Buchanan Ingersoll
ATTORNEYS

Donald E. Segal
202 452 7959
segalde@bipc.com

1776 K Street, N.W.
Suite 800
Washington, DC 20006-2365

T 202 452 7900
F 202 452 7989

www.buchananingersoll.com

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VIA FIRST CLASS MAIL & MESSENGER

Dockets Management
Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No 2003N -0233
Response to request for submission of additional information to support the use of enzacamene [3-(4-methylbenzylidene)-camphor], which is sold under the trade name of Eusolex® 6300, as generally recognized as safe and effective for OTC use as a sunscreen

Dear Sir or Madam:

On August 21, 2002, in response to a request by FDA, Merck KGaA submitted a time and extent application (TEA) in support of the use of the active ingredient enzacamene [3-(4-methylbenzylidene) camphor], up to 4%, as a sunscreen single active ingredient and in combiniation with other sunscreen active ingredients. In the Federal Register of July 11, 2003, FDA announced that it had reviewed Merck KGaA's TEA and determined that enzacamene was eligible for consideration in the OTC monograph system. 68 FR 41386-87. In that same notice FDA requested the submission, by October 9, 2003, of data and information "to determine whether these conditions can be generally recognized as safe and effective (GRAS/E) for their proposed OTC use."

The status of enzacamene (Eusolex® 6300) has been pending before the FDA for thirty years. During this time, extensive documentation has been submitted to the FDA in support of the safety and efficacy of this sunscreen. The initial submissions were made in response to the call for data at the outset of the OTC sunscreen Monograph process. (Docket No. 78N-0038). Based upon these submissions, the panel found that Eusolex® 6300 safe and effective and recommended that it have Category I status. [1] This Category I status was changed in the ANPR[2] on the basis that there was no data establishing the marketing of Eusolex® 6300 in the U.S. prior to December 4, 1975.

[1] Meeting Minutes of September 30 and October 1, 1975.
[2] ANPR, 43 Fed. Reg. 38206. (August 25, 1978).

In response to that change in status of Eusolex® 6300, a Citizen Petition (Docket No. 78N-0038) was filed by Merck KGaA on December 17, 1980 requesting reconsideration and seeking to reopen the rulemaking process. During the ensuing years and the continued pendancy of this Citizen Petition, voluminous additional submissions were made in support of the safety and efficacy of Eusolex® 6300. See, for example, submissions of August 15, 1985 and April 12, 1999. The April 12, 1999 submission included the studies that formed the basis for the final approval of Eusolex® 6300, in September 1998, by the Scientific Committee impaneled to review and approve sunscreen products for the European Community.

The most recent submissions made on Eusolex® 6300 were made as part of the TEA application (Docket No. 96N-0277). These submissions contained extensive safety data, based on thirty years of worldwide marketing history, and literature references demonstrating the sunscreen's efficacy.

We respectfully request that all prior submissions made to the FDA in support of Eusolex® 6300 by Merck KGaA, and its predecessors and affiliates including but not limited to those made in connection with the referenced Citizen Petition, the current TEA, and the original OTC rulemaking process be incorporated and made a part of these proceedings. Additionally, we respectfully request that the record of the initial panel discussions finding Category I status for this compound, also be included in the record. For your reference, enclosed as Attachment A is a list of all submissions that have been made by Merck KGaA and its predecessors, on Eusolex® 6300 over the past thirty years.

As part of its TEA application, Merck KgaA requested interim marketing rights. We reiterate that request. There have now been two independent determinations made by expert scientific panels in the U.S. and Europe finding Eusolex® 6300 to be both safe and effective. Based upon the policies announced in the ANPR for the Time and Extent Regulations, and the fact that the initial OTC panel found Eusolex® 6300 Category I, Eusolex® 6300 qualifies for interim marketing status. This could be accomplished through an announced enforcement policy or by some other mechanism. FDA has acknowledged that such a procedure is appropriate to treat similarly situated products in a fair and equitable manner. 67 Fed. Reg. 3060, 3068 (January 23, 2002). Given the extraordinary passage of time; the numerous submissions of data, and the extensive and recognized marketing history, such action by FDA is long overdue.

We look forward to your prompt review of our materials and our request for interim marketing status.

Very truly yours,

Donald E. Segal
Robert G. Pinco

Enclosure
cc: Ina Höfgen-Müeller
Gerry Rachanow

ATTACHMENT A

Date of Submission	Identification of Submission
December 18, 1973	Submission by Greiter Corp. to OTC Review of data and information on five sunscreening chemicals and products made with those chemicals.
May 1, 1974	Supplemental data submitted by EM Labs to OTC Review regarding various Eusolex compounds.
March 15, 1974	Letter from EM Labs to OTC Review mentioning that recent efforts to market several sunscreening substances in the U.S. have met resistance because they are regarded as OTC drugs.
November 1974	Clinical trial material (Sydney, Australia).
July 22, 1975	EM Labs submission to OTC Review of reports on clinical testing of Eusolex 6300.
March 30, 1976	Supplement to OTC Drug Review submission made on 12/18/73. Contains information on additional clinical studies carried out in Australia.
February 17, 1977	Submission of scientific data on sunscreen testing by Greiter Corp. to FDA's OTC staff.
June 1, 1977	Letter to OTC Panel from K.L. Milstead stating that Greiter Corp. has marketed several sunscreen products in the U.S. during the past 3 years.
September 21, 1979	Short letter to FDA
January 8, 1980	Short letter to FDA
December 17, 1980	Petition from EM Industries to reopen rulemaking record for OTC sunscreen drugs to include additional information. - Expresses surprise that Eusolex 6300 was placed in Category II in the proposed monograph, since Panel minutes of 9/30/75 and 10/1/75 recommended Category I. - States that human use of the substance in the U.S. began in 1976 and has continued

	to increase since that date. - Encloses pre-clinical data (five reports of studies conducted from 1973-1980) and clinical trial material (Hamburg 2/20/80).
August 15, 1985	Request to Reopen the Rulemaking Record Respecting the Proposed Monograph for Sunscreen Drug Products for Over-The-Counter Human Use, 43. Fed. Reg. 38206 (Aug. 25, 1978) to Include Additional Information (Docket No. 78N-0038)
September 17 1988	Submission by Company in response to FDA request for information and chemical samples to support prior Sunscreen Monograph submission on Eusolex 6300; Submission included: - Validation of the Analytical Methods for Eusolex 6300; - Material Safety Data Sheet for Eusolex 6300; - Monographs for Eusolex 6300; - Certificate of Analysis for the "Primary Standard"; - Chemical Samples for Eusolex 6300.
September 11, 1990	DMF
April 12, 1999	Supplement to Petition to Reopen Rulemaking record Respecting Sunscreen Drug Products for OTC. (Docket No. 78N-0038)
July 20, 2000	Request for a meeting to discuss regulatory issues.
August 21, 2002	Time and Extent Application ("TEA") for Priority Review (Docket No. 96N-0277).
October 28, 2002	Additional Information for the Eusolex® 6300 TEA for Priority Review (Docket No. 96N-0277)