20004

Janet Woodcock, M.D.
Jane Axelrad, Esq.
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
White Oak Office Building 51(WO51)
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Appeal of Denial of Winston Laboratories, Inc.'s User Fee Waiver Request (Waiver Request 2008.062; Request for Reconsideration 2009.030)

Dear Mr. Hutt, Dr. Woodcock, and Ms. Axelrad:

On April 8, 2009, on behalf of Winston Laboratories, Inc. ("Winston"), Mr. Hutt submitted an appeal to me via email in my capacity as the U.S. Food and Drug Administration's ("FDA's" or "Agency's") deciding official ("User Fee Appeals Officer") in matters involving user fee appeals to the Office of the Commissioner. This appeal involved a dispute over a request for a waiver of the application fee for a new drug application (NDA) for Civanex (civamide (zucapsaicin)) cream ("Civamide NDA").

After carefully considering the April 8 e-mail, its attachments, all prior correspondence, and other relevant documents, I have concluded that, although Winston employs fewer than 500 persons and does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce, the Civamide NDA would not be the first human drug application that Winston or its affiliate submits to the Secretary for review. Accordingly, I find that Winston does not meet the statutory criteria for a small business fee waiver and I am denying Winston's appeal of CDER's denial of its request on that ground for a waiver of the application fee associated with the submission of the Civamide NDA.

I. Background

A. Prescription Drug User Fees and the Waiver Process

The Prescription Drug User Fee Act of 1992, as amended by the Food and Drug Administration Modernization Act of 1997 and further amended with the Prescription Drug User Fee

Amendments of 2002 and 2007 ("PDUFA"), requires FDA to assess user fees for certain applications, products, and establishments. 21 U.S.C. § 376h(a). PDUFA authorizes FDA to grant waivers and reductions (hereafter referred to just as "waivers") from these fees under limited circumstances. 21 U.S.C. §379h(d).

An entity who believes it qualifies for a small business waiver is encouraged to submit a request for a waiver approximately 90 days before the application is to be submitted. *See* FDA, *Attachment G – Draft Interim Guidance Document for Waivers and Reductions in User Fees*, at 23-26 (July 16, 1993) ("1993 FDA Draft Guidance"). A company seeking a waiver after the filing of an application must submit a written request to the "Waiver Officer" within 180 days after the fee is due. 21 U.S.C. § 379h(h)(i).

FDA will grant or deny the waiver request based on the submitted materials and will notify the requester, in writing, of its decision. An entity may request reconsideration of a denial by submitting a letter to FDA, explaining its reasons for believing that the waiver denial was in error, and submitting any additional information necessary to support that position. *See* 1993 FDA Draft Guidance, at 26. FDA will then review all the relevant information and either grant or deny the entity's waiver reconsideration request. *Id.*

An entity may appeal a denial of its waiver reconsideration request to the Agency's "User Fee Appeals Officer" by submitting a letter that should explain the reasons for the appeal, should contain references only to materials already submitted, and should not contain any new information. FDA's decision on an appeal submitted to the "User Fee Appeals Officer" will constitute final agency action on that waiver request. *See id.* at 26-27.

B. Winston's Request for a Waiver of Certain User Fee

In accordance with the *1993 FDA Draft Guidance*, in advance of submitting the Civamide NDA, on May 21, 2008, Winston submitted a request for a waiver of the application fee that would be due upon the NDA's submission. Letter from S. Phillips to B. Friedman (May 21, 2008) ("Waiver Request"). In the Waiver Request, Winston asserted that it was entitled to a waiver of the application fee associated with the Civamide NDA, under 21 U.S.C. § 379h(d)(1)(D). Winston stated in support of its request that it had one affiliate, had eleven employees (as of May 21, 2008), and had not submitted any previous human drug applications for review. Waiver Request, at 2.

If Winston is not granted the requested application fee waiver, under the authority of PDUFA, as amended, an application fee of $1,247,200 will be due upon submission of the Civamide NDA.[1] *See* 21 U.S.C. § 379h(a)(1)(B).

[1] This assumes that the Civamide NDA is submitted during Fiscal Year ("FY") 2009, that is, by September 30, 2009. *See* 73 Fed. Reg. 45017 (Aug. 1, 2008). If the Civamide NDA is submitted after that date, the application fee for FY 2010, which has not yet been established, would apply.

C. CDER's Initial Denial of Winston's Waiver Request

CDER denied Winston's request for a waiver of the application due at the submission of the Civamide NDA by letter dated December 1, 2008. Letter from J. Axelrad to S. Phillips (December 1, 2008), at 1 ("December 2008 Denial"). CDER considered whether Winston met the standard for granting a waiver of the application user fee associated with the submission of the Civamide NDA under the small business waiver provision, 21 U.S.C. § 739h(d)(1)(D).

The small business waiver provision of PDUFA provides for a waiver of the application fee for the first human drug application submitted by a small business or its affiliate to FDA for review. A waiver is granted under this provision if the following criteria are met:

(1) The business employs fewer than 500 persons, including employees of its affiliates. [21 U.S.C. § 379h(d)(4)(A)]
(2) The business does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce. [21 U.S.C. § 379h(d)(4)(A)]
(3) 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. [21 U.S.C. § 379h(d)(4)(B).]

Based on a determination by the Small Business Administration (SBA) that Winston and its affiliates employ fewer than 500 employees, *see* SBA Size Determination No. 4-2008-55 (August 13, 2008) ("SBA Size Determination"), CDER concluded that Winston met the first criterion for granting a small business waiver. December 2008 Denial, at 2. However, CDER concluded that Winston did not meet the third criteria under the small business waiver provision because the Civamide NDA will not be the first human drug application to be submitted by Winston or its affiliates. *Id.* CDER's conclusion was based on information contained in the public record and in submissions to FDA concerning the relationship between GenDerm Corporation ("GenDerm") and Northbrook Testing Co., Inc. ("Northbrook"), and Dr. Joel Bernstein, Chief Executive Officer and founder of Winston.[2] *Id.* Because CDER concluded that Winston did not meet the third criterion for a small business waiver, CDER did not consider the second criterion, whether Winston or its affiliates have a human drug product introduced or delivered for introduction into interstate commerce. *Id.* at 3.

In support of its conclusion that a human drug application had been previously submitted by Winston or its affiliates, CDER relied upon information contained in the public record and in submissions to FDA about the relationship between Dr. Bernstein and GenDerm. *Id.* at 2. Because Dr. Bernstein was the founder and Chairman of GenDerm, CDER considered GenDerm to be an affiliate of Winston. GenDerm had previously submitted NDA 20-318, Carbamide Peroxide Solution, for FDA's review and approval, and, therefore, CDER concluded that the Civamide NDA would not be the first human drug application submitted by Winston or its affiliates. *Id.*

[2] The SBA concluded that Dr. Joel Bernstein controls Winston by virtue of the ownership of 61% of Winston's stock by Dr. Bernstein and his immediate family. SBA Size Determination. This conclusion was adopted by CDER and was not disputed by Winston. December 2008 Denial, at 2; Reconsideration Denial, at 3.

In addition, CDER also cited evidence in the public record and in submissions to the Agency that Dr. Bernstein was the president of Northbrook. *Id.* Because of this relationship between Dr. Bernstein and Northbrook, CDER also considered Northbrook to be an affiliate of Winston. Northbrook submitted NDA 19-690, Papulex (nicotinamide) to FDA for its review. *Id.* Ownership of the NDA was later transferred to GenDerm and subsequently to Winston. *Id.* Because of the submission of NDA 19-690 by Northbrook, CDER further concluded that the Civamide NDA would not be the first human drug application submitted by Winston or its affiliates. *Id.*

CDER recognized that GenDerm and Northbrook were not included in the list of affiliates considered by the Small Business Administration in making its size determination and noted that the SBA does not consider firms that are no longer in business in determining a company's affiliates. *Id.* CDER explained that, in determining whether to grant a small business waiver, "*FDA* considers *all* affiliates, even those no longer in existence." *Id.* (emphasis added). Accordingly, based on the relationships between Dr. Bernstein, Winston, GenDerm, Northbrook, CDER concluded that GenDerm and Northbrook are considered affiliates of Winston and, because these two companies previously submitted NDAs, the Civamide NDA would not be the first human drug application submitted by Winston or its affiliates.

D. Winston's Reconsideration Request

By letter dated December 9, 2008, Winston requested that CDER reconsider its denial of Winston's waiver request. Letter from J. Bernstein to J. Axelrad (December 9, 2008), at 1-2 ("Reconsideration Request"). Winston asserted that Winston is not an affiliate of Northbrook and GenDerm, explaining that:

- "Northbrook was dissolved in 1984, 14 years before Winston was originally incorporated."
- GenDerm was sold to Medicis on December 3, 1997. Joel Bernstein, CEO of Winston, was not a controlling shareholder in GenDerm, "own[ing] 27% of GenDerm while the venture capitalists who controlled the Board of Directors owned over 50%." After the sale of GenDerm to Medicis in 1997, according to Winston, no shareholder of Winston, including Dr. Bernstein, has owned any shares of GenDerm.

Id. In support of its assertion, Winston also cited the opinion of five attorneys with whom they consulted, all of which "expressed the unequivocal opinion that Winston is not an affiliate of Northbrook or GenDerm." *Id.*

E. CDER's Response to the Request for Reconsideration of Its Initial Denial

By letter dated February 2, 2009, CDER affirmed its finding that Winston met the first criterion for a small business waiver, in that Winston and its affiliates employ less than 500 persons. Letter from J. Axelrad to J. Bernstein (Feb. 2, 2009), at 2 ("Reconsideration Denial"). CDER also concluded that Winston met the second criterion for a small business waiver, i.e., that

Winston and its affiliates do not have a drug product that has been approved under a human new drug application and introduced or delivered for introduction into interstate commerce.

With regard to the third criterion, CDER's Reconsideration Denial addressed the issue raised by Winston of whether Northbrook and GenDerm could be considered affiliates of Winston and, accordingly, whether the Civamide NDA will be the first human drug application submitted to FDA by Winston or its affiliates. CDER confirmed the findings in its December 2008 Denial that Northbrook and GenDerm are considered affiliates of Winston for the purposes of PDUFA and that the new drug applications submitted by Northbrook and GenDerm render Winston ineligible for a small business waiver. *Id.* Therefore, CDER upheld its decision to deny Winston's waiver request for the application fee associated with the submission of the Civamide NDA. *Id.* at 3.

With respect to Winston's affiliation with Northbrook, CDER noted that Winston provided no information to refute CDER's finding that, as President of Northbrook, and CEO of Winston, Dr. Joel Bernstein controlled both entities, or that Northbrook submitted NDA 19-690, Papulex (nicotinamide), under Dr. Bernstein's signature. With respect to Winston's contention that Northbrook could not be considered an affiliate of Winston because Northbrook was dissolved 14 years before Winston was incorporated, CDER re-emphasized that there is "no requirement in the definition of affiliate [in PDUFA] that all relevant parties be in existence at the same time." Reconsideration Denial at 3. Accordingly, CDER again concluded that the Civamide NDA would not be the first human drug application submitted by Winston or its affiliates. *Id.*

CDER also affirmed its conclusion that GenDerm is an affiliate of Winston. CDER considered Winston's assertion that, despite Dr. Bernstein's role as founder, Chairman, and Chief Executive of GenDerm, he did not control GenDerm because he was a minority shareholder and venture capitalists controlled GenDerm's Board of Directors. *Id.* at 2. CDER concluded that Winston provided no evidence that, at the time of submission of NDA 20-318, Carbamide Peroxide Solution, by GenDerm, Dr. Bernstein did not control, or have the power to control, GenDerm. *Id.* at 4. CDER therefore found that Dr. Bernstein had the power to control both GenDerm and Winston and the companies are affiliated for the purposes of determining whether Winston or its affiliates have previously submitted a human drug application. *Id.* In addition, CDER rejected Winston's assertion that it was relevant that GenDerm submitted a new drug application prior to the enactment of PDUFA, noting that there is nothing in the statutory language that indicates that the third criterion for a small business waiver depends on the timing of the submission of the NDA. *Id.* Consequently, CDER reaffirmed its conclusion that GenDerm and Winston are affiliates, that GenDerm has submitted an NDA for FDA's review, and that, accordingly, the Civamide NDA would not be the first human drug marketing application submitted by Winston or its affiliates. *Id.*

II. Analysis of Winston's Appeal

A. Contentions in Winston's Appeal

In its present appeal, submitted by Mr. Hutt via an e-mail dated April 8, 2009, Winston requested a waiver of the application fee that would be due in connection with the submission of the

Civamide NDA. E-mail from P. Hutt to M. Lumpkin dated April 8, 2009 ("Appeal"). Winston asserted that the denial of its request for reconsideration of CDER's denial of its user fee waiver request was incorrect because CDER's denial relied on a finding that Northbrook and GenDerm, two now-defunct entities, were affiliates of Winston. *Id.* Winston further explained that CDER's interpretation of "affiliate" to include entities that no longer exist was in conflict with the definition accepted by five attorneys consulted by the company, as well as an employee of the SBA. *Id.*

Finally, Winston asserted (for the first time) that, although it was clearly entitled to a waiver under the small business waiver provision, it also qualifies for a waiver of the application fee because "the assessment of the fee would present a significant barrier to innovation because of limited resources available to such person or other circumstances." *See* Appeal (quoting 21 U.S.C. § 379h(d)(1)(D)). Winston stated that it "currently has approximately $2.5 million in cash and investments, a burn rate of $400,000 per month, and no income." Appeal. Winston further asserted that the company cannot afford to pay the application fee and remain in business. *Id.*

B. Legal Standards for PDUFA Fees and Waivers

1. Application Fees

PDUFA provides that:

> each person that submits, on or after September 1, 1992, a human drug application or a supplement shall be subject to a fee as follows:
>
> (i) A fee established under subsection (c)(5) for a human drug application for which clinical data (other than bioavailability or bioequivalence studies) with respect to safety or effectiveness are required for approval.

21 U.S.C. § 739h(a)(1)(A).

2. Fee Waivers

Under PDUFA, a waiver of fees may be granted under several circumstances. PDUFA provides for a waiver where the applicant involved is a small business submitting its first application to FDA for review. *See* 21 U.S.C. § 379h(d)(1)(D). The small business waiver provision entitles a small business to a waiver when the company meets the following criteria:

(1) The business employs fewer than 500 persons, including employees of its affiliates.
(2) The business does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce.
(3) 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.

Id. § 379h(d)(4).

FDAMA, which amended PDUFA in 1997, provided that the "person" subject to fees in the waiver provisions "shall include an affiliate thereof." *See* FDAMA § 103(h). As amended, PDUFA further defines "affiliate" as:

> 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(11). FDA has interpreted "affiliate" in this and other responses to PDUFA fee waiver requests to include entities that existed at different times, including those who are no longer in existence. December 2008 Denial, at 2; Reconsideration Denial, at 3.

FDA's *Draft Interim Guidance Document for Waivers and Reductions in User Fees* discusses the small business waiver and suggests procedures for requesting such a waiver. *1993 FDA Draft Guidance*, at 11-12, 22-24, 27-28. The draft guidance discusses the first two criteria currently used by FDA in determining whether a company qualifies for a small business waiver, quoting the statutory definition of "affiliate" referenced above. *Id.* at 11. In addition, citing to the legislative history of PDUFA, the draft guidance states that "[t]he number of employees [of an applicant for a small business waiver] is to be calculated in accordance with the procedures and regulations of the [SBA]." *Id.* at 12 (citing H. Rep. No., 102-895 (1992) at 17). The third criterion for determining whether a company qualifies for a small business waiver, that the application in question is the first submitted by a company and its affiliates, is not discussed in the draft guidance because this limitation was added by FDAMA, which was enacted after the promulgation of the draft guidance.[3]

C. Merits of Winston's Appeal

For the reasons set forth in detail below, I am denying Winston's appeal of CDER's denial of Winston's fee waiver request for the application fee associated with the submission of the Civamide NDA. I concur with CDER's findings that Winston employs fewer than 500 persons and does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce. In addition, based on the information provided by CDER and Winston, I have concluded that a fee waiver is not warranted because the Civamide NDA would not be the first human drug marketing application submitted by Winston or its affiliates.

It is not disputed that Winston is a small business in accordance with the definition in PDUFA, that is, that Winston has fewer than 500 employees and does not market a drug product that is the subject of an approved application. *See* December 2008 Denial, at 2; Reconsideration Denial, at

[3] Similarly, I note that much of the draft guidance's discussion of the procedures associated with granting a small business waiver is no longer pertinent because it reflects the statutory standard as of PDUFA's enactment in 1992, rather than the current version, as amended by FDAMA.

2. The key issue raised in Winston's Appeal is whether, for the purposes of determining if an NDA is the first human drug application submitted by a small business or its affiliate, the term affiliate includes companies that no longer exist. The resolution of this issue is dispositive in determining whether the Civamide NDA would be the first human drug marketing application submitted by Winston or its affiliates.

As set forth in more detail above, CDER concluded that two now-defunct companies, Northbrook Testing Company ("Northbrook") and GenDerm, which were founded by Joel Bernstein, Chief Executive Officer and majority shareholder of Winston, are affiliates of Winston. CDER found that Dr. Bernstein controls Winston and controlled both GenDerm and Northbrook in his capacity as Chairman and Chief Executive Officer of GenDerm and President of Northbrook. Further, because Northbrook and GenDerm each had previously submitted an NDA, CDER concluded that the Civamide NDA would not be the first NDA submitted by Winston or its affiliates. Accordingly, CDER determined that Winston does not qualify for a small business user fee waiver under 21 U.S.C. § 379h(d)(1)(D).

For the reasons set forth below, I find, as did CDER, that Northbrook is an affiliate of Winston under the PDUFA's statutory definition of "affiliate." However, I find that there is not sufficient evidence to determine whether or not GenDerm and Winston are affiliates. These findings are consistent with the purpose of PDUFA and public policy considerations.

1. Scope of the term "affiliate"

As noted above, the key issue raised in Winston's Appeal is whether, for the purposes of determining if an application is "the first human drug application that a small business or its affiliate submits to [FDA] for review," the term affiliate includes companies that no longer exist.

Under PDUFA, an affiliate is defined as "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(11). On its face, the statutory definition is silent with regard to whether companies that are no longer in business may be considered affiliates. There are no FDA regulations implementing or further interpreting this provision. In its responses to this user fee waiver request and other request, FDA has consistently interpreted the term affiliate to include companies that existed in the past, a position which I believe is supported by the purpose of the statutory provision.

In its Appeal, Winston relies on the opinion of five attorneys consulted by the company in support of its assertion that Northbrook and GenDerm cannot be considered affiliates because they are no longer in existence. Winston, however, provided no legal analysis or support for the conclusions of these legal experts. I, therefore, do not find the citation to these attorneys' positions persuasive.

Winston's Appeal also relies on an e-mail sent from SBA's Manager of Size Determination/COC Programs, responding to an inquiry from Northbrook and stating that a company that has been out of business for 20 years cannot be considered an affiliate "if the [size] *determination* is made

after the date of the entity's dissolution." *See* E-mail to D. Starr from D. Gordon, Small Business Administration (February 11, 2009) ("Gordon E-mail") (emphasis added). As a preliminary matter, the conclusion in the Gordon E-mail is clearly limited to the context of making size determinations.[4] Based on its text, there is no reason to believe that Mr. Gordon's response contemplates the definition of affiliate in the broader regulatory context of PDUFA. I do not find Mr. Gordon's e-mail persuasive, then, to the issue at hand, whether, for the purposes of determining if a company or its affiliates have previously submitted a human drug application, the term affiliate includes companies no longer in business.

Moreover, even if the Gordon E-mail were relevant, it is not binding on FDA's determination of whether an application has previously been submitted by a company or its affiliates. While the Agency may in practice consult with the SBA prior to determining whether a company meets the *size requirements* to qualify for a small business waiver, in keeping with Congressional intent, FDA does not consult, and is not required to consult or make decisions in accordance with, the SBA with regard to the other criterion for determining if a company is entitled to a small business waiver. The legislative history of PDUFA indicates that Congress intended for FDA to *determine the size of an applicant* in accordance with the regulations of the Small Business Administration. H. Rep. No., 102-895 (1992) at 17 (emphasis added). Notably, Congress did not instruct FDA to make the overall determination whether a company qualifies for the small business fee waiver in accordance with the SBA's regulation. Further, PDUFA was amended in 1997 by FDAMA, which provided for a waiver, rather than deferral, of the application fee for small business, but made that waiver available only for the first human drug application submitted by a company or its affiliates. Nowhere in the legislative history of FDAMA did Congress indicate that it intended for FDA to be influenced or bound by the SBA's interpretation of the term affiliate in determining whether an application had previously been submitted by a company or its affiliates.

It is true that, when making a size determination, SBA only considers existing companies with a current relationship to the company.[5] The SBA's regulation does not attempt to limit the definition of affiliate, but rather limits the types of affiliates that will be considered by the SBA in determining the number of persons employed by a company. This limitation is consistent with FDA's *Draft Interim Guidance Document for Waivers of and Reductions in User Fees,* which states that "the factors that support a small business determination may change rapidly." *1993 FDA Draft Guidance,* at 30. Indeed, in light of this reality, FDA suggests that companies submit requests for small business waivers no sooner than 90 days before they expect to submit their NDAs, and has indicated that it will reevaluate a firm's small business status one year after granting such a waiver request. *Id.* at 29-30. It is logical, then, that the SBA's size determination would be based only on current affiliates in existence at the time of the determination. Accordingly, the SBA's Size Determination for Winston did not include a consideration of Northbrook or GenDerm.[6]

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[4] This is consistent with the SBA's regulations, which provide that employees of a former affiliate are not counted in determination of number of employees if affiliation ended before determination was made. *See* 13 C.F.R. § 121.106(b)(4)(ii).

[5] 13 C.F.R. § 121.106(b)(4)(ii).

[6] I note that reliance on a company's current affiliates in making a size determination is not inconsistent with a broad interpretation of affiliate for the purposes of PDUFA. Even if the employees of now-defunct affiliates were

In contrast to the process for making a size determination, which require consideration of a company's status *at the time* the determination is made, PDUFA contemplates that FDA examine past events in order to determine whether an NDA is the first human drug application submitted by a company or its affiliates. Therefore, it is reasonable, indeed, arguably *necessary*, to consider whether companies that may no longer exist should be considered affiliates of that company and whether they have submitted applications. Given the clear purpose of this provision and the fact that the statute's plain language includes no temporal limitation to prevent the consideration of now defunct companies, it is reasonable to consider companies that are no longer in business to be affiliates of an applicant for a small business waiver.

Moreover, policy considerations support a broader interpretation of the term affiliate. Under the interpretation promoted by Winston, a company could obtain a fee waiver for its "first human drug application," dissolve the company, establish a new company that is essentially a duplicate of the first, and obtain a fee waiver for its next NDA (which would technically be the "first" NDA of *that* incarnation of the company). This cycle could be repeatedly indefinitely. PDUFA's emphasis that a waiver is only available for the *first* human drug application submitted by "a small business or its affiliate," and not for subsequent applications, 21 U.S.C. § 379h(d)(4)(B) (emphasis added), instead of all applications submitted by a "small business," *id.* § 379h(d)(1)(D), certainly suggests that Congress intended to prevent such abuse. To adopt an interpretation that would permit companies to easily circumvent the limitation on the small business waiver put in place by Congress is not sound public policy.

2. Control by Dr. Bernstein of GenDerm and Northbrook

PDUFA defines "affiliate" as "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(11). Because it is undisputed that Dr. Bernstein controls Winston, if Dr. Bernstein controlled, or had the power to control, Northbrook or GenDerm, respectively, either company is considered an affiliate of Winston. As explained below, I find, as did CDER, that Northbrook is an affiliate (as defined by PDUFA) of Winston, but find that there is not sufficient evidence to determine whether or not GenDerm is an affiliate (as defined by PDUFA).

CDER concluded that Dr. Bernstein, in his capacity as Founder and President of Northbrook, controlled the company. Reconsideration Denial, at 3. Winston provided no evidence or argument to rebut this assertion, and did not challenge this conclusion in its Appeal. Accordingly, I affirm CDER's finding that, based on the relationship between Dr. Bernstein and Northbrook, Dr. Bernstein controlled Northbrook and, therefore, Winston and Northbrook are considered affiliates for the purposes of PDUFA.

With respect to Dr. Bernstein's relationship with GenDerm, CDER also found that Dr. Bernstein controlled GenDerm and, therefore, Winston and GenDerm are affiliated. CDER's conclusion

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explicitly considered in making a size determination, the result would be the same as if they were not considered because these companies, by function of no longer existing, no longer have employees.

was based on Dr. Bernstein's position as Founder, Chairman, and Chief Executive Officer of GenDerm. Reconsideration Denial, at 3-4. In its Reconsideration Request, Winston presented evidence to challenge this conclusion, stating that Dr. Bernstein owned 27% of the company, while venture capitalists owned over 50% of the company and "controlled the Board of Directors."[7] Reconsideration Request, at 2. In its Reconsideration Denial, CDER accepted this assertion but found that Winston "provided no evidence that at the time of submission of NDA 20-318, Carbamide Peroxide Solution, Dr. Joel Bernstein did not control, or did not have the power to control, GenDerm." Reconsideration Denial, at 4.

Although PDUFA does not require showing that one entity exercised control over another entity, only that the first entity has *the ability* to do so, *see* 21 U.S.C. § 379g(11), I find that the evidence presented by Winston raises questions about whether Dr. Bernstein controlled, or had the ability to control, GenDerm. In absence of evidence to the contrary, it is reasonable to conclude that a person in Dr. Bernstein's position with respect to GenDerm controls, or has the ability to control, the company. However, if there is evidence that another entity has a controlling share of stock or otherwise controls the company, this conclusion cannot be presumed.[8] Merely signing a regulatory submission in the capacity of the Chairman and Chief Executive Officer of a company does not compel a conclusion that the individual exercises control over a company. On the other hand, it is not clear how widely held the stock was, whether the venture capitalists voted as a collective entity or as individuals, and when the venture capitalists became majority shareholders and obtained control of the Board of Directors in relation to the submission of NDA 20-318.

I, therefore, find that there is not sufficient evidence to determine whether Dr. Bernstein controlled, or had the ability to control, GenDerm, and accordingly to determine whether Winston and GenDerm are affiliates for the purposes of PDUFA. However, because the answer to this question is not dispositive in deciding this appeal, it is unnecessary for present purposes to answer the question of GenDerm's affiliation.

3. Previous Submission of NDA by Winston or its Affiliates

My finding that there is not sufficient evidence to determine whether GenDerm and Winston are affiliated does not disrupt CDER's ultimate conclusion that Winston is not entitled to a small business user fee waiver. As referenced above, I find that Northbrook and Winston are affiliates. It is undisputed that Northbrook previously submitted NDA 19-690, Papulex (nicotinamide). Therefore, Winston does not meet the third criterion for granting a small business waiver, that the application in question is the first human drug application submitted by the applicant or its affiliates. *See* 21 U.S.C. § 379h(d)(4)(B).

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[7] Winston further explained in its Reconsideration Request that GenDerm was sold to Medicis in December 1997 and no shareholder of Winston, including Dr. Bernstein, has held any shares of GenDerm since that sale. Reconsideration Request, at 2. I concur with CDER that this is not relevant to the issue of whether Dr. Bernstein controlled, or had the power to control, GenDerm when GenDerm submitted NDA 20-318, Carbamide Peroxide Solution. Reconsideration Denial, at 4.

[8] *Cf.* 13 C.F.R. § 121.103(c)(3) ("If a concern's voting stock is widely held and no single block of stock is large as compared with all other stock holdings, *the concern's Board of Directors and CEO or President will be deemed to have the power to control the concern* in the absence of evidence to the contrary." (emphasis added)).

4. Barrier to Innovation

In its Appeal, Winston also asserted that the company is entitled to a waiver of the application fee associated with the Civamide NDA because "the assessment of the fee would present a significant barrier to innovation because of limited resources available to such person or circumstances." *See* Appeal (quoting 21 U.S.C. § 379h(d)(1)(B)). As FDA has interpreted this provision in other responses to PDUFA fee waiver requests, a waiver of fees on this ground may be granted if the following two criteria are met: (1) the product for which the waiver is being requested is innovative and (2) the fee would be a significant barrier to the entity's ability to develop, manufacture, or market innovative products.

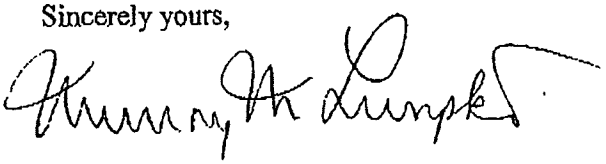
This issue was not raised by Winston in any previous submissions or considered by CDER in its Denial and Reconsideration Denial.[9] Therefore, I decline to make a finding with regard to Winston's request for a waiver on this ground. I note, however, that there is no barrier to the submission of multiple user fee waiver requests and that Winston may submit an additional request for a waiver on this ground to CDER's Associate Director for Policy.

III. Conclusion

Based on my review of the entire record, the statute, its purpose and legislative history, and FDA guidance, I conclude that Winston's waiver request should not be granted. I find that Winston meets the first two criteria for granting a small business waiver, i.e., that it employs fewer than 500 employees and it does not market a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce. 21 U.S.C. § 379h(d)(4)(A). However, as explained above, based on the purpose of the statutory provisions at issue and public policy considerations, I find that, for the purposes of PDUFA, the term "affiliate" includes companies that are no longer in existence. Based on this interpretation and information provided in the record below, I find that Northbrook is an affiliate of Winston and that Northbrook previously submitted an NDA to FDA for review. I, therefore, conclude that the Civamide NDA would not be the first human drug application that Winston or its affiliates have submitted to FDA for review. *See id.* § 379h(d)(4)(B). For that reason, I conclude that Winston does not meet the statutory criteria set forth in 21 U.S.C. § 379h(d) and is not entitled to a small business waiver.

Accordingly, Winston's fee waiver request is denied.

Sincerely yours,



Murray M. Lumpkin, M.D.
Deputy Commissioner for International Programs

[9] As referenced above, an appeal to FDA's User Fee Appeals Officer should contain references only to materials already submitted, and should not contain any new information. *1993 FDA Draft Guidance*, at 26.