

LAW OFFICES  
JACOB, MEDINGER & FINNEGAN, LLP

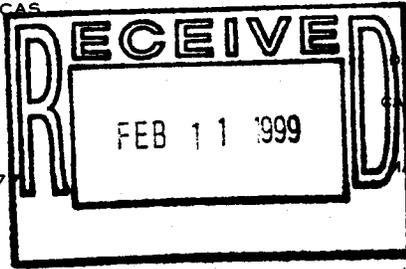
1270 AVENUE OF THE AMERICAS

ROCKEFELLER CENTER

NEW YORK, N. Y. 10020

(212) 332-7700

TELECOPIER: (212) 332-7777



PETER ALEXANDER CROSS, P.C.  
TIMOTHY M. FINNEGAN, P.C.  
EDWIN J. JACOB, P.C.  
ANN T. LADD  
GLENN J. POGUST  
BARRY S. SCHAEVITZ  
CHESTER J. WRABLESKI, P.C.

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NANCY RUTH RYAN  
JUN CHUL WHANG

OF COUNSEL  
JOHN E. FORTUNATO  
FRANK H. MEDINGER

February 10, 1999

**Via Federal Express**

C.W. Jameson, Ph.D.  
National Toxicology Program  
Report on Carcinogens  
Building 4401 Room 3127  
79 Alexander Drive  
Research Triangle Park, NC 27709

Dear Dr. Jameson:

Enclosed are 15 copies of United States Tobacco Company's Supplemental Comments regarding the National Toxicology Program's consideration of smokeless tobacco for listing in the Ninth Report on Carcinogens. The purpose of this submission is to bring to NTP's attention two recently published case-control studies relating to smokeless tobacco and oral cancer.

I understand that NTP has not yet made its final recommendation to the Secretary of Health and Human Services regarding the listing of smokeless tobacco in the Ninth Report on Carcinogens, and I trust that NTP will consider the enclosed submission in making its final recommendation.

Please contact me if you have any questions regarding the enclosed submission.

Very truly yours,

Chester J. Wroblewski

Enc.

**National Toxicology Program  
Review of Smokeless Tobacco  
for Possible Listing in the  
Ninth Report on Carcinogens**

**Supplemental Comments of  
United States Tobacco Company**

**February 10, 1999**

**Supplemental Comments of**  
**United States Tobacco Company**  
**regarding**  
**National Toxicology Program Review of Smokeless Tobacco**  
**for Possible Listing in the Ninth Report on Carcinogens**

United States Tobacco Company, together with several other manufacturers of smokeless tobacco products, submitted comments to the National Toxicology Program (“NTP”) on October 15, 1997 in connection with NTP’s consideration of smokeless tobacco for listing in the Ninth Report on Carcinogens. Based upon several analyses of the epidemiological and experimental data relating to smokeless tobacco and cancer furnished with those comments, the smokeless tobacco manufacturers submitted that NTP should not classify smokeless tobacco as either “known to be a human carcinogen” or “reasonably anticipated to be a human carcinogen.”

Among the analyses submitted with the smokeless tobacco manufacturers’ October 1997 comments was one by Dr. Kenneth D. MacRae, a Reader in Medical Statistics at the Imperial College School of Medicine of the University of London,

a Fellow of the Royal Statistical Society and a member of the editorial committee of the British Medical Journal. Dr. MacRae reviewed the epidemiological data relating to smokeless tobacco and cancer, and concluded as follows:

It is my opinion that the epidemiological data do not support the conclusion that smokeless tobacco has been shown to be a cause of cancer in humans. Nor, in my opinion, does the epidemiological data, taken as a whole, support a finding that the use of smokeless tobacco is a risk factor for oral cancer. Accordingly, I do not believe that the epidemiological data support NTP's classifying smokeless tobacco among substances that are either "known to be human carcinogens" or "reasonably anticipated to be human carcinogens."<sup>1</sup>

The purpose of these supplemental comments is to bring to NTP's attention two case-control studies relating to smokeless tobacco and oral cancer which were published in 1998 and which underscore the validity of Dr. MacRae's 1997 conclusion. Copies of the two studies are being furnished with these comments. Both case-control studies were carried out in Sweden where a substantial portion of the adult population is reported to use smokeless tobacco. Both studies reported that there was no significantly increased risk of oral cancer associated with the use of smokeless tobacco in their study populations.

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<sup>1</sup> Submission of Kenneth D. MacRae, Ph.D. to NTP dated October 10, 1997 at pages 2-3.

Schildt, et al., (1998) reported an odds ratio of 0.7 (95% CI 0.4-1.1) for active snuff users. The authors concluded that “our results do not support any association between the use of oral snuff and oral cancer.”<sup>2</sup> Lewin, et al., (1998) examined the possible relationship between oral snuff and head and neck cancer. The authors stated that “[i]n our study, relative risks were usually close to RR = 1. Age at start, total number of years of use, and total amount used in a lifetime had little or no impact on RR.”<sup>3</sup> The authors concluded that “[o]verall, the use of oral snuff had little or no effect on risk.”<sup>4</sup>

United States Tobacco Company submits that these recently published studies, together with the analyses submitted in 1997, demonstrate that NTP should not classify smokeless tobacco as either “known to be a human carcinogen” or “reasonably anticipated to be a human carcinogen.”

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<sup>2</sup> Elsy-Britt Schildt, et al., *Oral Snuff, Smoking Habits and Alcohol Consumption in Relation to Oral Cancer in a Swedish Case-Control Study*, Int. J. Cancer: 77: 341-346, at 345 (1998).

<sup>3</sup> Freddi Lewin, et al., *Smoking Tobacco, Oral Snuff, and Alcohol in the Etiology of Squamous Cell Carcinoma of the Head and Neck. A Population-Based Case-Referent Study in Sweden*, Cancer, 82(7): 1367-1375, at 1374 (1998).

<sup>4</sup> Id. at 1369.