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February 5, 2002

The Honorable Donald S. Clark  
Secretary  
Federal Trade Commission  
600 Pennsylvania Avenue, NW  
Washington, DC 20580

Re: Request for Advisory Opinion

Dear Secretary Clark:

U.S. Smokeless Tobacco Company ("USSTC"), a subsidiary of UST Inc. ("UST"), requests that the Commission, pursuant to section 1.1 of its Rules of Practice, issue an advisory opinion regarding the acceptability of communicating in advertising that smokeless tobacco products are considered to be a significantly reduced risk alternative as compared to cigarette smoking. Such action by the Commission would address an issue of significant public interest to adult tobacco consumers, USSTC, and other smokeless tobacco manufacturers.

For decades, the public health community in the United States has asserted that cigarette smoking is the most deadly epidemic of modern times. For almost as long, the message of the public health community to cigarette smokers has been monolithic: stop all use of tobacco. Over the past several years, however, an increasing number of public health advocates have voiced doubts about what some have called the "quit or die" approach to smoking cessation. Rather than rely entirely on programs intended to achieve total cessation of tobacco use, this segment of the public health community is urging that a more pragmatic goal be adopted -- that of tobacco "harm reduction." One method of achieving tobacco harm reduction, according to a growing number of researchers, is to encourage those cigarette smokers who do not quit to switch to smokeless tobacco products.

The FTC may wish to consider holding a workshop to address the appropriateness of conveying tobacco harm reduction information as part of smokeless tobacco advertising. A workshop would assist in educating the Commission prior to the issuance of an advisory opinion, and would facilitate public discussion of this novel and important issue.

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## **I. Introduction**

Since the Surgeon General's Report in 1964,<sup>1</sup> there has been substantial public health discussion about the potential health effects of tobacco use. Various public health organizations have identified the risks of cigarette smoking as including cancer (*e.g.*, lung, oral cavity, esophagus, larynx, pancreas, bladder, kidney), chronic obstructive pulmonary disease, myocardial infarction, and stroke.<sup>2</sup> The Surgeon General has indicated that the ideal way to avoid such health risks is to abstain from cigarette smoking.<sup>3</sup> Nonetheless, 47 to 50 million adults in the U.S. continue to smoke cigarettes.<sup>4</sup> This number represents approximately 25 percent of all U.S. adults.<sup>5</sup>

The Surgeon General determined in 1986 that use of smokeless tobacco products "can cause cancer."<sup>6</sup> Moreover, federally-mandated rotating warnings on smokeless tobacco product packaging and advertising state that smokeless tobacco "may cause mouth cancer," "may cause gum disease and tooth loss," and "is not a safe alternative to cigarettes."<sup>7</sup> There is, however, a

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<sup>1</sup> U.S. Department of Health Education & Welfare, *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service* (1964).

<sup>2</sup> Stratton K, Sherry P, Wallace R, Bondurant S (eds.). *Clearing the smoke. Assessing the science base for tobacco harm reduction.* Institute of Medicine. National Academy Press, Washington, D.C., 2001, at pp. 367-68.

<sup>3</sup> U.S. Department of Health & Human Services, *Preventing Tobacco Use Among Young People: A Report of the Surgeon General* (1994); *see also Smoking As A Health Hazard*, American College of Cardiology Position Statement, available at <http://www.acc.org/clinical/position/72565.pdf>.

<sup>4</sup> The National Center For Chronic Disease Prevention and Health Promotion ("National Center For Chronic Disease Prevention") estimates that 47 million adults in the United States smoke cigarettes. *Targeting Tobacco Use: The Nation's Leading Cause of Death*, Tobacco Information and Prevention Source ("TIPS") (2001). The U.S. Department of Health and Human Services ("HHS") estimates that more than 57 million Americans currently smoke cigarettes. *Preventing Death and Disease From Tobacco Use*, Fact Sheet (Jan. 8, 2001). Other reports suggest that the number of smokers in the United States is between 46.5 and 50 million. *Cigarette Smoking Among Adults - United States, 1999, MMWR Highlights* (Oct. 12, 2001) Vol. 50, No. 40; *Treating Tobacco Use and Dependence*, U.S. Public Health Service, Fact Sheet (June 2000).

<sup>5</sup> The National Center For Chronic Disease Prevention estimates that the adult smoking rate was 23.5 percent in 1999. *Cigarette Smoking Among Adults - United States, 1999, MMWR Highlights* (Oct. 12, 2001), Vol. 50, No. 40. HHS estimates that 25 percent of all adults smoke. U.S. Public Health Service, *Treating Tobacco Use and Dependence*, Fact Sheet (June 2000).

<sup>6</sup> U.S. Department of Health & Human Services, *The Health Consequences of Using Smokeless Tobacco: A Report of the Advisory Committee to the Surgeon General* (1986).

<sup>7</sup> Comprehensive Smokeless Tobacco Health Education Act of 1986, 15 U.S.C. §§ 4401-4408.

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growing body of scientific literature that supports the conclusion that cigarette smokers who do not quit can reduce their health risks substantially if they switch to smokeless tobacco products.

USSTC requests that the Commission issue an advisory opinion supporting the use of statements in advertising that provide the public with truthful and substantiated information about the harm reduction that a growing number of public health advocates believe can result from switching from cigarettes to smokeless tobacco products.<sup>8</sup> The benefits of making such information available to consumers would be twofold: it would provide ready access to scientific opinion that otherwise would be difficult or costly to obtain, and it would help adult consumers make better educated choices about the tobacco products they use.<sup>9</sup> As the federal agency with authority over tobacco advertising, the FTC should act affirmatively to provide guidance in this area.

USSTC believes that the types of information it proposes to communicate in advertising are truthful, non-misleading and substantiated. At the same time, USSTC recognizes that cross-category (*i.e.*, smokeless tobacco advertisements directed at adult smokers) comparative advertising of reduced risk tobacco products raises issues which currently are the subject of ongoing public health debate. Providing USSTC with an advisory opinion would inform USSTC and other smokeless tobacco manufacturers of the criteria the FTC will apply when considering such statements. At a minimum, FTC consideration of these issues would advance the public debate on the issue of tobacco harm reduction, and increase the amount of information available to the public regarding reduced risk alternatives to cigarette smoking. Indeed, as part of its consideration of this request, the FTC may wish to hold a public workshop or similar forum to facilitate a full exchange of views on the issues involved.

## **II. Background**

UST Inc. is a New York Stock Exchange listed company with headquarters in Greenwich, Connecticut. USSTC is the world's leading producer and marketer of moist smokeless tobacco or "moist snuff."<sup>10</sup> Copenhagen and Skoal -- two of the Company's brands -- are America's best-selling moist snuff products. Two other brands -- Rooster and Red Seal -- were introduced within the last five years, and hold established positions in the marketplace. A

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<sup>8</sup> This information would be communicated together with other statements in USSTC's smokeless tobacco product advertising.

<sup>9</sup> This request for an advisory opinion concerns tobacco use by adult tobacco consumers. USSTC markets its products to adults only and believes that only adults should be permitted to purchase or use any kind of tobacco product.

<sup>10</sup> Smokeless tobacco comes in several forms: moist snuff, dry snuff, and chewing tobacco, which comes in loose, plug or twist forms.

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new pouch product -- Revel -- is currently in test market. USSTC maintains manufacturing and processing facilities in Franklin Park, Illinois, Hopkinsville, Kentucky, and Nashville, Tennessee.

In 1997, USSTC was the only smokeless tobacco company to support the proposed tobacco resolution. When the proposal failed to pass the Congress, USSTC became the only smokeless tobacco company to enter into the Smokeless Tobacco Master Settlement Agreement ("STMSA") with Attorneys General of various U.S. states and territories. Pursuant to the STMSA, USSTC is providing a total of \$100 million, over a 10-year period, to the American Legacy Foundation for programs to reduce youth usage of tobacco and combat youth substance abuse, and for enforcement purposes.<sup>11</sup> Moreover, USSTC agreed to limitations on its advertising and marketing efforts, even though this put USSTC at a competitive disadvantage with other smokeless tobacco manufacturers.<sup>12</sup>

### **III. Proposed Statements Conveying Information About Tobacco Harm Reduction Would Be Truthful and Non-Deceptive**

#### ***A. Statements in Advertising***

Congress enacted the Comprehensive Smokeless Tobacco Health Education Act of 1986 (Smokeless Act), in part, "to inform the public of any dangers to human health resulting from the use of smokeless tobacco products."<sup>13</sup> Among other things, the Smokeless Act requires that all smokeless tobacco product packaging and advertising (except billboard advertising) display one

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<sup>11</sup>Youth usage of smokeless tobacco, as reported in surveys conducted by various federal government agencies and by the University of Michigan, has declined substantially in recent years. For example, the authors of last year's report on the University of Michigan's Monitoring the Future national survey noted that "[t]he use of smokeless tobacco by teens has been decreasing gradually from recent peak levels in the mid-'90s, and the overall declines have been substantial." Johnston LD, O'Malley PM, Bachman JG. *Monitoring the Future national results on adolescent drug use: Overview of key findings 2000*. (NIH Publication No. 01-4923). Bethesda, MD: National Institute of Drug Abuse, p. 34 (2001).

<sup>12</sup> These restrictions include, among other things, eliminating outdoor advertising of smokeless tobacco products, such as billboards and signs in arenas, stadiums, shopping malls, video-game arcades, and on public transit. In addition, USSTC voluntarily limited itself to one brand-name sponsorship in any 12-month period, and agreed to discontinue distribution to the public of non-tobacco merchandise, such as caps and T-shirts, bearing the brand name, logo, or trademark of any smokeless tobacco product.

<sup>13</sup> 15 U.S.C. § 4401(a)(1).

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of three rotating warnings.<sup>14</sup> USSTC has and will continue to include on all of its smokeless tobacco product packaging and advertising the appropriate federally-mandated health warnings.

USSTC proposes to disseminate advertisements with the following or similar statements:<sup>15</sup>

*The Surgeon General in 1986 concluded that smokeless tobacco “is not a safe substitute for smoking cigarettes.” While not asserting that smokeless tobacco is “safe,” many researchers in the public health community have expressed the opinion that the use of smokeless tobacco involves significantly less risk of adverse health effects than smoking cigarettes. For those smokers who do not quit, a growing number of researchers advocate switching to smokeless tobacco products.*

As the scientific publications discussed below make clear, this statement accurately references the views and opinions of a substantial number of respected public health advocates and researchers that use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking. Indeed, there is considerable agreement in the scientific community on this point.<sup>16</sup> The statement also recognizes the conclusion of the 1986 Surgeon General’s Report, while communicating that a growing number of public health advocates and researchers propose use of smokeless tobacco products as a reduced risk product for those cigarette smokers who do not quit. As explained below, this representation is both truthful and substantiated.

## **B. Evidentiary Standard Under Section 5**

Section 5 of the Federal Trade Commission Act<sup>17</sup> requires a reasonable basis for all express and implied claims conveyed by advertising statements. The level of substantiation

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<sup>14</sup> The Smokeless Act mandates three different warnings: *WARNING: THIS PRODUCT MAY CAUSE MOUTH CANCER; WARNING: THIS PRODUCT MAY CAUSE GUM DISEASE AND TOOTH LOSS; WARNING: THIS PRODUCT IS NOT A SAFE ALTERNATIVE TO CIGARETTES.* Id. § 4402(a)(1).

<sup>15</sup> USSTC recognizes that the Commission’s practice is not to pre-approve any particular advertisement and it does not seek such approval. The language cited is included for illustrative purposes; USSTC’s request for an advisory opinion relates to its desire to communicate to adult consumers the broader concept of tobacco harm reduction through cross-category comparative statements in its advertising.

<sup>16</sup> Attachment A contains a discussion of significant issues relating to smokeless tobacco in the context of tobacco harm reduction, together with excerpts from 50 scientific publications, many of which were peer-reviewed, that assert or support the proposition that the use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking.

<sup>17</sup> 15 U.S.C. §§ 41 *et seq.*

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required to meet this standard largely depends on the nature of the claims being made, how they are presented in the context of the entire advertisement, and how they are qualified.<sup>18</sup> In providing guidance for health and safety claims by dietary supplement manufacturers, the FTC has described the substantiation standard as follows:

The FTC's standard for evaluating substantiation is sufficiently flexible to ensure that consumers have access to information about emerging areas of science. At the same time, it is sufficiently rigorous to ensure that consumers can have confidence in the accuracy of information presented in advertising.<sup>19</sup>

With regard to statements in advertising related to tobacco harm reduction issues, such as those proposed for smokeless tobacco, a relatively high level of substantiation -- "competent and reliable scientific evidence" -- may be required.<sup>20</sup>

**C. *Representations in the Proposed Statements are Adequately Substantiated***

USSTC possesses a reasonable basis for all express and implied claims conveyed by its proposed statements. As reflected in Attachment A, there is considerable agreement in the scientific community that the use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking. In the past several years, dozens of scientific publications -- many of which were peer reviewed -- have asserted or supported this view.<sup>21</sup> There is also growing support in the public health community that, as part of an overall strategy to reduce harm from tobacco use, cigarette smokers who do not quit should be encouraged to switch to smokeless tobacco products.<sup>22</sup>

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<sup>18</sup> See *In re Cliffdale Assocs., Inc.*, 103 F.T.C. 110, 176 (1984), reprinted in an appendix to a letter dated Oct. 14, 1983, from the Commission to the Honorable John D. Dingell, Chairman, Committee on Energy and Commerce, U.S. House of Representatives ("Deception Statement").

<sup>19</sup> *Dietary Supplements: An Advertising Guide for Industry* 8 (1998).

<sup>20</sup> Competent and reliable scientific evidence is often defined as "tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." *Id.* at 9.

<sup>21</sup> See Attachment A.

<sup>22</sup> *Id.* at 6-8.

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At the same time, it should be noted that some critics reject “reduced harm” strategies, favoring only those public health strategies aimed at preventing or stopping tobacco use altogether.<sup>23</sup> And a recent report of the Institute of Medicine calls for more testing of the harm reduction benefits of smokeless tobacco products before urging their use as part of a tobacco harm reduction strategy.<sup>24</sup>

USSTC’s proposed statements, of which the above text is a possible example, accurately portray the views of public health researchers about the risks of smokeless tobacco as compared to cigarette smoking. The statements also would convey that a growing number of researchers advocate that smokers who do not quit be encouraged to switch to smokeless tobacco products. USSTC has taken care not to overstate the evidence or its significance. In addition, it acknowledges the Surgeon General’s conclusion concerning smokeless tobacco products,<sup>25</sup> while informing the public about the views of public health researchers who contend that smokeless tobacco is a reduced risk alternative to cigarette smoking.<sup>26</sup>

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<sup>23</sup> *Id.* at 8-9.

<sup>24</sup> Stratton K, Sherry P, Wallace R, Bondurant S (eds.). *Clearing the smoke. Assessing the science base for tobacco harm reduction.* Institute of Medicine. National Academy Press, Washington, D.C., 2001, discussed in Attachment A at 1-3.

<sup>25</sup> *See, e.g., FTC v. National Comm’n on Egg Nutrition*, 517 F.2d 485 (7th Cir. 1975).

<sup>26</sup> For purposes of background, Attachment B presents an overview of the scientific literature regarding smokeless tobacco and health. While it is USSTC’s position that smokeless tobacco has not been shown to be a cause of any human disease, it is not necessary to agree with that position or resolve that issue in order to accept the proposition that smokeless tobacco has a significant and legitimate role to play in a public health strategy aimed at tobacco harm reduction.

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**IV. The FTC Should Provide an Advisory Opinion to USSTC to Encourage the Communication of Useful and Accurate Information to Adult Consumers**

**A. *The FTC Has Jurisdiction and is the Appropriate Agency to Consider USSTC's Proposed Statements and to Issue an Advisory Opinion***

USSTC respectfully requests that the FTC provide an advisory opinion permitting advertising which incorporates information regarding the current debate about tobacco harm reduction, such as the exemplar statement set forth in section III.A. above. USSTC currently does not make cross-category comparative statements in its advertising.

The Commission may issue advisory opinions with respect to an intended course of action when “[t]he matter involves a substantial or novel question of fact or law and there is no clear Commission or court precedent” or “[t]he subject matter of the request and consequent publication of Commission advice is of significant public interest.”<sup>27</sup>

The Commission is the appropriate agency to provide guidance on the proposed comparative statements for smokeless tobacco products. It has direct authority over smokeless tobacco advertising under the Federal Trade Commission Act and the Smokeless Act. Further, the FTC is uniquely experienced in addressing the kind of health-related statements at issue here and in providing guidance to business. For example, in its *Enforcement Policy Statement on Food Advertising*, the Commission provided guidance on the use of nutrient content and health claims in food advertising,<sup>28</sup> and more recently it provided guidance on dietary supplement advertising claims.<sup>29</sup> These and other business and consumer education efforts by the Commission<sup>30</sup> have provided a measure of certainty to companies seeking to advertise certain attributes of their products, and provided information to consumers in an unsettled legal environment. Commission guidance with respect to comparative health risk statements for smokeless tobacco products would provide similar benefits to business and adult consumers.

USSTC recognizes, of course, the widespread interest within the government regarding issues relating to tobacco products generally, and understands the FTC may wish to consult with

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<sup>27</sup> 16 C.F.R. § 1.1 (a)(1)(2).

<sup>28</sup> This policy statement followed the Food and Drug Administration's issuance of food labeling regulations implementing the Nutrition Labeling and Education Act of 1990.

<sup>29</sup> *Dietary Supplements: An Advertising Guide For Industry* (1998).

<sup>30</sup> See, e.g., *Complying with the Made in USA Standard* (Dec. 1998); *Dot Com Disclosures: Information about Online Advertising* (2000).

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agencies within the Department of Health and Human Services, among others, in developing the requested advisory opinion.<sup>31</sup>

**B. *An Advisory Opinion is Warranted Because Cross-Category Comparative Reduced Risk Statements Present Novel Legal Issues for Which There is No Clear Precedent***

There is little doubt that cross-category comparative reduced risk statements in smokeless tobacco advertising raise novel legal issues. Although principles underlying the Commission's regulation of health claims in food and dietary supplement advertising, as well as its actions in prior tobacco advertising matters,<sup>32</sup> are relevant, there is no clear precedent governing the use of cross-category comparative reduced risk statements in the advertising of tobacco. The Commission has not addressed the complex issues involved here concerning tobacco use and the views of the public health community.

**C. *The Tobacco Harm Reduction Statements at Issue Are of Significant Public Interest to the Consuming Public and Are Best Addressed Through an Advisory Opinion***

The subject matter of the requested advisory opinion and its publication are of significant public interest. At stake are important issues of public health and the ready availability of accurate information about comparative health risks. An advisory opinion that addresses parameters for reduced risk statements in advertising will encourage the publication of accurate information about the comparative risks associated with the use of various forms of tobacco and help adult consumers make more informed choices about the tobacco products they use.

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<sup>31</sup> For example, a coalition of public health organizations and anti-smoking advocacy groups recently petitioned FDA to regulate what the petitioners believe to be five non-traditional tobacco or nicotine products, including tobacco lozenges, nicotine water, and three brands of so-called "safer" cigarettes, under the Food, Drug, and Cosmetic Act as drugs, drug delivery devices or food products.

<sup>32</sup> In April 2000, Santa Fe Natural Tobacco Company, Inc., and Alternative Cigarettes, Inc., entered into agreements with the Federal Trade Commission stemming from allegations that the two companies implied in their advertisements that their cigarettes were safer to smoke than other cigarettes because they contained no additives. The complaints also alleged that the two companies falsely implied in their advertising that herbal cigarettes did not pose the health risks associated with tobacco cigarettes. *In re Santa Fe Natural Tobacco Co.*, FTC File No. 992-3026 (Apr. 27, 2000); *In re Alternative Cigarettes, Inc.*, FTC File No. 992-3022 (Apr. 27, 2000). See also *In re R.J. Reynolds Tobacco Co.*, FTC File No. 992-3025 (Mar. 3, 1999). These matters, however, dealt primarily with questions of ad interpretation, not whether there was sufficient evidence to substantiate what were viewed as implied claims that the advertised cigarettes were safer than conventional cigarettes.

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In recent years, FTC advertising policy has consistently recognized the need to permit proponents of all sides of an issue to make their cases to the public, allowing consumers to make informed choices.<sup>33</sup> For example, in the area of food advertising, the Commission's Enforcement Policy Statement avoided overly stringent regulatory requirements that would inhibit or prevent truthful claims about the relationship between diet and disease. The Commission recognized that, "there may be certain limited instances in which carefully qualified health claims may be permitted under Section 5 although not yet authorized by the FDA, if the claims are expressly qualified to convey clearly and fully the extent of the scientific support."<sup>34</sup>

Some of those who have studied the history of tobacco advertising believe that adverse consequences may result from undue restrictions on health-related claims. In *The Ghost of Cigarette Advertising Past*,<sup>35</sup> an analysis of over 40 years of the FTC's efforts concerning cigarette advertising, Dr. John E. Calfee argues that restrictions on the cigarette manufacturers' ability to describe important product attributes effectively stifled incentives to produce and market lower risk alternatives. According to Dr. Calfee, such restrictions ultimately undermine competition among tobacco products and create adverse consequences for public health.<sup>36</sup> Allowing substantiated and properly qualified cross-category comparative reduced risk statements in advertising, as proposed here, will avoid such effects.

To assist in educating itself prior to the issuance of an advisory opinion, the FTC may wish to hold a workshop, or similar public forum, to facilitate public discussion of harm reduction benefits and the appropriateness of cross-category comparative reduced risk statements in tobacco advertising. Panels could include medical and public health experts, public interest and advocacy groups, industry members, and representatives from other federal and state agencies. Such workshops have proved quite successful in shedding light on complex issues faced by the Commission, particularly in matters involving public health.<sup>37</sup> A workshop to air the scientific and advertising issues involved here could be similarly beneficial to the Commission, as well as to the public in general.

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<sup>33</sup> See, e.g., J. Howard Beales, III & Timothy J. Muris, *State and Federal Regulation of National Advertising* 81 (1993). See also *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, \_\_\_, 121 S. Ct. 2404, 2426 (2001) in which the Court stated, "[t]obacco retailers and manufacturers have an interest in conveying truthful information about their products to adults, and adults have a corresponding interest in receiving truthful information about tobacco products."

<sup>34</sup> *Enforcement Policy Statement on Food Advertising* 20 (May 1994).

<sup>35</sup> *Regulation*, Vol. 10, No. 02 (1986), reprinted in *Regulation* (Summer 1997).

<sup>36</sup> *Id.* at 38-39.

<sup>37</sup> The Commission's 1997 conference on weight loss products and programs, for example, increased public awareness of the benefits of small amounts of weight loss and led to highly successful self-regulatory efforts.

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We appreciate your attention to this matter. Please contact me at (202) 508-6025, or my colleague, Dana Rosenfeld, at (202) 508-6032, for any further information you may require.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Daniel C. Schwartz". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Daniel C. Schwartz

Enclosures

cc: Chairman Timothy J. Muris  
Commissioner Sheila F. Anthony  
Commissioner Mozelle W. Thompson  
Commissioner Orson Swindle  
Commissioner Thomas B. Leary

J. Howard Beales, III, Director, Bureau of Consumer Protection  
Lydia B. Parnes, Deputy Director, Bureau of Consumer Protection  
C. Lee Peeler, Deputy Director, Bureau of Consumer Protection  
Mary K. Engle, Acting Associate Director, Division of Advertising Practices  
Gerard Butters, Assistant Director, Bureau of Economics

## **An Overview of Significant Issues Relating to Smokeless Tobacco in the Context of Tobacco Harm Reduction**

### **I. Introduction**

Numerous methods have been suggested by public health advocates for achieving tobacco harm reduction, including urging cigarette smokers to smoke fewer cigarettes, developing “less hazardous” cigarettes and creating alternative nicotine delivery systems, such as nicotine inhalers. A growing number of tobacco harm reduction proponents, however, are arguing for an additional method for achieving their goal. Based on the generally accepted view in the scientific community that smokeless tobacco use involves significantly less risk of adverse health effects than cigarette smoking, they would encourage those cigarette smokers who do not quit to switch to smokeless tobacco products. Set forth below is a review of some of the more important issues relating to smokeless tobacco in the context of tobacco harm reduction.

### **II. The IOM Report**

A logical starting point for discussion of smokeless tobacco in the context of tobacco harm reduction is the 600 page report issued last year by the Institute of Medicine (IOM) entitled “Clearing the Smoke. Assessing the Science Base for Tobacco Harm Reduction” (IOM Report). The IOM was established in 1970 by the National Academy of Sciences to examine policy matters pertaining to public health, and acts under the Academy’s congressional charter to be an advisor to the federal government and to assess issues relating to medical care, research and education. The IOM tobacco harm reduction project was undertaken at the request of, and was supported by, the U.S. Food and Drug Administration.

The IOM Report explains the need for a tobacco harm reduction strategy as follows:

Despite overwhelming evidence and widespread recognition that tobacco use poses a serious risk to health, some tobacco users cannot or will not quit. For those addicted tobacco users who do not quit, reducing the health risks of tobacco products themselves may be a sensible response. This is why many public health leaders believe that what has come to be called “harm reduction” must be included as a subsidiary component of a comprehensive public health policy toward tobacco.<sup>1</sup>

Tobacco “harm reduction” is defined in the IOM Report as follows:

*For the purposes of this report, a product is harm-reducing if it lowers total tobacco-related mortality and morbidity even though use of that product may involve continued exposure to tobacco-related toxicants. Many different policy strategies may contribute to harm reduction. However, this report focuses on tobacco products that may be less harmful or on pharmaceutical preparations that may be used alone or concomitantly with decreased use of conventional tobacco.<sup>2</sup>*

It is clear from this definition of “harm reduction” that, in the view of the IOM, it is not necessary to demonstrate that a product is “safe” or “harmless” in order for that product to play a role in tobacco harm reduction.<sup>3</sup>

The IOM Report had the following to say with respect to smokeless tobacco products:

Smokeless tobacco products are associated with oral cavity cancers, and a dose-response relationship exists. However, the overall risk is lower than for cigarette smoking, and some products such as Swedish snus may have no increased risk. It may be

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<sup>1</sup> Stratton K, Shetty P, Wallace R, Bondurant S (eds.). Clearing the smoke. Assessing the science base for tobacco harm reduction. Institute of Medicine. National Academy Press, Washington, D.C., 2001, at p. 201.

<sup>2</sup> Id. at p. 2.

<sup>3</sup> It should be noted that it is USSTC’s position that smokeless tobacco has not been shown to be a cause of any human disease, and nothing in this review should be interpreted as a concession by USSTC to the contrary. It is not necessary, however, to agree with USSTC’s position on the smokeless tobacco and health issue in order to accept the proposition that smokeless tobacco has a significant and legitimate role to play in a public health strategy aimed at tobacco harm reduction.

considered that such products could be used as a PREP [Potential Reduced-Exposure Product] for persons addicted to nicotine, but these products must undergo testing as PREPs using the guidelines and research agenda contained herein.<sup>4</sup>

There has been criticism of the IOM Report's recommendation that all products proposed for use in the context of a tobacco harm reduction strategy require substantial and elaborate scientific testing to demonstrate their harm reduction benefits. For example, Clive Bates of the UK's Action on Smoking and Health has made the following comments:

The report places very substantial evidential requirement on those seeking to bring PREPs to the market with a health related claim. The easiest approach for the public health and regulatory community is to demand near complete certainty before approving the marketing of any PREPs. At first sight this appears prudent, but it is actually a *transfer* of risk from the regulator to the smoker. With insurmountable evidential hurdles in place, the regulator may sleep easy in a cocoon of professional skepticism.<sup>5</sup>

The IOM Report's focus on the need for further research and demonstration of harm reduction benefits may be understandable in the context of new or novel tobacco products or so-called "safer" cigarettes. When it comes to smokeless tobacco, however, there is considerable agreement in the scientific community that the use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking.

### **III. Scientific Support for the Proposition That Smokeless Tobacco Involves Significantly Less Risk than Cigarette Smoking**

Attached to this review is a compilation of excerpts from 50 publications in the scientific literature, many of which were peer-reviewed, which assert or support the proposition that the

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<sup>4</sup> Stratton K, et al. Clearing the smoke. Assessing the science base for tobacco harm reduction, at p. 434.

use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking. These publications were authored or co-authored by over 50 researchers or public health advocates and appeared in approximately 40 different scientific journals or books, most having been published over the past several years.

Dr. Brad Rodu, a Professor in the Department of Pathology at the University of Alabama at Birmingham and a Senior Scientist at the UAB Comprehensive Cancer Center, and several of his colleagues, are the most widely published researchers on the issue of smokeless tobacco and tobacco harm reduction. They have authored nearly a dozen publications and Dr. Rodu has published a book entitled “For Smokers Only – How Smokeless Tobacco Can Save Your Life,” in which he maintains that smokeless tobacco is “98 percent less dangerous” than cigarette smoking.

Dr. Rodu’s analysis is based on two assumptions. First, he accepts the view of the Centers for Disease Control and Prevention that cigarette smoking is responsible for approximately 419,000 deaths each year in the United States, as follows:<sup>6</sup>

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<sup>5</sup> Bates C. Clearing the smoke or muddying the water? (Editorial) *Tobacco Control* 2001; 10: 87-88.

<sup>6</sup> Centers for Disease Control and Prevention. Cigarette smoking – attributable mortality and years of potential life lost. *MMWR* 1993; 42: 645-649.

Cancers	
- Lip, oral cavity, pharynx	6,475
- Esophagus, larynx, kidney, bladder, etc.	24,927
- Trachea, lung, bronchus	116,920
Cardiovascular diseases	179,820
Respiratory diseases	84,475
Pediatric diseases	1,711
Burns	1,362
Environmental tobacco smoke	3,000
TOTAL	418,690

Second, Dr. Rodu calculates that if all 46 million cigarette smokers in the United States switched to smokeless tobacco there would be “at worst, 6,000 deaths from oral cancer” each year.

Dr. Rodu has summarized his analysis as follows:

If all smokers were instead addicted to smokeless tobacco, only 12,000 new cases of oral cancer (with a 50 percent survival rate) could be expected each year. This is only one-twentieth of all cancers that now result from smoking, and one-tenth of smoking related lung cancer cases! I haven't even mentioned the reduction in heart disease and emphysema deaths yet. *If all 46 million smokers used smokeless tobacco instead, the United States would see, at worst, 6,000 deaths from oral cancer, versus the current 419,000 deaths from smoking-related cancers, heart problems, and lung disease.*<sup>7</sup>

Dr. Rodu and one of his colleagues have also performed an analysis from which they conclude that a cigarette smoker's life is shortened by 7.8 years as a result of his smoking, compared to 15 days for a smokeless tobacco user:

We estimated the life expectancy of 35-year old white males with three patterns of tobacco use: non-users, cigarette smokers and smokeless-tobacco users.

\* \* \*

The results indicate that the average remaining life expectancy of a 35-year old smokeless-tobacco user is 45.92 years, only 0.04 year less than that of a non-user. . . . This 15-day reduction in life expectancy is in sharp contrast to the 7.8 years lost by smokers.<sup>8</sup>

#### **IV. Recommendation That Cigarette Smokers Who Do Not Quit Should Switch to Smokeless Tobacco**

A growing number of tobacco harm reduction proponents recommend that those cigarette smokers who do not quit should switch to smokeless tobacco products. Examples of researchers or public health advocates who recommend this course of action are as follows:

- As early as 1980, LR Kirkland, a physician at Emory University Hospital, made the following proposal in the *New England Journal of Medicine*:

I urge physicians to encourage snuff and chewing tobacco as alternatives to cigarettes. No one disputes the role of snuff and similar products as the cause of oral leukoplakia, but there is a vast difference in the frequencies of oropharyngeal carcinoma and cigarette-induced lung cancer. If five new “dippers” are created to avert creation of one new cigarette smoker, then progress has been made.<sup>9</sup>

- In 1985, four British researchers made the following observation in the *Lancet*:

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<sup>7</sup> Rodu B. For smokers only. How smokeless tobacco can save your life. Sulzburger & Graham Publishing, Ltd., New York; 1995 at p. 131.

<sup>8</sup> Rodu B, Cole P. Tobacco-related mortality. (Letter to the Editor). *Nature* 1994; 370: 184.

<sup>9</sup> Kirkland LR. The nonsmoking uses of tobacco. (Letter to the Editor). *NEJM* 1980; 303: 165.

Unlike tobacco smoking, use of wet snuff carries no risk of lung cancer, bronchitis, or emphysema, and no risk of cardiovascular disease has been demonstrated.

\* \* \*

If all smokers in Britain switched to [smokeless tobacco] sachets about 50 000 premature deaths per year might eventually be saved at an annual cost of less than 1000 deaths from mouth cancer.<sup>10</sup>

- Since 1995, Dr. Rodu and his colleagues have strongly recommended that “inveterate” cigarette smokers switch from cigarettes to smokeless tobacco products:

A switch to a safer delivery system, smokeless tobacco, will allow the 46 million smokers in this country (and the people they live with) to live longer, healthier lives.<sup>11</sup>

What do switchers accomplish? Our research shows that they will live, on average, as long as those smokers who quit nicotine altogether. They reduce their risks for smoking-related illness and death, which is the goal of all existing smoking cessation efforts. There is, of course, no debate about the ideal way to achieve this goal: complete tobacco abstinence. But that ideal is not always attainable since many smokers are unable to give up nicotine. Switching to smokeless tobacco is a small compromise with the ideal which reaps large individual and public health gains.<sup>12</sup>

- More recently, Dr. Lars Ramström, Director of the Stockholm Institute for Tobacco Studies, published an article entitled “Snuff – An Alternative Nicotine Delivery System,” in which he made the following statement:

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<sup>10</sup> Russell MAH, Jarvis MJ, West RJ, Feyerabend C. Buccal absorption of nicotine from smokeless tobacco sachets. (Letter to the Editor). *Lancet* 1985; 1: 1370.

<sup>11</sup> Rodu B. For smokers only. How smokeless tobacco can save your life, at p. 18.

While snuff use may entail some health risks, there is good evidence that these are substantially lower than those associated with smoking. Switching from smoking to snuff use would therefore represent a reduction in health risk.<sup>13</sup>

- And a few months ago, Karl Fagerström, a Swedish researcher, was quoted in a *New Scientist* article making a similar recommendation:

Swedish men have the lowest rate of lung cancer in Europe, according to WHO figures, and the lowest risk of dying from a smoking-related disease – just 11 per cent compared with 25 per cent in Europe as a whole. Karl Fagerström of the Helsingborg Smokers' Information Centre, a smoking cessation clinic, is in no doubt that snus should take the credit. "It's very hard to argue that there are other factors responsible," he says. "It's very common to switch from smoking to snus. If they can't give up smoking then I suggest snus because it's much less dangerous than setting fire to tobacco. . . ."<sup>14</sup>

There is no real dispute in the public health community that the use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking. Yet there are some anti-tobacco advocates who object to encouraging cigarette smokers who do not quit to switch to smokeless tobacco products. For example, late last year, Dr. Gregory N. Connolly of the Massachusetts Department of Public Health made the following comments:

Tobacco companies – Swedish or American – want to make money and the health of people is not part of the bottom line. The Swedish experiment could become an "increased harm experiment" where continued smoking is supported, clean indoor air laws weakened, and pharmaceutical companies that promote

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<sup>12</sup> Rodu B, Cole P. Would a switch from cigarettes to smokeless tobacco benefit public health? - Yes. *Priorities* 1995; 7: 24-30.

<sup>13</sup> Ramström L. Snuff – an alternative nicotine delivery system. In: Ferrence R, Slade J, Room R, Pope M (eds.). *Nicotine and public health*. The American Public Health Foundation, Washington D.C., 2000; Chapter 9, at p. 172.

<sup>14</sup> Wilson C. My friend nicotine. *New Scientist* 2001; 10: 28-31, at p. 30.

cessation products driven out of the marketplace. Since tobacco products are not regulated, we should be very cautious in arguing that one product is “safer” than another. It is a dynamic environment where all tobacco manufacturers will work together to promote each other’s products and addiction to nicotine. We should be very careful in choosing our tobacco bedfellows.<sup>15</sup>

## V. **Individual Risk Versus Population Risk**

One concern raised by some in the public health community with respect to “reduced risk” tobacco products is that while a product might reduce the health risk to an individual, the aggregate public health impact on the population might be negative. Thus, for example, it is argued that if a “safer” cigarette reduced the health risks associated with cigarette smoking by 10 percent, but resulted in a 20 percent increase in cigarette use (either through new smokers or by causing some smokers who otherwise would have quit to continue smoking), the aggregate public health impact would be negative. Professor Kenneth E. Warner of the University of Michigan gives the following example:

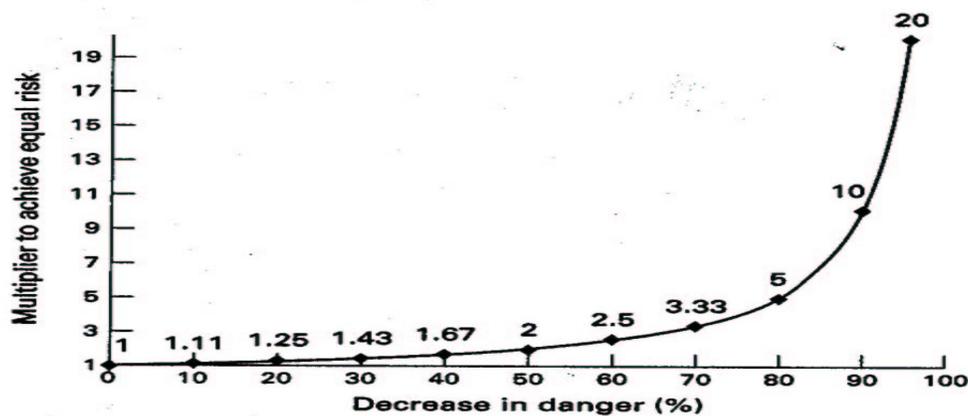
[C]onsider the implications of Star Enterprise’s advertising that its new cigarette, Advance, yields fewer nitrosamines than conventional cigarettes. Informed that most cigarette smoke contains nitrosamines and that nitrosamines are carcinogenic, would smokers preparing to quit flock to the new cigarette instead, believing that it would greatly reduce their risk of smoking-induced lung cancer? The net health consequences are unclear: for those smokers who would have continued smoking anyway, switching to Advance might well reduce risk. For smokers who would have quit, or former smokers induced to start smoking again by the availability of this purportedly “safer” product, the active marketing of a low-nitrosamine cigarette clearly would *increase*

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<sup>15</sup> Connolly GN. Suckers today; smokers tomorrow? *Tobacco Control* 2001; 10: 304.

risk. The net impact would depend on the unpredictable balance between such effects.<sup>16</sup>

Professor Lynn Kozlowski, Head of the Pennsylvania State University Department of Biobehavioral Health, has developed a “risk/use equilibrium” chart<sup>17</sup> to assess the issue of individual risk reduction versus aggregate population impact. The chart compares the “decrease in danger (%)” displayed on the horizontal axis to the “multiplier to achieve equal risk” on the vertical axis.



According to Professor Kozlowski’s analysis, a tobacco product which reduces risk by only 10 percent raises a difficult public health issue because an 11 percent increase in use of the product would offset the risk reduction in the population as a whole, and an increase in excess of 11 percent would result in a negative public health impact on the population as a whole. On the other hand, a tobacco product which results in a reduced risk in excess of 90 percent presents a

<sup>16</sup> Warner KE. Reducing harm to smokers: Methods, their effectiveness and the role of policy. In: *Regulating Tobacco*. Rabin RL, Sugarman SD (eds.) Oxford University Press, Oxford. 2001. Chapter 5, at pp. 133-134.

<sup>17</sup> Kozlowski L, Strasser AA, Giovino GA, Erickson PA, Terza JV. Applying the risk/use equilibrium: use medicinal nicotine now for harm reduction. (Editorial). *Tobacco Control* 2001; 10: 201-203.

relatively easy public health issue since the increase in usage necessary to offset the reduction in risk is so substantial – more than 1,000 percent – that it is highly unlikely to occur.

Given the predominant view in the public health community that the risk of adverse health effects associated with smokeless tobacco products is slight compared to that of cigarette smoking, researchers believe it is highly unlikely the public health benefit of cigarette smokers switching to smokeless tobacco would ever be offset by increased usage of smokeless tobacco.

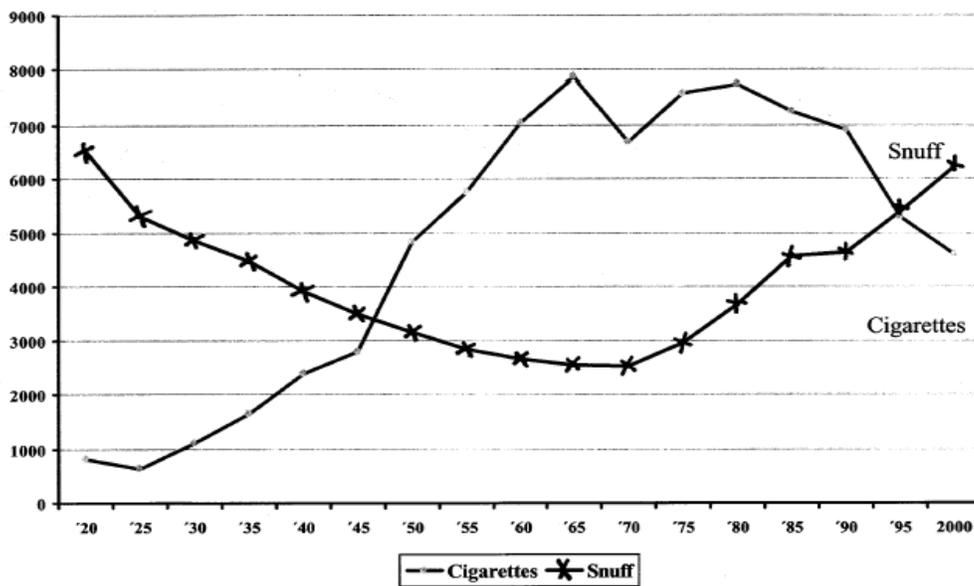
## **VI. The Swedish Experience**

Some proponents of encouraging “inveterate” cigarette smokers to switch to smokeless tobacco products point to the history of cigarette smoking and smokeless tobacco use in Sweden as support for their view. Swedish males have the highest rate of smokeless tobacco use and the lowest rate of cigarette smoking of any Western country, and the daily use of smokeless tobacco by Swedish males now exceeds that of cigarettes (18.2 percent daily smokeless tobacco users versus 17.1 percent daily cigarette smokers).<sup>18</sup> The following chart<sup>19</sup> illustrates the changing pattern of tobacco use in Sweden during most of the past century, including the fact that smokeless tobacco use has overtaken cigarette smoking in recent years for the first time since World War II.

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<sup>18</sup> Henningfield JE, Fagerström KO. Swedish Match Company, Swedish snus and public health: a harm reduction experiment in progress? *Tobacco Control* 2001; 10: 253-257, at p. 254.

<sup>19</sup> Adapted from Swedish Match’s Third Quarter Results, October 23, 2001, as posted on Company’s web site. The figures cited reflect reported taxable shipments of snuff and cigarettes, measured in tons.



Tobacco and health researchers have linked Sweden’s low rate of “tobacco-related mortality” to its high prevalence of smokeless tobacco use and low prevalence of cigarette smoking:

Sweden, with a long tradition of smokeless tobacco use (16% of adult males use smokeless tobacco daily) and the highest penetration of NRT [nicotine replacement therapy] use, is the only European country that has reached (19%) the World Health Organization’s target of 20% smokers in the adult population by the year 2000; about 35% of all nicotine consumed comes from nonsmoked deliver[y] forms. The tobacco-related mortality in Sweden is by far lower than in any other European or North American country, although nicotine consumption may not be lower than in other countries.<sup>20</sup>

Last year’s *New Scientist* article summarized the Swedish experience in the context of tobacco harm reduction:

<sup>20</sup> Balfour DJK, Fagerström KO. Pharmacology of nicotine and its therapeutic use in smoking cessation and neurodegenerative disorders. *Pharmacol Ther* 1996; 72: 51-81, at p. 71.

[S]mokers [in Sweden] aren't faced with the quit-or-die dilemma. Instead of using a nicotine replacement therapy with the aim of quitting both smoking and ultimately nicotine, they can continue using tobacco as a recreational drug, safe in the knowledge that it probably won't kill them. It's all down to a product called "snus," a form of moist ground tobacco that you pop between your lip and gum.<sup>21</sup>

\* \* \*

The "Swedish experiment," as it has come to be known, has inspired some health campaigners to press for a more enlightened approach to the smoking epidemic. It's a concept they call "harm reduction." "If you look at Sweden, we have a living example of the concept in action," says Clive Bates, director of ASH.<sup>22</sup>

Some have raised a question as to whether the Swedish experience is applicable to the United States, asserting that Swedish moist snuff products contain lower levels of so-called tobacco-specific nitrosamines (some of which have been reported to be laboratory carcinogens) than U.S. moist snuff products. For example, Professor Newell Johnson in an article published last year entitled "Tobacco Use and Oral Cancer: A Global Perspective" conceded that "on present evidence, snuff habits as they exist in Scandinavia and probably in the United States carry lower risk of serious health hazards"<sup>23</sup> than cigarette smoking, but also made the following comment:

In Scandinavia it is clear that local snuff is not a major risk factor: two recent case-control studies of oral cancer cases in Sweden have failed to show an association. This is because Swedish snus is not fermented and contains much lower nitrosamine levels than fermented tobaccos. The view that smokeless tobacco use may be associated with a lower risk of oral cancer in the United States has

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<sup>21</sup> Wilson C. My friend nicotine, at p. 29.

<sup>22</sup> Id. at p. 30.

<sup>23</sup> Johnson N. Tobacco use and oral cancer: A global perspective. *J Dent Educ* 2001; 65: 328-339, at p. 328.

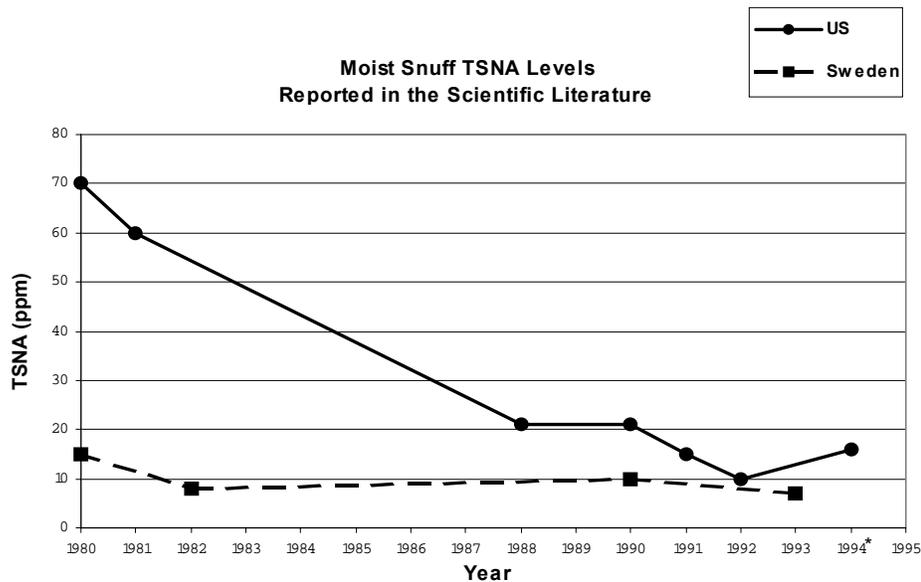
led to a movement to advocate the practice as a less dangerous alternative to smoking and an aid to nicotine withdrawal in those addicted to smoking.<sup>24</sup>

In fact, there is currently no significant difference in tobacco-specific nitrosamine (TSNA) levels in U.S. moist snuff products compared to Swedish moist snuff. Data reported in the scientific literature by researchers from the American Health Foundation, together with data published by Swedish researchers,<sup>25</sup> show that the average levels of TSNA in the major U.S. moist snuff products decreased 77% between 1980 and 1994, and that currently there is no significant difference between the levels of TSNA in those products compared to Swedish moist snuff products. A chart depicting this data follows:

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<sup>24</sup> Id. at pp. 332-333.

<sup>25</sup> Andersson G, Bjornberg G, Curvall M. Oral mucosal changes and nicotine disposition in users of Swedish smokeless tobacco products: A comparative study. *J Oral Pathol Med* 1994; 23: 161-167 (1993 Swedish data); Djordjevic MV, Brunnemann KD, Hoffmann D. The need for regulation of carcinogenic N-Nitrosamines in oral snuff. *Food Chem Toxicol* 1993; 31: 497-501 (1992 U.S. data and all earlier data); Hoffmann D, Djordjevic MV, Fan J, Zang E, Glynn T, Connolly GN. Five leading U.S. commercial brands of moist snuff in 1994: assessment of carcinogenic N-Nitrosamines. *J Natl Cancer Inst* 1995; 87: 1862-1869 (1994 U.S. data).



TSNA = Total of reported levels of NNN, NNK, NAT and NAB on dry weight basis in parts per million

US = Average of reported TSNA levels for leading American moist snuff products which, according to the researchers, “accounted for 84% of the snuff sales on the US market (Maxwell, 1992),” excluding anomalous data for 1986

Sweden = Average of reported TSNA levels for three unidentified Swedish moist snuff products

\* No comparable data reported in the scientific literature for any period after 1994

This view is supported by a report issued in 1997 by the Swedish National Board of Health and Welfare, which concluded:

Recent data suggest that the differences [in TSNA levels reported in American and Swedish moist snuff] have grown smaller, and that it is now questionable to make a sharp distinction between use of American and Swedish moist snuff when assessing risks at least where TSNA content is concerned.<sup>26</sup>

<sup>26</sup> Ahlbom A, Olsson UA, Pershagen G. Health hazards of moist snuff. *SoS Report* 1997; 11:3-29, at p. 7.

## **VII. Conclusions**

Among the conclusions that can be drawn from this review and the attached compilation of statements from the scientific literature are the following:

1. Smokeless tobacco products have a significant and legitimate role to play in a public health strategy aimed at tobacco harm reduction.
2. There is considerable agreement in the scientific community that the use of smokeless tobacco involves significantly less risk of adverse health effects than cigarette smoking.
3. There is growing support in the public health community for including smokeless tobacco as a component of a comprehensive tobacco harm reduction strategy by encouraging those cigarette smokers who do not quit to switch to smokeless tobacco products.

**Statements Published in the Scientific Literature Asserting or Supporting the View  
that Smokeless Tobacco Use Involves Significantly Less Risk  
of Adverse Health Effects Than Cigarette Smoking**

1. Anderson A. Can't quit, won't quit. (Editorial). *New Scientist* 2001; 10: 3.
  - What kills smokers is not the drug they are addicted to but all the disease-causing gunk in the smoke they inhale to get their fix. The good news is that there are now much safer ways of taking nicotine; the bad is that governments are failing to ensure these products are taken up. Across Europe, for instance, cigarettes containing all sorts of untested additives continue to be sold. Yet a comparatively safe form of chewing tobacco is banned.
  
2. Wilson, C. My friend nicotine. *New Scientist* 2001; 10: 28-31.
  - [S]mokers [in Sweden] aren't faced with the quit-or-die dilemma. Instead of using a nicotine replacement therapy with the aim of quitting both smoking and ultimately nicotine, they can continue using tobacco as a recreational drug, safe in the knowledge that it probably won't kill them. It's all down to a product called "snus", a form of moist ground tobacco that you pop between your lip and gum. Snus comes in two forms, either loose or packed in small portions like miniature tea bags. Both deliver nicotine direct to the bloodstream.

Among Sweden's 3.4 million men, snus is more popular than smoking: about 19 per cent use snus and 17 per cent smoke. That's easily the lowest rate of smoking in Europe—half the rate of Norway, for example—and it translates into an excellent health record. Swedish men have the lowest rate of lung cancer in Europe, according to WHO figures, and the lowest risk of dying from a smoking-related disease—just 11 per cent compared with 25 per cent in Europe as a whole. Karl Fagerström of the Helsingborg Smokers' Information Centre, a smoking cessation clinic, is in no doubt that snus should take the credit. "It's very hard to argue that there are other factors responsible," he says. "It's very common to switch from smoking to snus. If they can't give up smoking then I suggest snus because it's much less dangerous than setting fire to tobacco. . . ."

The evidence that snus improves public health becomes even stronger when you consider Swedish women. They hardly touch the stuff—only around 2 per cent use it—so act as a built-in control to the experiment. And their record on smoking-related diseases is nothing out of the ordinary. Swedish women are just as likely as any others to die from smoking, and their lung cancer rates are comparable with those of other Scandinavian countries. (pp. 29 – 30).

3. Asplund K. Snuff – how dangerous is it? The controversy continues. (Editorial). *J Intern Med* 2001; 250; 457-461.

- We are confronted with extremely difficult questions: Are there circumstances that could justify doctors to recommend the use of smokeless tobacco? What about the smoking patient who asks if he/she should try snuff dipping instead? And even more challenging: in pragmatic public health work, is snuff friend or foe?

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Obviously, from a medical point of view, the only reasonable norm is nonuse of tobacco. The goal should be a tobacco-free society. On the route towards this goal, we face enemies that are more perilous than others. My personal opinion is that we should not squander our forces. We should concentrate them on the fight against cigarettes – they are the overwhelming threat to people’s health, snuff being only a mini-monster in comparison. (pp. 459 – 460).

4. Bates C. Clearing the smoke or muddying the water? (Editorial). *Tobacco Control* 2001; 10: 87-88.

- While I do not wish to see a rush of novel tobacco products making health claims, there are immediate real problems arising from the “self serving caution” of regulators. For example, this applies to the refusal of some regulators to approve harm reduction indications for pharmaceutical NRT [nicotine replacement therapy], the regulatory barriers facing a nicotine gum manufacturer that wants to compete directly with cigarettes as a supplier of lifestyle branded nicotine, and the clumsy regulation of certain oral tobaccos that have substantially lower health risks than cigarettes. (p. 88).

5. Cole P, Rodu B. Analytic Epidemiology: cancer causes. *Cancer: principles & practice of Oncology*. Lippincott Williams & Wilkins, Pennsylvania 2001: 241-252.

- **CANCER OF THE ORAL CAVITY (OCC)**. This condition, including cancer of the pharynx, is caused by smoking with a RR [relative risk] of about 5.

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Use of smokeless tobacco imposes a moderate RR of 2 for OCC. However, the risk may be declining because the suspect carcinogens in smokeless

- tobacco, naturally-occurring tobacco-specific nitrosamines (TSNAs), have been reduced over the past two decades. In Sweden, where *per capita* consumption of smokeless tobacco is very high, TSNAs levels are undetectable and recent studies report no OCC attributable to the use of Swedish products. (p. 246).
- During the last 20 years in the USA many anti-smoking campaigns shifted their focus from preventing deaths caused by smoking to preventing tobacco use. If we refocus attention on deaths from smoking we can learn a valuable lesson from Sweden, the only country which has met the World Health Organization's goal of a less than 20% prevalence of smokers. It also has Europe's lowest rates of lung cancer, larynx cancer, OCC, and bladder cancer. How were these benchmarks attained? There may be several explanations, but it is certainly relevant that Sweden has the highest *per capita* use in Europe of smokeless tobacco. (pp. 249 – 50).
6. Galanti MR, Wickholm S, Gilljam H. Between harm and dangers. Oral snuff use, cigarette smoking and problem behaviours in a survey of Swedish male adolescents. *Eur J Public Health* 2001; 11: 340-345.
- The prevalence of smokeless tobacco use (moist snuff) in Sweden is among the highest world-wide and snuff is gaining popularity as a less harmful alternative to cigarettes. (Abstract, p. 340).
  - The use of Swedish oral tobacco (moist snuff) has not been consistently associated with relevant health hazards, and is therefore regarded as relatively safe compared to cigarette smoking. (p. 342).
7. Galanti MR, Nordgren P, Gilljam H. "Nicotine niche" or way out? The use of oral snuff among Swedish current and former smokers. *3<sup>rd</sup> SRNT Europe Conference* 19 – 22 September 2001, p. 52.
- To date, there is no convincing evidence of major adverse health effects associated with the use of the Swedish smokeless tobacco "*snus*". It has also been claimed that *snus* availability may have substantially contributed to lower the adult smoking prevalence.
8. Henningfield JE, Fagerström KO. Swedish Match Company, Swedish snus and public health: a harm reduction experiment in progress? *Tobacco Control* 2001; 10: 253-257.

- The most powerful means to reduce the diseases caused by tobacco use are to prevent the initiation of use and to help users to achieve complete and lasting abstinence. For tobacco users who are unwilling or unable to completely give up their tobacco use, the possibility is increasingly being considered that such persons might be able to reduce their risk of disease and premature mortality by reducing their exposure to tobacco toxins.

\* \* \*

In Sweden, the tobacco marketing and regulatory situation has been different from that of most other countries in several respects, and Sweden has become one of the first developed nations to see a significant decline in tobacco attributable mortality. This decline has been associated with changing consumer preferences and regulatory policies that have contributed to a partial shift in nicotine intake from the most hazardous form (cigarettes) to less hazardous forms (snus form of smokeless tobacco and nicotine replacement medications). It is not clear to us how to apportion the contribution of the aforementioned specific factors in the reduction of overall tobacco attributable mortality risk. Nonetheless, we believe that the situation in Sweden might be considered a real world experiment in harm reduction that is in progress although we are concerned that not all of the signs are positive. (p. 253).

- [R]eductions in smoking are possible in an environment that includes a range of accessible nicotine delivering alternatives to cigarettes. [W]e believe it is probable that for persons who sustain their nicotine intake, education about the dangers of smoking and the marketing of alternative products can contribute to shifts in the nature of nicotine product use. . . . [R]educed tobacco toxin exposure can lead to reduced premature mortality and this is not necessarily undermined by increasing prevalence of use of non-cigarette sources of nicotine. These effects and public health benefits have been predicted and discussed elsewhere.

. . . Swedish snus contains ingredients that are more toxic than would be permitted in foods or medicines, and there are adverse health consequences, including oral diseases and addiction, although the adverse consequences are less severe than those produced by cigarette smoking. (p. 255).

9. Johnson N. Tobacco use and oral cancer: A global perspective. *J Dent Educ* 2001; 65: 328–339.

- All forms of tobacco represent risk factors for oral cancer, but on present evidence, snuff habits as they exist in Scandinavia and probably in the United States carry lower risks of serious health hazards, including oral cancer. (Abstract, p. 328).
- In Scandinavia it is clear that local snuff is not a major risk factor: two recent case-control studies of oral cancer cases in Sweden have failed to show an association. This is because Swedish snus is not fermented and contains much lower nitrosamine levels than fermented tobaccos.

The view that smokeless tobacco use may be associated with a lower risk of oral cancer in the United States has led to a movement to advocate the practice as a less dangerous alternative to smoking and an aid to nicotine withdrawal in those addicted to smoking. This approach has been condemned on the grounds that it can lead to nicotine addiction and it ignores both the potential role of snuff in other cancers and cardiovascular diseases and the fact that other ethically accepted forms of nicotine replacement therapy . . . are widely available. It is of interest, therefore, to consider two recent Swedish studies: one showed a RR [relative risk] for myocardial infarction of 0.89 (95 percent CI [Confidence Interval] 0.62-1.29) in snuff users, compared to 1.87 (95 percent CI 1.40-2.48) in smokers. Another study from health screenings of 135,036 construction workers showed that the RR for death due to cardiovascular disease was 1.4 (1.2-1.6) for this group, compared to 1.9 (1.7-2.2) for smokers. No increased risk among snuff users who had never smoked was found among men with Crohn's disease and ulcerative colitis in a case-control study. The possibility of increased risk of cancer at other sites has not been fully addressed. Nevertheless, on present evidence, snuff habits as they exist in Scandinavia and, probably in the United States, carry low risks of serious health hazards, including oral cancer. (pp. 332-333).

10. Stratton K, Shetty P, Wallace R, Bondurant S (eds.). Clearing the smoke. Assessing the science base for tobacco harm reduction. Institute of Medicine. National Academy Press, Washington, D.C., 2001

- Smokeless tobacco products are associated with oral cavity cancers, and a dose-response relationship exists. However, the overall risk is lower than for cigarette smoking, and some products such as Swedish snus may have no increased risk. It may be considered that such products could be used as a PREP [Potential Reduced-Exposure Product] for persons addicted to nicotine, but these products must undergo testing as PREPs using the guidelines and research agenda contained herein. (p. 434).

11. Warner KE. Reducing harm to smokers: methods, their effectiveness, and the role of policy. In: Rabin RL, Sugarman SD (eds.). *Regulating tobacco*. Oxford University Press 2001: 111-142.
- Until recently the entire effort to help addicted smokers has rested on encouraging them to quit, to sever their ties to nicotine completely. Sweanor (1997) argues that this approach condemns millions of them to an early and avoidable grave. Among the alternatives to quitting smoking for those who cannot quit, as well as for those who do not want to quit but do wish to reduce risk, are reductions in the daily consumption of cigarettes and substitution of less harmful nicotine-delivery systems for cigarettes. Additional, more controversial possibilities include substitution of less dangerous tobacco products for cigarette smoking (e.g., smokeless tobacco or cigarettes modified to be less toxic) and the use of novel cigarette-like products developed by the cigarette manufacturers that are marketed as reducing risk. In each case, compared to the dangers posed by the unaltered smoking pattern, the alternative holds the potential of reducing the smoker's risk. (p. 114).
  - *Substitution of Less Dangerous Tobacco Products* For the nicotine addict who cannot find satisfaction in NRT products, switching from smoking cigarettes to less hazardous forms of tobacco consumption could conceivably reduce risk considerably. In recent years, Rodu (1995), an oral pathologist at the University of Alabama, and his colleagues (Tilashalski, Rodu, and Cole 1998; Rodu and Cole 1999) have argued in favor of converting "inveterate smokers" to smokeless tobacco use. His argument is straightforward, though not without its detractors (Tomar 1996): many confirmed smokers, he believes, can find smokeless tobacco an acceptable substitute for cigarettes, recognizing the risk-reduction benefits it confers in contrast to continued smoking. And smokeless tobacco use, although definitely not without disease risks of its own, is unarguably less risky than smoking. (pp. 118 – 19).
12. Bates C. Taking the nicotine out of cigarettes-why it is a bad idea. *Bulletin of the World Health Organization* 2000; 78: 944.
- If removing nicotine will not work, what is the alternative? . . . . Regulators should be concentrating on cleaning up the delivery system, and tending to *increase* the amount of nicotine in the smoke relative to toxic smoke constituents such as tar and carbon monoxide. Regulatory pressure may be used to force selective reduction of tobacco toxins relative to nicotine by the use of chemically active filters, a switch from burning to heating tobacco, and greater use of oral tobacco, tobacco distillates and perhaps, ultimately, to nicotine delivery devices that do not use tobacco at all but, unlike current nicotine replacement therapies (patches and gum, etc.), deliver a psychoactive

- and satisfying dose of nicotine to the addict. None of these approaches avoids all harm – far from it – but the evolution (rather than prohibition) of addictive nicotine delivery products represents an important strategy in reducing tobacco-related deaths in the 21<sup>st</sup> century. (p. 944).
13. Ramström L. Snuff – an alternative nicotine delivery system. In: Ferrence R, Slade J, Room R, Pope M (eds.). *Nicotine and public health*. The American Public Health Foundation, Washington D.C., 2000; Chapter 9: 159-178.
    - Experts from the Institute of Environmental Medicine at the Karolinska Institute . . . . conclude that long-term use of snuff does not have any marked effects on the major risk factors for cardiovascular disease. (p. 167).
    - If snuff dipping had been a major contributor to oral cancer, Sweden’s high levels of snuff dipping in the late 1960s and later should have been reflected in high death rates for oral cancer about 1990 compared with other countries. Instead, Sweden has lower rates for male oral cancer than [Canada, Denmark, France, Ireland, and the U.S.A.]. (p. 169).
    - While snuff use may entail some health risks, there is good evidence that these are substantially lower than those associated with smoking. Switching from smoking to snuff use would therefore represent a reduction in health risks. (p. 172).
  
  14. Sweanor DT. Is it the nicotine or the tobacco? *Bulletin of the World Health Organization* 2000; 78: 943.
    - [L]ess deadly tobacco products should have regulatory advantages over the most deadly products. Tobacco products that do not require combustion (such as the “snus” sold in Sweden) offer clear advantages. So, too, do products that primarily heat rather than burn tobacco. But the marketing of these products should not obscure the greater advantages of “cleaner” delivery systems and of cessation, and the marketing of such products should only be allowed within a strong, resourced and expert regulatory oversight to ensure that such products are truly reducing aggregate harm. (p. 943).
  
  15. Benowitz NL. Editorial comment: Snuff, nicotine and cardiovascular disease: Implications for tobacco control. *J Am Coll Cardiol* 1999; 34: 1791-1793.
    - Rapid delivery of nicotine through cigarette smoke is expected to produce more deleterious effects on the arterial circulation than nicotine absorbed

- more slowly through the buccal mucosa, as is the case with the use of snuff. (p. 1791).
- Overall, the epidemiologic and experimental data suggest that nicotine absorbed from smokeless tobacco, nicotine gum or transdermal nicotine is not a significant risk factor for accelerating coronary artery disease or causing acute cardiovascular events. (p. 1792).
16. Borland R, Scollo M. Opportunities for harm minimization in tobacco control. *Drug Alcohol Rev* 1999; 18: 345-353.
- An alternative approach is to accept the addiction and alter the product to make it less harmful, an approach first suggested by Russell in 1994. Harm minimization at the level of delivery system could encompass: 1, modifications that would make cigarettes less harmful; 2, nicotine replacement therapies that could be used not simply to assist people to quit, but also to help them reduce tobacco consumption, or even temporarily abstain from smoking; and 3, tobacco replacement products that might act as replacements for cigarettes; that is, products that would deliver nicotine in a manner that was similarly satisfying (to the user), but with less of the dangerous by-products (this could be done by chewing, or inhaling vapour rather than smoke). (p. 348).
  - It is known that long-term use of oral snuff, a form of tobacco used widely in Sweden and the United States, is less harmful than tobacco smoking. (p. 350).
17. Ephros H, Blitz M. More to it than smokeless. (Letter to the Editor) *JADA* 1999; 130: 1558.
- Early in the article, data are presented on ST [smokeless tobacco] use. This is immediately followed by statistics on oral and oropharyngeal cancer in the United States. Some readers might gather from this that ST is associated with a majority or at least a significant percentage of oral cancer cases. That, of course, is not true. Most oral cancer in the United States is related to the use of alcohol and/or smoked tobacco products. There is anecdotal evidence to connect ST use with oral and oropharyngeal cancer, but epidemiologic data from this and other countries are not conclusive. (p. 1558).

18. Huhtasaari F, Lundberg V, Eliasson M, Janlert U, Asplund K. Smokeless tobacco as a possible risk factor for myocardial infarction: A population-based study in middle-aged men. *J Am Coll Cardiol* 1999; 34: 1784-1790.
- The present observations would show that, from a cardiovascular perspective, the deleterious effects of snuff dipping are much less than those of cigarette smoking. This is a complicated message. Faced with anti-smoking campaigns and restrictions on sales of cigarettes, it is tempting for the tobacco industry to turn to less controversial alternatives, i.e. various forms of smokeless tobacco. (p. 1789).
19. Rodu B, Cole P. Nicotine maintenance for inveterate smokers. *Technology* 1999; 6: 17-21.
- [M]odern smokeless tobacco products have three major benefits to offer the inveterate smoker. First, although smokeless tobacco is perceived as hazardous, it poses only about two percent of the mortality risk of smoking. Even the risk of oral cancer—the one consequential health effect of smokeless tobacco—is only one-half that of continued smoking. Smokeless tobacco causes none of the other health effects of smoking, including lung cancer, emphysema, and cardiovascular diseases. Second, nicotine is absorbed from smokeless tobacco in a manner very similar to that from smoking, therefore the craving of inveterate smokers usually is eliminated. In fact, serum nicotine levels from smokeless tobacco use remain elevated longer than they do from smoking, and tobacco consumption is reduced. In part for this reason, the third benefit of smokeless tobacco is that it is less expensive than cigarettes. . . . A major consideration regarding smokeless tobacco relates to its image as socially unacceptable. However, newer products are packaged in small, single-dose paper pouches that are imperceptible during use. In a recent pilot study, 16 of 63 inveterate smokers used smokeless tobacco to quit, and the product was accepted by both men and women. (p. 19).
20. Dretchen K, Slade J, Kessler D, Koop CE, et al. Conference on tobacco dependence: innovative regulatory approaches to reduce death and disease: selected excerpts from conference proceedings. In: Warner KE, Peck CC, Woosley RL, Henningfield JE, Slade J, Page J. Tobacco dependence: Innovative regulatory approaches to reduce death and disease. *Food and Drug Law J Supplement* 1998; 53: 115-137.
- I [Ken Warner] did want to mention just two interesting substances that we ought to be thinking about as we go through this discussion. One is Snus [Swedish snuff], which has been mentioned here previously. This is the smokeless tobacco that is in widespread use, for many decades now, in Sweden that is very low in cancer-causing nitrosamines, and quite high in

nicotine. The evidence is that it increases health risks compared to that of nontobacco users very little. There appears to be a slight oral cancer risk. There is no evidence of an elevated cardiovascular risk. So this is a population of long-term heavily dependent nicotine users who are not observing significant health consequences over a period of decades. (p. 130).

21. Fagerström KO, Ramström L. Can smokeless tobacco rid us of tobacco smoke? *Am J Med* 1998; 104: 501-503.

- In 1996 a commission under the National Board of Health and Welfare in Sweden concluded, with the help of a broad range of scientific evidence including two new well-controlled studies that Swedish *snus* did not seem to increase the incidence of upper airway cancer. Furthermore, from an international perspective, Swedish males have low rates of oral cancer despite their high level of smokeless tobacco use.

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The Swedish National Board of Health and Welfare concluded in its report that “the health risks related to smokeless tobacco are with great probability lower than those related to smoking.” (p. 502).

- [The authors of this study] would like to encourage further research with smokeless tobacco because Swedish epidemiological data show that it may be used in a risk reduction approach, and United Nations Focal Point on Tobacco or Health has released a report from a meeting of experts who recommended the use of alternative and safer forms of nicotine to reduce smoking. Such studies should recognize that smokeless tobacco may work well and better than current nicotine replacement medications for highly dependent smokers who are at greatest risk for developing tobacco related diseases and that, by working with relatively minimal intervention, it may be cost effective. (p. 503).

22. Jimenez-Ruiz C, Kunze M, Fagerström KO. Nicotine replacement: A new approach to reducing tobacco-related harm. *Eur Respir J* 1998; 11: 473-479.

- The most effective forms of modification are those products that do not heat or burn tobacco, i.e. smokeless tobacco. Some such preparations, e.g. moist snuff (“snus”) used in Sweden, do not appear to cause oral or other cancers. In addition, snuff appears much less likely to cause cardiovascular disease than cigarette smoking. (p. 473).

- [I]t appears that Swedish users of smokeless tobacco (snuff), who ingest similar amounts of nicotine to smokers, do not have a higher incidence of coronary disease than nontobacco users. (p. 476).
  - It is interesting to note that Sweden, which has the lowest incidence of tobacco-related harm among developed countries, has unintentionally been used as a reduced smoking paradigm. Sweden has relatively few smokers. . . . However, approximately 28% of adult Swedes use nicotine daily, the explanation being that approximately one third of all nicotine consumed is in the form of moist snuff. . . . The practice of using snuff has not been found to significantly increase mortality. Thus, reduced smoking and/or abstinence combined with alternative nicotine delivery devices appears to be an untapped resource in the quest to reduce tobacco-related harm. (p. 477).
23. Lewin F. Smokeless tobacco. In: Ramström L, Uranga R, Hendrie A (eds.). *Social and economic aspects of reduction of tobacco smoking by use of alternative nicotine delivery systems (ANDS)*, Adis International Limited, United Nations. 1998: 10.
- Two recent case-referent studies in Sweden that analysed overall snuff use, years since stopping, age at initiation, duration of use and total consumption showed no evidence for any increased risk of cancer of the upper aerodigestive tract. In comparison, the overall risks were 5.0 for ever-smokers and 8.0 for current smokers. In summary, the lack of health risks observed with Swedish snuff suggest that it could offer an alternative to cigarette smoking. (p. 10).
24. Nilsson R. A qualitative and quantitative risk assessment of snuff dipping. *Regul Toxicol Pharmacol* 1998; 28: 1-16.
- [I]t seems appropriate to emphasize that whereas snuff dipping is more common in Sweden than in any other western country, the population has a relatively low incidence for cancer of the oral cavity, well below, e.g., the U.S. average. . . .
- While certain physicians are engaged in a crusade to stop all uses of tobacco in a way that is reminiscent of the moods prevailing during the era of alcohol prohibition in the United States, some experts have compared the relative risks involved for active smoking with that of snuff dipping and arrived at the conclusion that turning active smokers to snuff users will drastically reduce the risk of cancer and cardiovascular disease. (Citations omitted, p. 2).
- Upon reviewing . . . two recent Swedish epidemiological studies . . . the Swedish Government Agency for Health and Welfare noted that “although

these studies cannot exclude such a relationship, no significant association between snuff dipping and cancer in humans can be established” and further that these findings “have raised doubt as to the scientific justification for the currently used hazard labeling, ‘Causes cancer.’” In light of new evidence, the agency also suggested that the Swedish government renegotiate the issue with the [Commission of the European Communities].

The total ban on oral snuff imposed by the Commission of the European Communities—but not on nasal snuff products or on any other tobacco product—does not seem to be based on rational scientific considerations. . . . This author agrees fully with the opinion of Hoffmann and co-workers (1981) at the American Health Foundation: “Although we concur with other scientists” . . . “that snuff use may be a feasible alternative to cigarette smoking, we feel that no efforts should be spared to reduce the concentration of alkaloid derived N-nitrosamines in snuff, since the use of this type of tobacco product has been associated with an increased risk for cancer of the oral cavity.” (Citations omitted, p. 13).

25. Ramström L, Uranga R, Hendrie A (eds.). *Social and economic aspects of reduction of tobacco smoking by use of alternative nicotine delivery systems (ANDS)*, Adis International Limited, United Nations. 1998: 17.
  - [I]t is now evident that the risk of death and disease is related to not only the amount but also the nature of tobacco exposure; for example, daily cigarette smoking is far more dangerous than occasional use of Swedish snuff.
  
26. Tilashalski K, Rodu B, Cole P. A pilot study of smokeless tobacco in smoking cessation. *Am J Med* 1998; 104: 456-458.
  - Traditional smoking cessation programs have had limited success and only among smokers who can achieve nicotine abstinence. Inveterate smokers may benefit from strategies that focus instead on providing nicotine by a means other than cigarette smoking. Smokeless tobacco is a potential alternative for inveterate smokers because we have estimated its adverse health effects may be as low as 2% of those of smoking. (p. 456).
  
27. Ahlbom A, Olsson UA, Pershagen G. Health hazards of moist snuff. *SoS-Report* 1997; 11: 3-29.

- Taken together, the data suggest that long-term use of snuff does not have any marked effects on the major risk factors for cardiovascular disease. (p. 17).
  - The health hazards of snuff are in all likelihood smaller than those associated with smoking. (p. 20).
28. Bolinder G. Smokeless tobacco – a less harmful alternative? In: Bolliger CT, Fagerström KO. (eds.) *The Tobacco Epidemic: Progress in Respiratory Research*. Volume 28; Karger Publishing, Basel. 1997: 199-212.
- [C]ompared with the extremely high risk of developing cancer due to tobacco smoking (according to the WHO, 33% of all cancers in the industrialized world are caused by smoking), it seems as if the risks associated with the use of smokeless tobacco are obviously of minor importance. (p. 203).
  - The risk of adverse health effects is evidently less serious in smokeless tobacco users than in smokers . . . . (p. 208).
29. Borland R. Minimizing the harm from nicotine addiction. *Health Promotion J Australia* 1997; 7: 138-141.
- Tobacco smoke contains more than 4000 different chemicals, many of which are known poisons, mutagens and carcinogens. It is generally accepted that most of the damage from smoking is due to components in the tar, and to a lesser extent, the carbon monoxide (CO). The contribution of the nicotine is believed to be lower, but still considerable. The strongest evidence for this is that smokeless tobacco, which has little tar, appears to be less harmful than the smoked product. (p. 138).
30. Balfour DJK, Fagerström KO. Pharmacology of nicotine and its therapeutic use in smoking cessation and neurodegenerative disorders. *Pharmacol Ther* 1996; 72: 51-81.
- If nicotine preparations could be developed that were acceptable to smokers, there is the possibility of eliciting a substantial reduction in tobacco smoking, while not necessarily maintaining complete abstinence.
- Such use of NRT [nicotine replacement therapy], although controversial for those hoping for a total extinction of nicotine use, without doubt would do more service to mankind and public health than what NRT could contribute in

smoking cessation. Sweden, with a long tradition of smokeless tobacco use (16% of adult males use smokeless tobacco daily) and the highest penetration of NRT use, is the only European country that has reached (19%) the World Health Organization's target of 20% smokers in the adult population by year 2000; about 35% of all nicotine consumed comes from nonsmoked delivery forms. The tobacco-related mortality in Sweden is by far lower than in any other European or North American country, although nicotine consumption may not be lower than in other countries. (Citations omitted, p. 71).

31. Barker BF, Barker GJ. Oral tobacco use. (Letter to the Editor). *Oral Surg Oral Med Oral Pathol Radiol Endod* 1996; 81: 132.

- It cannot be denied that serious diseases and death rates associated with the use of tobacco are far greater for those who smoke cigarettes than for those who use smokeless tobacco. (p. 132).

32. Dunlap C. Smokeless tobacco. (Letter to the Editor). *Oral Surg Oral Med Oral Pathol Radiol Endod* 1996; 81: 376.

- The central theme [of Vigneswaran's article, Tobacco use and cancer,] was that smokeless tobacco use is far safer than other forms of tobacco use. To me, the theme rings true. I have been in oral pathology for 32 years and have yet to see a single case of oral carcinoma arising precisely at the site where tobacco is held. There has been a hand full, probably fewer than a half-dozen, who used smokeless tobacco and eventually developed carcinoma, but the carcinomas were not at the spot where the tobacco was held. I have seen far more people with oral cancer who had no risk factors.

Although I don't approve of smokeless tobacco use, I think the carcinogenicity of smokeless tobacco has been overstated and the authors are essentially correct in their assessment of this issue.

33. Rodu B, Cole P. The rewards of smoking cessation. (Letter to the Editor). *Epidemiology* 1996; 7: 111-112.

- Lifelong smokeless tobacco use has little impact on life expectancy, and this analysis shows that switching to smokeless tobacco has essentially the same effect on life expectancy as does quitting smoking. This finding is important because new options are needed for smoking cessation programs. The National Cancer Institute's Community Intervention Trial for Smoking Cessation confirms that existing resource- and labor-intensive quit smoking

programs are not very successful, largely because conventional approaches offer no alternative to giving up nicotine entirely, an unattainable goal for many smokers. Furthermore, these programs are unnecessarily limited, as they do not accommodate the fact that there are now several ways to satisfy a tobacco user's desire for nicotine without the health effects of smoking. Smoking cessation programs may become more successful when their providers recognize that the benefits of quitting smoking can be achieved without quitting nicotine altogether. (p. 112).

34. Vigneswaran N, Tilashalski K, Rodu B, Cole P. Oral tobacco use. (Letter to the Editor). *Oral Surg Oral Med Oral Pathol Radiol Endod* 1996; 81: 133.

- As stated by the Barkers [in Oral Tobacco Use], "It cannot be denied that serious diseases and death rates . . . are far greater for those who smoke cigarettes than for those who use smokeless tobacco (ST)." In fact, the health risks related to ST use are only 2% those of smoking, and the smoker who switches reduces risks for *all* smoking-related illnesses. . . .

All current cessation strategies require smokers to overcome tobacco and nicotine addiction entirely to gain health benefits. A switch to ST permits smokers to achieve most of the benefits of quitting smoking without quitting nicotine altogether. . . .

Actual data show that the products of tobacco combustion, but not necessarily nicotine, are associated with deaths from hypertension, ischemic heart disease, cerebrovascular diseases, and atherosclerosis, whereas ST use is not associated with mortality from myocardial infarction. . . .

[T]he scientific and medical foundation for smokers switching to ST is solid. The average lifelong smoker loses almost 8 years of life compared with the nonuser of tobacco, whereas the ST user's loss is 15 days. (p. 133).

35. Vigneswaran N, Tilashalski K, Rodu B, Cole P. Smokeless tobacco. (Letter to the Editor). *Oral Surg Oral Med Oral Pathol Radiol Endod* 1996; 81: 377.

- Our proposal [that inveterate cigarette smokers switch to smokeless tobacco], however, has a clear and legitimate scientific basis:
  1. The risk of oral cancer from smokeless tobacco use is only half that from smoking.
  2. Smokeless tobacco use carries no excess risk for other cancers or for lung and heart diseases that kill over 400,000 smokers every year.

3. Smoking is the most dangerous nicotine delivery system. Lifelong cigarette smokers lose almost 8 years of life on average compared with nonusers of tobacco: in contrast, smokeless tobacco users lose only 15 days.
  4. One third of current smokeless tobacco users are former smokers.
36. Benowitz NL. Medical implications. In: Davis RM (ed). Smoking cessation: Alternative strategies. Session III: Implications of alternative treatment goals. In: *Tobacco Control* 1995; 4: (suppl 2): S44-S48.
- A potentially useful analysis is the epidemiology of snuff use in Sweden. Snuff users have plasma or urine nicotine and cotinine levels as high or higher than cigarette smokers. A recent epidemiological study reported that snuff dippers had the same odds ratio for myocardial infarction as those who did not use tobacco. In comparison, the odds ratio for cigarette smokers was substantially higher than that of either snuff users or those who used no tobacco. (p. S46).
37. Rodu B. For smokers only. How smokeless tobacco can save your life. Sulzburger & Graham Publishing, Ltd., New York; 1995.
- [S]mokeless tobacco products allow you, the hard-core and long-term smoker, to take back a measure of control over your health by indulging in a far safer form of tobacco use. (Introduction, p. 8).
  - A switch to a safer delivery system, smokeless tobacco, will allow the 46 million smokers in this country (and the people they live with) to live longer, healthier lives. (p. 18).
  - If we look at “safe” to mean relatively safe or “safer,” something the government warnings inately avoid here, then use of smokeless tobacco products is far safer than cigarette smoking. . . .
- Statistical dangers of using smokeless tobacco do exist, but they are considerably smaller than the dangers related to smoking cigarettes. (p. 29).
- What about smokeless tobacco use and the development of heart disease? Within the past two years a couple of studies regarding this issue have come from Sweden (the smokeless tobacco capital of the world). In the first . . . [t]he results showed that smoking resulted in an increased risk for heart attacks, while smokeless tobacco use carried no risk. In a second study . . . smokeless tobacco use carried some risk for dying from heart disease in men

who were between 35 and 54 when the study started. . . . [T]he recorded risk for users of snuff was much smaller than for those who were either light or heavy smokers. In fact, the risk in smokeless tobacco users was the same as smokers who had quit from one to five years previously.

\* \* \*

[R]egarding heart disease, it appears that *switching to smokeless tobacco is as beneficial as quitting smoking*.

What counts for you, then, is the fact that smokeless tobacco use carries fewer risks for all diseases than smoking, including . . . lung disease. (pp. 55 – 56).

- If nicotine were responsible for circulatory problems, then users of smokeless tobacco, which contains as much nicotine, would suffer from heart disease and strokes at equivalent rates as smokers. However, there is strong evidence that this is not the case. Use of smokeless tobacco carries reduced risks for cardiovascular diseases compared with cigarette smoking. (p. 102).
- If all smokers were instead addicted to smokeless tobacco, only 12,000 new cases of oral cancer (with a 50 percent survival rate) could be expected each year. This is only one-twentieth of all cancers that now result from smoking, and one-tenth of smoking related lung cancer cases! I haven't even mentioned the reduction in heart disease and emphysema deaths yet. *If all 46 million smokers used smokeless tobacco instead, the United States would see, at worst, 6,000 deaths from oral cancer, versus the current 419,000 deaths from smoking-related cancers, heart problems, and lung disease.*

\* \* \*

Relative to cigarettes, smokeless tobacco products are a godsend. (p. 131).

- [T]he average remaining life expectancy of a 35-year-old smokeless tobacco user is 45.92 years, which is merely four-hundredths of a year less than the nonuser of tobacco. Statistically speaking, use of full-bodied tobacco products with all the nicotine of cigarettes will cost the smokeless tobacco user only *fifteen days* of life! That's about 2,780 more days than the cigarette smoker lives. (p. 133).
- As an alternative to cigarette smoking, smokeless tobacco is not perfectly safe, it is just *98 percent* less dangerous. (p. 181).
- Since smokeless tobacco users live eight years longer than smokers, it is absolutely unethical to continue to deny smokers information that could save their lives. (p. 182).

38. Rodu B, Cole P. Would a switch from cigarettes to smokeless tobacco benefit public health? - Yes. *Priorities* 1995; 7: 24-30.

- [S]mokeless tobacco use is 98 percent safer than cigarette smoking. Thus, it can save lives of smokers and of those persons who breathe second-hand smoke.
- Contrary to a popular misperception, all forms of tobacco are not equally risky. Smokeless tobacco causes neither lung cancer nor other diseases of the lung, and users have no excess risk for heart attacks. In fact, the only consequential—but infrequent—adverse health effect of smokeless tobacco use is oral cancer. In 1981, writing in *The New England Journal of Medicine*, Dr. Deborah Winn and colleagues established that smokeless tobacco users are four times more likely to develop oral cancer than are nonusers of tobacco. However, this relative risk is only about one half the relative risk of oral cancer from smoking.
- The number of deaths from smoking is almost 70 times higher than the number from smokeless tobacco use. In terms of life expectancy, the smokeless-tobacco user loses only about 15 days on average, compared with the eight years lost by the smoker.

Another major health benefit: smokers who switch to smokeless tobacco produce no passive smoke to harm others. The American Heart Association estimates that 40,000 Americans die annually from diseases related to second-hand smoke. No one dies from the secondary effects of smokeless tobacco use. Thus, this proposal could be recommended solely on the basis of lives saved through the elimination of the effects of passive smoking.

- What do switchers accomplish? Our research shows that they will live, on average, as long as those smokers who quit nicotine altogether. They reduce their risks for smoking-related illness and death, which is the goal of all existing smoking cessation efforts. There is, of course, no debate about the ideal way to achieve this goal: complete tobacco abstinence. But that ideal is not always attainable since many smokers are unable to give up nicotine. Switching to smokeless tobacco is a small compromise with the ideal which reaps large individual and public health gains.
- Substituting smokeless tobacco for smoking is a wise risk-reduction strategy because it reduces *all* smoking related risks and introduces no new risks.
- Providing information about an alternative to smoking that is 98 percent safer is not only consistent with the highest standards of medical ethics, it is mandated by them.

39. Tilashalski K, Lozano K, Rodu B. Modified tobacco use as a risk-reduction strategy. *J Psychoactive Drugs* 1995; 27: 173-175.

- A novel approach for smoking cessation has been proposed: that cigarette smokers unable or unwilling to quit change to smokeless tobacco (ST) use. In fact, surveys reveal that as many as 7% of former smokers have already modified their tobacco use to ST, which they perceive as less risky despite repeated warnings by medical authorities.

Data indicate that former smokers who now use ST have indeed chosen a safer mode of tobacco use that serves as a positive risk-reduction strategy. (Citations omitted, p. 173).

40. Vigneswaran N, Tilashalski K, Rodu B, Cole P. Tobacco use and cancer. *Oral Surg Oral Med Oral Pathol Radiol Endod* 1995; 80: 178-182.

- Previous research has demonstrated that the relative risk of oral cancer with smokeless tobacco use is 4.2, about half of the risk from smoking (relative risk = 10 to 15). Mortality data from populations with sustained high-frequency smokeless tobacco use do not support the mistaken prediction of an epidemic of oral cancer with increasing smokeless tobacco use. In fact, the risks of smokeless tobacco use compare so favorably with those of smoking that smokers who switch to smokeless tobacco reduce their risks for all tobacco-related illnesses including oral cancer. Although some criticize this proposal as less than an ideal solution for the nation's smokers, full adoption of this strategy would eventually save over 400,000 lives each year. (Abstract, p. 178).
- [L]arge scale vital statistics from Sweden and France strongly support the suggestion that if tobacco is to be used, it should be in the form of ST [smokeless tobacco] and not cigarettes. The population that uses ST in lieu of smoking is, in effect, protected from lung cancer and other major smoking-related diseases and suffers little or no increased risk of oral cancer. (p. 180).
- A recent proposal has recommended ST use as an alternative for adult smokers who are unable or unwilling to stop smoking. Crucial to this proposal is the realization that ST use carries a lower risk of oral cancer than does continued smoking and has virtually no other consequential adverse effects. (p. 180).
- A switch to ST use for inveterate smokers can be . . . justified – if not ethically mandated. Full adoption of this strategy would eventually save over 400,000 lives each year, a 98% reduction in deaths from *all* tobacco-related illnesses.

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Although all tobacco use carries some risk, a reduction in risks for these inveterate smokers by a switch to ST will save lives. (p. 180).

41. Rodu B. Editorial: An alternative approach to smoking control. *Am J Med Sci* 1994; 308: 32-34.

- The author . . . proposes that smokeless tobacco be recommended as a cigarette substitute by persons who cannot stop smoking. This proposal is made because smokeless tobacco is associated with far fewer and considerably less serious health consequences than is smoking. . . . A public health policy that recognizes smokeless tobacco as an alternative to smoking would benefit individuals confronted with the unsatisfactory options of abstinence or continuing to smoke. (Abstract, p. 32).
- Because smokeless tobacco causes far fewer and considerably less serious health effects than does smoking, it should be promulgated as an alternative to cigarettes for smokers unable or unwilling to overcome their nicotine addiction. (p. 32).
- Smokeless tobacco is an excellent substitute for cigarette smoking because it delivers similar nicotine levels but results in far fewer and less serious health consequences. . . .

The only major health concern about smokeless tobacco is oral cancer. However, the association is not strong . . . .

Oral cancer mortality rates are not elevated significantly among populations with above-average smokeless tobacco use. . . . Sweden long has been the world's highest per capita consumer of smokeless tobacco, however, annual death rates for oral cancer have averaged 2.8 per 100,000 over the past 30 years.

Other adverse effects of smokeless tobacco, such as leukoplakia and gingival recession, can be diagnosed readily and monitored. These conditions, although undesirable, pale in comparison to lung cancer and other disorders related to cigarette smoking.

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Although it is more desirable for individuals to overcome a nicotine addiction entirely, those failing smoking cessation therapy can benefit by changing their addiction to smokeless tobacco use.

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By effective delivery of similar nicotine doses for only a fraction of the health risks associated with smoking, smokeless tobacco is a solution to the dilemma of total abstinence versus continuation of smoking. . . . Rather than condemning the addiction itself, this proposal focuses instead on smokers, providing them with a rationale to fundamentally change their addiction and related health risks. (p. 33).

42. Rodu B, Cole P. Tobacco-related mortality. (Letter to the Editor). *Nature* 1994; 370: 184.

- We suggest that abstinence is not the only approach to reducing tobacco-related mortality: for smokers addicted to nicotine who would not otherwise stop, a permanent switch to smokeless tobacco could be an acceptable alternative to quitting. (p. 184).

43. Whidden P. Smokeless fire. (Letter to the Editor). *Nature* 1994; 371: 564.

- A massive shift towards the use of oral tobacco by smokers would considerably cut the tens of thousands of deaths caused by tobacco-smoke pollution.

44. Kozlowski LT. Reduction of tobacco health hazards in continuing users: Individual behavioral and public health approaches. *J Substance Abuse* 1989; 1: 345-357.

- There is no doubt that smokeless tobacco products are gram for gram less hazardous than smoked tobacco products. Smokeless tobacco products present no fire risks. . . . No added doses of smoke toxins (e.g. carbon monoxide, tar) get into the lungs of the user of oral or nasal snuff. There are no apparent lung cancer risks of using smokeless tobacco. It may be appropriate here to emphasize again that I do not suggest that smokeless tobacco products are safe. Nonetheless, these products are unquestionably less risky than smoked tobacco products.

One advantage of smokeless products is that it is easier to ration the dose. . . . In other words, when one limits smokeless tobacco to a certain amount per day, one does not have the same compensatory dosing problems found with smoked tobacco products. (Citations omitted, pp. 352-53).

45. Peto R. Control of tobacco-related disease. In: *The Value of Preventive Medicine*. The Ciba Foundation Symposium 110. Pitman, London. 1985; pp. 126-142.

- As well as thinking about the composition of cigarettes, we should also think about the use of tobacco in a much less hazardous form, including perhaps not only the usual alternatives such as pipes and cigars, but also various forms of “smokeless” tobacco (including nasal snuff, chewing tobacco, and “dipping” tobacco—that is, powdered tobacco that is usually held between the gum and cheek). The exact hazards associated with such habits are not yet known, but the preliminary evidence thus far available suggests that they are unlikely to be substantial in comparison with the vast mortality now being produced by tobacco smoking (unless promotion of smokeless tobacco among the young engenders nicotine addiction that eventually leads to smoking). (Citation omitted, p. 127).
- If this [snuff dipping] or some other such habit were to become widespread and did to any substantial extent replace smoking (particularly of cigarettes), then the net effect would be likely to be a reduction in tobacco-induced mortality. For, although snuff dipping causes a vast increase in the *relative* risk of cancer of the gum and cheek (together with the same sort of risks of cancers of other parts of the mouth that smoking produces), the *absolute* excess risks of death from oral cancer associated with the habit in the South-Eastern United States appear to be at most a few per cent of the total risk of death produced by cigarette smoking. Although the absolute risks in other populations might, of course, be considerably different (especially if some diseases other than oral cancer are found to be increased by tobacco “dipping”) the use of smokeless tobacco is still likely to be much less hazardous than is tobacco smoking, especially of cigarettes. (Citation omitted, p. 128).

46. Russell MAH, Jarvis MJ, West RJ, Feyeravend C. Buccal absorption of nicotine from smokeless tobacco sachets. (Letter to the Editor). *Lancet* 1985; 1: 1370.

- Unlike tobacco smoking, use of wet snuff carries no risk of lung cancer, bronchitis, or emphysema, and no risk of cardiovascular disease has been demonstrated.

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If all smokers in Britain switched to [smokeless tobacco] sachets about 50 000 premature deaths per year might eventually be saved at an annual cost of less than 1000 deaths from mouth cancer.

47. Kozlowski LT. Less-hazardous tobacco use as a treatment for the “smoking and health” problem. In: Smart RG, Cappell HD, Glaser FB, Israel Y, Kalant H, Popham RE, Schmidt W, Sellers EM (eds.) *Research Advances in Alcohol and Drug Problems*. Volume 8. Plenum Press, New York; 1984: Chapter 11, pp. 309-329.

- This chapter will argue that the use of less-hazardous tobacco, if prohibitionistic impulses can be put aside, may have an important role in the treatment of the smoking and health problem. . . . The phrase “less-hazardous tobacco use” is meant to be inclusive. Cigarettes, for example, are the most hazardous tobacco products overall. . . . On the other hand, some less-hazardous tobacco products are less-hazardous in certain respects no matter how they are used: chewing tobacco, for example, carries no risks of fire and essentially no risk of lung disease. (p. 310).
- There is really no dispute about whether smokeless tobaccos present fewer hazards to the user than do smoking tobaccos. Smokeless tobaccos expose the lungs to essentially no tobacco toxins. No carbon monoxide and no tar is produced. The oral cancers associated with oral smokeless tobaccos are substantially less lethal and are more easily diagnosed than lung cancers. In addition, smokeless tobaccos pose no problems of second-hand smoke and no risks of fire. (Citations omitted, p. 319).

48. Kozlowski LT. Pharmacological approaches to smoking modification. In: Matarazzo JD, Weiss SM, Herd JA, Miller NE, Weiss SM (eds.) *Behavioral Health. A handbook of health enhancement and disease prevention*. John Wiley & Sons, New York; 1984: Chapter 45, pp. 713-728.

- Some less hazardous forms of tobacco use (smokeless tobaccos, pipes, cigars) are pharmacotherapies that can be self-applied easily by those who are poorly motivated to modify their smoking. (p. 714).
- The use of smokeless tobaccos is not associated with lung cancer, chronic obstructive lung disease, or bronchitis. Oral smokeless tobaccos are associated with oral cancers, however, and manufactured nasal snuff may cause nasopharyngeal cancer, although direct evidence is lacking for such an effect.

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Smokeless tobaccos not only act to eliminate the possible problems of passive smoking, they also eliminate the definite problems of passive fire-starting. (Citations omitted, p. 724).

49. Russell MAH, Jarvis MJ, Devitt G, Feyerabend C. Nicotine intake by snuff users. *Br Med J* 1981; 283: 814-817.

- From our results snuff use may clearly be an efficient method of nicotine intake. This suggests that it might prove sufficiently acceptable to smokers, not only as a temporary substitute to help those who are trying to give up smoking but as a long-term alternative to continued cigarette smoking. . . .

Unlike tobacco smoke, snuff is free of tar and harmful gases such as carbon monoxide and nitrogen oxides. Since it cannot be inhaled into the lungs, there is no risk of lung cancer, bronchitis, and emphysema.

\* \* \*

[T]he rapid absorption of nicotine from snuff confirms its potential as an acceptable substitute for smoking. Switching from cigarettes to snuff would substantially reduce the risk of lung cancer, bronchitis, emphysema, and possibly coronary heart disease as well, at the cost of a slight increase in the risk of cancer of the nasopharynx (or oral cavity in the case of wet snuff). Another advantage of snuff is that it does not contaminate the atmosphere for non-users. (p. 816).

50. Kirkland LR. The nonsmoking uses of tobacco. (Letter to the Editor). *NEJM* 1980; 303: 165.

- The English authors propose snuff as a healthier substitute for cigarettes; the American author unrealistically eschews all forms of tobacco. Rather than oppose the advertising of “smokeless tobacco,” I urge physicians to encourage snuff and chewing tobacco as alternatives to cigarettes. No one disputes the role of snuff and similar products as the cause of oral leukoplakia, but there is a vast difference in the frequencies of oropharyngeal carcinoma and cigarette-induced lung cancer. If five new “dippers” are created to avert creation of one new cigarette smoker, then progress has been made.

## Smokeless Tobacco and Health

The principal disease claimed to be associated with smokeless tobacco is oral cancer.<sup>1</sup>

The purpose of this attachment is to provide an overview of the scientific studies published to date regarding smokeless tobacco and oral cancer.<sup>2</sup>

### **I. Overview**

There are 34 epidemiological studies published in the scientific literature that report data or information regarding smokeless tobacco and oral cancer. Epidemiological studies – “case-control” or “cohort” studies – investigate diseases in human populations by statistical methods and identify factors that are statistically associated with the occurrence of those diseases. More than half of the epidemiological studies relating to smokeless tobacco and oral cancer (20 of the 34 studies) do not report a statistically significant association between smokeless tobacco use and oral cancer. Furthermore, the overwhelming majority of the more recent studies do not report a statistically significant association between smokeless tobacco use and oral cancer.<sup>3</sup>

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<sup>1</sup> While claims have been made that smokeless tobacco may be associated with cancers at other sites, the 1986 Surgeon General’s Report concluded that the evidence relating to such cancers is “sparse” and that the results are “inconclusive.” 1986 Surgeon General’s Report at xxiii. Studies published since that time do not contradict that conclusion.

<sup>2</sup> This overview does not deal with studies pertaining to smokeless tobacco products used in Asia or India because those products frequently incorporate materials such as slaked lime and betel nut, and are therefore substantially different from U.S. or Western Europe smokeless tobacco products.

<sup>3</sup> There have also been approximately 30 animal studies (listed below) in which nearly 1,000 animals (hamsters, mice, rats and monkeys) have been exposed orally to smokeless tobacco. The results of this research are consistent with the overall negative findings of the epidemiological literature – *i.e.*, oral cancer did not develop in any of the exposed animals in 23 of these studies. Peacock & Brawley 1959, Peacock et al. 1960, DiPaolo 1962, Dunham et al. 1966, Smith et al. 1970, Homburger 1971, Dunham et al. 1974, Homburger et al. 1976, Hirsch & Thilander 1981, Hirsch & Johansson 1983, Das et al. 1983, Hirsch et al. 1984, Antoniadis et al. 1984, Shklar et al. 1985, Park et al. 1985, Mendel et al. 1986, Park et al. 1986, Hirsch et al. 1986, Hecht et al. 1986, Park et al. 1987, Mendel et al. 1987, Larsson et al. 1989, Johansson et al. 1989, Chen 1989, Worawongvasu et al. 1991, Johansson et al.

In 1986, the Surgeon General's Report concluded that smokeless tobacco "can cause cancer." At the time of the Surgeon General's Report, the most frequently cited study supporting this conclusion was Winn et al. 1981 ("Winn"), a case-control study of mostly elderly women from North Carolina. However, as discussed below, substantial scientific research relating to smokeless tobacco and oral cancer has been conducted since the publication of the Surgeon General's Report, leading the European Union to eliminate the phrase "causes cancer" from smokeless tobacco warning labels.

## **II. Epidemiological Studies**

Figure 1 below summarizes the epidemiological studies relating to smokeless tobacco and oral cancer. The left hand column lists those studies that report data or information indicating no statistically significant association between smokeless tobacco use and oral cancer in the population studied ("negative studies"). The right hand column lists those studies that report data or information indicating a statistically significant association between smokeless tobacco use and oral cancer in the population studied, or in a subgroup thereof ("positive studies").

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1991, Johansson et al. 1991, Summerlin et al. 1992, Ashrafi et al. 1992, Patel et al. 1993.

Fig. 1 Epidemiological Studies Relating to Smokeless Tobacco and Oral Cancer

	Negative	Positive
<i>Literature published in last 10 years</i>	Lee et al. 2000 Schwartz et al. 1998 Lewin et al. 1998 Schildt et al. 1998 Muscat et al. 1996 Bundgaard et al. 1995 Mashberg et al. 1993 Marshall et al. 1992 Sterling et al. 1992	<i>Kabat et al. 1994</i> <sup>4</sup> Zahm et al. 1992 Maden et al. 1992
<i>Literature published in last 20 years</i>	Franco 1989 Spitz et al. 1988 Young et al. 1986  [1986 Surgeon General's Report published]	<i>Blot et al. 1988</i> Stockwell & Lyman 1986
	Wynder et al. 1983 Winn et al. 1982	Bjelke & Schuman 1982
	Whitaker et al. 1979 Wynder & Stellman 1977 Browne et al. 1977 Smith et al. 1970, 1975 Martinez 1969 Wynder et al. 1957	Winn et al. 1981 Westbrook et al. 1980 <i>Williams &amp; Horm 1977</i> Vincent & Marchetta 1963 Vogler et al. 1962 <i>Peacock et al. 1960</i> Wynder, Bross et al. 1957 Moore et al. 1953

Figure 1 illustrates several points. First, as stated above, the overwhelming majority of the more recent epidemiological studies are negative. This is true whether one considers all the studies published (i) over the course of the last ten years (75% of the studies are negative), (ii) since the publication of the 1986 Surgeon General's Report (71% of the studies are negative),

<sup>4</sup> The four positive studies indicated by italics (Kabat et al. 1994, Blot et al. 1988, Williams & Horm 1977, Peacock et al. 1960) report a statistically significant association only in a small subgroup of the population studied (e.g., females who do not smoke). These studies are otherwise negative.

or (iii) over the course of the last twenty years since the publication of Winn (70% of the studies are negative).

Moreover, Figure 1 shows that, at the time of the 1986 Surgeon General's Report, 50% of these studies were not published. Finally, Figure 1 illustrates that, since the publication of Winn, fourteen negative studies have been published and six positive studies have been published. As discussed below, none of the six positive studies replicates the findings of Winn.

It is beyond the scope of this attachment to provide an in depth analysis of each of the 34 epidemiological studies. The following is an overview of certain studies that warrant some discussion by virtue of their size, their focus on smokeless tobacco, and/or their recent publication. In addition, some discussion will be provided of the six positive studies that have been published since Winn.

The two most recent large-scale epidemiological studies that focus on smokeless tobacco are Schildt et al. 1998 and Lewin et al. 1998. Both studies were carried out in Sweden,<sup>5</sup> where a substantial portion of the adult population is reported to use moist snuff and where the cancer registry system accounts for almost 99% of all head and neck cancers.<sup>6</sup>

In Schildt et al. 1998, the study population consisted of 354 oral cancer cases and 354 controls. The authors concluded: "Oral snuff was not found to be a risk factor for oral cancer in

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<sup>5</sup> Claims have been made that Swedish studies are not pertinent to an evaluation of U.S. moist snuff products because U.S. moist snuff products allegedly have higher levels of so-called tobacco-specific nitrosamines ("TSNA") than Swedish moist snuff products. Such claims are without merit. As discussed more fully in Attachment A, there is currently no significant difference in TSNA levels in U.S. moist snuff products compared to Swedish moist snuff products. Furthermore, the 1986 Surgeon General's Report regarding smokeless tobacco did not make any distinction between epidemiological studies relating to smokeless tobacco and oral cancer conducted in the United States and studies conducted in Western Europe and the 1986 Report evaluated such studies from Sweden, Norway and the United Kingdom.

our study.”<sup>7</sup> In Lewin et al. 1998, the study population consisted of 545 head and neck cancers and 641 controls. The authors concluded that: “Overall, the use of oral snuff had little or no effect on risk.”<sup>8</sup>

Another large-scale, epidemiological study that focuses specifically on smokeless tobacco is Sterling et al. 1992. Sterling is one of the few U.S. epidemiological studies that is national in its scope, rather than limited to a particular state or a particular area of the country. It used the National Mortality Followback Survey and the National Health Interview Survey to compute risk estimates for mortality for all cancer, oral cancer, and cancer of the digestive organs for use of smokeless tobacco, controlling for potential confounding from smoking, drinking alcohol, and occupation. No statistically significant associations were found for any of these cancer groups.

The study most frequently cited at the time of the 1986 Surgeon General’s Report for the proposition that smokeless tobacco causes oral cancer was Winn et al. 1981. Winn is a retrospective case-control study conducted in the 1970s involving 232 cases comprised mostly of elderly women from the Piedmont region of North Carolina with oral and pharyngeal cancer and 410 controls. The authors, as well as other researchers, recognize that the study has limitations.<sup>9</sup>

One limitation is that the study group in Winn is not representative of smokeless tobacco consumers or the U.S. population in general. In addition, according to Dr. Deborah Winn, lead

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<sup>6</sup> Lewin et al. 1998 at 1367-68.

<sup>7</sup> Schildt et al. 1998 at 344.

<sup>8</sup> Lewin et al. 1998 at 1369.

<sup>9</sup> See Lewin et al. 1998 at 1374; Sterling et al. 1992 at 229-30.

author of the study, virtually all of the snuff used in the study was of the “dry” type.<sup>10</sup> This type of snuff has negligible usage and is not representative of smokeless tobacco products in the United States.<sup>11</sup>

Furthermore, because many of the subjects were deceased, information regarding their snuff usage, cigarette smoking, alcohol consumption, as well as other critical information, was obtained not from the subjects themselves, but rather from their next-of-kin. This method of data collection is disfavored in epidemiological studies because of the risk of error in reporting.

Winn is cited for its reported finding that snuff dipping for greater than 50 years resulted in a 47.5 relative risk for gum and buccal cancer. However, this relative risk is inconsistent with all other studies on the subject and was arrived at by excluding various strata of data from the calculations. No study published in the 20 years since the 1981 Winn study has replicated this finding.

There have been six positive studies published since Winn: Bjelke and Schuman 1982,<sup>12</sup> Stockwell and Lyman 1986, Blot et al. 1988, Maden et al. 1992, Zahm et al. 1992, and Kabat et al. 1994. None of these studies replicates the finding of Winn and each has limitations.

Two of the positive studies published since Winn (Blot et al. 1988 and Kabat et al. 1994) are generally negative in that they do not report a statistically significant association between smokeless tobacco and oral cancer in the overall population studied. Rather, they report a

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<sup>10</sup> Winn 1986 at 374; *see also* Winn & Pickle 1986 at 261.

<sup>11</sup> In 1999, dry snuff represented only about 3% of total U.S. sales of smokeless tobacco. Federal Trade Commission Report tbls. 1, 3c.

<sup>12</sup> Bjelke & Schuman 1982 was published in abstract form and provides no data and no discussion of the methods used.

statistically significant association only in a subgroup of the study population. In both studies, the subgroup is defined as females who do not smoke. Furthermore, in both studies, the number of non-smoking females upon which the association is based is six or fewer.

The remaining four studies also have limitations. For example, they do not account for the effect that cigarette smoking and alcohol consumption may have had on the associations reported.<sup>13</sup> Epidemiological studies generally take into account the confounding effect of risk factors such as cigarette smoking and alcohol consumption by statistically adjusting the results. However, Zahm et al. 1992, by way of example, reported a statistically significant association between smokeless tobacco and oral cancer, but noted that most of the subjects also used other tobacco products. The results were not adjusted to take that fact into account.<sup>14</sup> In addition, in Maden et al. 1992, the authors adjusted their results for cigarette smoking to account for confounding by alcohol consumption and adjusted their results for alcohol consumption to account for confounding by cigarette smoking. However, they did not adjust their results for smokeless tobacco to account for either cigarette smoking or alcohol consumption.<sup>15</sup>

Another limitation with at least some of the positive studies published since Winn is that the results are based on a small number of cases. For example, in Stockwell and Lyman 1986, the statistically significant association reported with respect to smokeless tobacco and oral

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<sup>13</sup> Approximately 75% of all oral and pharyngeal cancers in the United States have been attributed to the combined effect of cigarette smoking and alcohol consumption. Blot et al. 1988.

<sup>14</sup> Winn et al. 1982 analyzed data from the same study from which Zahm et al. 1992 collected their data and observed no oral or pharyngeal cancer deaths among those who used smokeless tobacco only.

<sup>15</sup> Two recent studies (Schwartz et al. 2001, Chen et al. 2001) combined cases from Maden with cases from a study of a similar population and adjusted for cigarette smoking and alcohol. The results of both studies regarding smokeless tobacco were not statistically significant.

cancer is based on five smokeless tobacco consumers. When an association is based on such a small number of individuals, the statistical significance may depend solely on the inclusion or deletion of one or two individuals among the cases.

Finally, none of the six positive studies published since Winn is generally cited in the scientific literature for the proposition that smokeless tobacco causes oral cancer. Rather, Winn and the 1986 Surgeon General's Report continue to be cited as support for that proposition.

### **III. European Community Warning**

As a result of more recent studies published relating to smokeless tobacco and oral cancer, the European Union issued a directive in June 2001<sup>16</sup> eliminating the warning "Causes cancer" from the warnings required on smokeless tobacco products sold in its Member States.<sup>17</sup> Dr. Lars Ramstrom, Director of the Stockholm Institute for Tobacco Studies, recently explained the genesis of the change in the European Union smokeless tobacco health warning. He noted that a report issued in 1997 by the Swedish National Board of Health and Welfare ("NBHW"),<sup>18</sup> which reviewed then recent studies relating to smokeless tobacco and oral cancer, caused the NBHW to "feel uneasy in its role as signatory of the legally prescribed [European Union] warning label on snuff packages: 'Causes cancer.' So the NBHW sent a letter to the Ministry of Health, drawing attention to the manifested lack of scientific basis for this warning label."<sup>19</sup>

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<sup>16</sup> Council Directive 2001.

<sup>17</sup> The warnings have been changed from "Causes cancer" and "Tobacco seriously damages health" (Council Directive 1992 (*citing* Council Directive 1989)) to "This tobacco product can damage your health and is addictive." (Council Directive 2001).

<sup>18</sup> Ahlbom et al. 1997.

<sup>19</sup> Ramstrom 2000 at 169.

As a result of this and other submissions, the European Union issued its new directive on tobacco labeling, endorsed by both the European Council and Parliament, eliminating “causes cancer” from the health warning on smokeless tobacco products.

#### **IV. Conclusion**

The majority of the epidemiological studies relating to smokeless tobacco do not report a statistically significant association between smokeless tobacco use and oral cancer. The proportion of negative studies has been even higher since the publication of Winn and the 1986 Surgeon General’s Report and no study published since Winn has replicated its result. Against this backdrop, it is USSTC’s position that smokeless tobacco has not been shown to be a cause of any human disease.<sup>20</sup>

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<sup>20</sup> It is not necessary to agree with USSTC’s position relating to smokeless tobacco and health in order to accept the proposition that smokeless tobacco has a legitimate role to play in a public health strategy aimed at tobacco harm reduction.

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