

ARTER & HADDEN^{LLP}

ATTORNEYS AT LAW

founded 1843

Austin
Cleveland
Columbus
Dallas
Dayton
Irvine
Los Angeles
San Antonio

100 Congress Avenue
Suite 1800
Austin, Texas 78701
telephone 512.479.6403
facsimile 512.469.3552

San Diego
San Francisco
Washington, D.C.
Woodland Hills
Affiliated Offices
Brussels, Belgium
Geneva, Switzerland

Direct Dial: (512) 479-6403
Email: abeinke@arterhadden.com

February 9, 1999

VIA FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 98N-0148
64 Federal Register 1629 (January 11, 1999)

COMMENTS OF METABOLIFE INTERNATIONAL, INC.

I. Introduction

On behalf of Metabolife International, Inc. ("Metabolife"), these comments are submitted for consideration by the Food and Drug Administration ("FDA") in the preparation of the United States position on the World Health Organization's ("WHO") proposal to add several substances to schedules of the 1971 United Nations Convention on Psychotropic Substances. FDA's January 11, 1999 *Federal Register* notice indicated that the United States position will be presented at the upcoming meeting of the United Nations Commission on Narcotic Drugs in Vienna, Austria. Although the FDA notice addressed several specific substances, Metabolife directs its comments only to the notification for the substance "ephedrine".

Metabolife is a California-based corporation that markets and sells dietary supplements throughout the United States. One of Metabolife's products, "Metabolife 356", is a dietary supplement which contains *ma huang*, an ephedrine alkaloid. Because of this product, Metabolife is very concerned with the WHO's recommendation to schedule ephedrine under the United Nations Convention on Psychotropic Substances, thereby making products containing ephedrine available only by medical prescription.

II. Metabolife's Position

Metabolife urges the FDA to develop a United States position that opposes the WHO recommendations to impose international manufacturing and distribution restrictions on ephedrine. Metabolife urges this position because it believes that (1) little or no scientific evidence exists to support the scheduling, and (2) no widespread pattern of abuse of ephedrine

8304 10 10 10 49:1

ARTER & HADDEN_{LLP}

Dockets Management Branch
Food and Drug Administration
February 9, 1999
Page 2

exists in the United States or worldwide. As a result, ephedrine should not be added to any schedule promulgated by the United Nations Commission on Narcotic Drugs. A recommendation supporting scheduling would unreasonably harm consumers who currently rely on ephedrine-containing dietary supplements for weight management and other health benefits. In addition, any recommendation which would make ephedrine-containing dietary supplements available only by medical prescription would have a significant detrimental effect on the hundreds of thousands of small business that are involved in the distribution and sale of these products.

III. Metabolife's Products Are Safe

The WHO Expert Committee on Drug Dependence recommendation to schedule ephedrine is based upon little or no scientific evidence. In fact, the factual record is clearly inconclusive with regard to ephedrine and contains no information that would support scheduling dietary supplements containing herbal ephedra. No distinction seems to be made between the two substances. Herbal ephedra has been consumed safely and beneficially for thousands of years. Today, herbal ephedra is widely and beneficially used throughout the United States and the world in a variety of food and dietary supplement products.

Metabolife has never been made aware of any adverse health events by consumers of its products. Metabolife has never received a notice from a consumer that any serious adverse health event has occurred because of ingestion of Metabolife 356. This claims-free history exists notwithstanding the wide spread media attention regarding dietary supplement products containing ephedrine. Last year, Metabolife sold approximately 60 million tablets per month of Metabolife 356. This amounts to about 720 million tablets of Metabolife 356 sold annually in the United States. Many of Metabolife's customers are repeat consumers that have been using Metabolife 356 for a number of years. These customers' continued use of the product without reporting any serious adverse effects demonstrates the safety of the product and that the customers are experiencing health benefits from using the product. These customers have experienced health benefits such as effective weight management, an overall sense of well-being, and a sense of empowerment or self-control over their bodies and lives.

In order to encourage the safe and appropriate use of its products, Metabolife has implemented a safety monitoring procedure. Each label of each bottle of Metabolife 356 includes a telephone number for a Metabolife customer service representative. The customer service representative refers all customer contacts concerning medical-type inquiries to a nurse practitioner for further review and processing. If a complaint presents a concern other than one of a temporary, non-serious nature or requests information about the interaction of Metabolife 356 with a prescription or OTC drug, the customer service representative is to recommend that

ARTER & HADDEN_{LLP}

Dockets Management Branch
Food and Drug Administration
February 9, 1999
Page 3

the caller seek professional health assistance immediately. Metabolife takes the health of its potential and existing customers very seriously.

In addition, Metabolife has devoted a significant amount of time and resources to ensure that its products are safe and effective. First, Metabolife is one of two companies which invested in animal studies to evaluate the health effects of its products. These 1994 studies evaluated an herbal compound containing ephedra and guarana at a cost of approximately \$200,000. Second, Metabolife engaged the Academy of Clinical, Environmental, Research and Informational Sciences ("ACERIS"), a non-profit certification company, to review the ingredients and label of Metabolife 356 for safety and quality assurance. This review also included an evaluation of the manufacturing plant where the product is produced. As a result of that 1997 review, Metabolife received a valuable quality assurance certification from ACERIS. Third, Metabolife funded a portion of a significant human study commissioned by the Ephedra Research Foundation which is being conducted at hospitals affiliated with Harvard University Medical School and Columbia University. Fourth, Metabolife sponsored a human clinical study on Metabolife 356 at Vanderbilt University Medical Center. The findings of that study were issued in January, 1998 and focused on the efficacy of the product for weight loss. This study concluded that Metabolife causes an increase in energy expenditure in normal, moderately obese human subjects which is independent of physical exercise. No adverse effects were observed or measured that affected the health of the subjects in the study.

IV. Metabolife Products Are Not Abused

While some countries have reported past or present abuse of ephedrine, these reports focus primarily on synthetic or pure ephedrine single-ingredient products. There is no evidence that herbal ephedra or dietary supplements containing herbal ephedra are subject to abuse. This lack of significant evidence of abuse of products containing herbal ephedra is largely due to the inherent differences between pure ephedrine and herbal ephedra. The body seems to absorb ephedrine alkaloids from herbal ephedra slower than from pure ephedrine. In addition, the presence of other alkaloids in herbal ephedra may offset the effects of the ephedrine itself. Without valid documentation of an abuse problem for herbal ephedra, no basis exists to conclude that the use of ephedra-containing products presents a public health or social problem which would justify the scheduling of these products.

Metabolife's consumer statistics also support the contention that dietary supplements containing ephedra are not abused. On an average, each customer that buys Metabolife 356 buys an average of 1.78 bottles per purchase. Each bottle contains 90 tablets. This information indicates that the purchasing habits of Metabolife customers support the contention that the typical consumer of dietary supplements containing ephedra does not abuse the product. The

ARTER & HADDEN_{LLP}

Dockets Management Branch
Food and Drug Administration
February 9, 1999
Page 4

product quantities purchased by Metabolife customers seem to support the judicious and appropriate use of the product for the intended health benefits.

Metabolife 356 and other dietary supplements containing ephedra are not precursors to amphetamines. As a result, these products cannot be abused with the intended purpose to convert the ingredients of these products to a dangerous drug, such as methamphetamine. As a List 1 chemical, pure ephedrine can be used in the manufacture of amphetamines. However, it is chemically impossible or, at least, extremely difficult to manufacture amphetamines from dietary supplements containing ephedrine alkaloids. A recent study showed that even a professional, legitimate scientific laboratory was unable to use dietary supplements containing ephedrine to manufacture amphetamines. Metabolife commissioned Hauer Laboratory Services to "attempt to produce methamphetamines from Metabolife 356 using the 'street' method published in *The Journal of Forensic Sciences*". The procedure produced a black tar-like material instead of methamphetamine crystals. The material was tested and was found to contain mostly ephedra alkaloids and caffeine. No methamphetamine was detected in the material. This analysis supports the empirical information Metabolife has gleaned from its sales records indicating that dietary supplements containing ephedrine are not purchased for use as precursors to amphetamines.

V. Scheduling Ephedrine Will Have A Serious Social And Economic Impact

Before scheduling a substance, the United Nations Commission on Narcotic Drugs is required to consider, among other things, the economic and social factors that may result from the decision. The social impact of such a decision would be wide spread. Many OTC products that contain ephedrine which are used by consumers for a variety of health needs would not be readily available. In addition, the over five million consumers of dietary supplements containing ephedrine would not be able to purchase these products without a medical prescription. Many of these consumers would be unable to continue to use the products and would fail to receive the health benefits they are currently enjoying.

In addition, the impact of scheduling ephedrine on businesses in the United States would be substantial. The dietary supplement industry alone has several hundred thousand small businesses that are involved in the marketing and distribution of dietary supplements containing ephedrine. All of these small businesses would be economically devastated.

VI. Conclusion

Ephedrine or herbal ephedra should not be added to the schedules of the 1971 United Nations Convention on Psychotropic Substances. Such scheduling is unnecessary and inappropriate. The WHO has not developed a factual record to support such an action. No

ARTER & HADDEN_{LLP}

Dockets Management Branch
Food and Drug Administration
February 9, 1999
Page 5

evidence has been presented to support the contention that widespread abuse of ephedrine-containing products is occurring. No evidence has been presented that indicates the use of ephedrine-containing products constitutes a serious health threat. There is no evidence that products containing herbal ephedra are used as precursors in the illicit manufacture of methamphetamine. Significant evidence does exist that the scheduling of ephedrine would have substantial adverse social and economic impacts on consumers and small businesses in the United States.

In light of this evidence, the United States should oppose efforts to scheduled ephedrine at the upcoming meeting of the United Nations Commission on Narcotic Drugs. If efforts to prevent the scheduling of ephedrine are not successful, the United States should strongly support efforts to exclude herbal ephedra and products containing herbal ephedra from the appropriate schedule.

Respectfully submitted,



Allen P. Beinke

Counsel for Metabolife International, Inc.

APB/lah

1 From [Redacted] Date 2/9/99

Sender's Name Allen Beinke Phone (512) 479-6403

Company ARTER & HADDEN, LLP

Address 100 Congress Ave., Ste. 1800

City Austin State TX ZIP 78701-4053

2 Your Internal Billing Reference Information 70404/83441

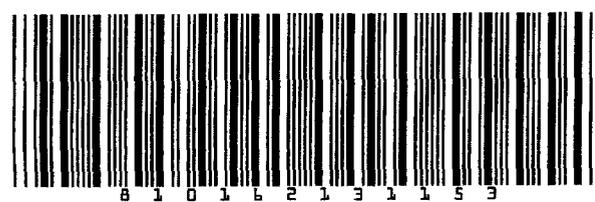
3 To (HFA-305) Recipient's Name Dockets Mgmt Branch

Company Food and Drug Administration

Address 5630 Fishers Lane, Room 1061

City Rockville State MD ZIP 20852

For HOLD at FedEx Location check here For WEEKEND Delivery check here



4a Express Package Service Packages under 150 lbs. FedEx Priority Overnight, FedEx First Overnight, FedEx 2Day, FedEx Express Saver

4b Express Freight Service Packages over 150 lbs. FedEx Overnight Freight, FedEx 2Day Freight, FedEx Express Saver Freight

5 Packaging FedEx Letter, FedEx Pak, FedEx Box, FedEx Tube, Other Pkg.

6 Special Handling Does this shipment contain dangerous goods? Dry Ice, Cargo Aircraft Only

7 Payment Bill to: Sender, Recipient, Third Party, Credit Card, Cash/Check



Total Packages, Total Weight, Total Declared Value, Total Charges

*When declaring a value higher than \$100 per shipment, you pay an additional charge.

8 Release Signature

Your signature authorizes Federal Express to deliver this shipment without obtaining a signature and agrees to indemnify and hold harmless Federal Express from any resulting claims.

Questions? Call 1-800-Go-FedEx (800)463-3339

322