



Neil L. Wilcox, DVM, MPH  
Senior Vice President &  
Chief Compliance Officer

(336) 335-7656  
Fax (336) 335-7752  
E-Mail: [nwilcox@lortobco.com](mailto:nwilcox@lortobco.com)

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

VIA ELECTRONIC SUBMISSION

**RE: COMMENTS OF LORILLARD TOBACCO COMPANY**

Request for Comments: Scientific Evaluation of  
Modified Risk Tobacco Product Applications  
Docket No. FDA-2011-N-0443

These comments are respectfully submitted by Lorillard Tobacco Company (Lorillard) in response to the questions in Section II of the Food and Drug Administration (FDA) notice of public workshop on the "scientific evaluation of modified risk tobacco product (MRTP) applications." 76 Fed. Reg. at 36544.

The Family Smoking Prevention and Tobacco Control Act (Act) requires an order from FDA before a MRTP can be introduced or delivered into interstate commerce.<sup>1</sup> The Act defines a MRTP as a tobacco product which is sold or distributed to reduce harm or risk of tobacco related disease if the product's label or advertising implicitly or explicitly represents that the product is less harmful or presents a lower risk of tobacco-related disease than one or more commercially marketed tobacco products or the product or its smoke contains a reduced level of, presents reduced exposure to, or is free of a substance.<sup>2</sup> The Act expressly contemplates that combustible tobacco products, including cigarettes, which meet the Act's requirements can qualify as MRTPs.

Modified Risk Tobacco Products and Reduced Harm

Of course, encouraging smoking cessation and discouraging smoking initiation should always remain the primary public health message. Smoking and its consequent effects on health have shown general declines for some decades now. The adult smoking rate decreased from 20.9% in 2005 to 19.3% in 2010. Despite these overall positive trends in terms of the public health, approximately 45 million US adults currently continue to smoke.<sup>3</sup> These continuing smokers are the exclusive target market for MRTPs in the FDA-regulated tobacco products marketplace.

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<sup>1</sup>Act, Section 911(a)

<sup>2</sup>Act, Section 911(b)

<sup>3</sup><http://www.cdc.gov/VitalSigns/AdultSmoking/index.html>

MRTPs will have the greatest benefit to the public health if they include the full spectrum of moderately to radically modified products in order to appeal to smokers who have not quit smoking. The benefits to smokers' health that could result from MRTPs can be realized only if such products are readily available and acceptable to smokers as replacements for traditional cigarettes.

The contemporary concept of a MRTP is founded upon a vast science base of analytical chemistry, laboratory experimentation and human disease epidemiology that has accumulated for decades. MRTPs were the focus of the NCI "less hazardous cigarette" program of the 1970s,<sup>4</sup> were examined in the Institute of Medicine's *Clearing the Smoke* report in 2001,<sup>5</sup> and continue to be a promising alternative to smoking cigarettes currently available on the market.

Although the reduction in smoking-related disease risks as a result of cigarette design changes over the last six decades has been questioned by some public health authorities, decreasing exposure to smoke, generally, and to harmful constituents in smoke, specifically, continues to be a viable risk reduction strategy based on the valid and well-established toxicological principle of dose-response.<sup>6</sup> This approach to risk reduction focuses on potentially decreasing the adverse health effects of smoking, given the reality of continued cigarette smoking by a substantial percentage of the US population.

#### Modified Risk is not Equivalent to No Risk

The continuum reproduced below from the 2011 TobPRAC report<sup>7</sup> represents the essence of the fundamentally similar views of a number of advisory bodies on the spectrum of potential MRTPs.

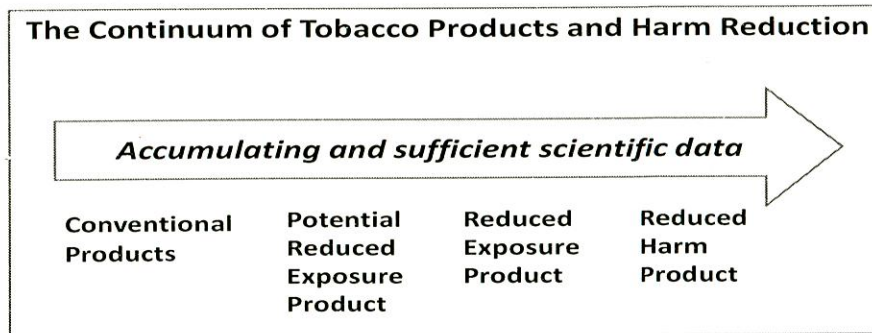
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<sup>4</sup> Parascandola, M. (2005). Lessons from the history of tobacco harm reduction: The National Cancer Institute's Smoking and Health Program and the "less hazardous cigarette". *Nicotine & Tobacco Research* 7(5): 779-789. Parascandola, M. (2011). Tobacco Harm Reduction and the Evolution of Nicotine Dependence. *American Journal of Public Health* 101(4): 632-641.

<sup>5</sup> Institute of Medicine, Committee to Assess the Science Base for Tobacco Harm Reduction, Board on Health Promotion and Disease Prevention. *Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction*. Washington, DC: National Academy Press; 2001.

<sup>6</sup> See, e.g., International Agency for Research on Cancer, *Tobacco Smoke and Involuntary Smoking*, Vol. 83: 171 (2004); NCI, Smoking and Tobacco Control Monograph 13, *Risks Associated with Smoking Cigarettes with Low Tar Machine-Measured Yields of Tar and Nicotine*, at 81 (2001); Henningfield, J.E. et al., *Guidance for research and testing to reduce tobacco toxicant exposure*, *Nic. & Tob. Res.*, vol. 7(6), 821-26 (2005).

<sup>7</sup> Peter G. Shields, Greg Connolly, K. Michael Cummings, Mirjana V. Djordjevic, Dorothy K. Hatsukami, Jack E. Henningfield, Matthew Myers, J. Richard J. O'Connor, Mark Parascandola, Vaughan Rees, Jerry Rice, and Mitchell Zeller (2011). *Providing a Science Base for the Evaluation of Tobacco Products*. Tobacco Product Assessment Consortium (TobPRAC)



The potential of MRTPs to benefit continuing smokers by reducing their exposures to one or many tobacco and smoke constituents that are believed to cause or promote serious illness can only be realized if such products are readily available to consumers and are sufficiently appealing to them to displace traditional cigarettes in the marketplace. There will not necessarily be bright line divisions between traditional cigarettes; modified cigarette products which may have relatively small, but meaningful, benefits to the public health; and radically different products which may have substantial public health benefits. Even modest, incremental advances in technologies that decrease smoking-related exposures may result in reductions in disease risk to smokers who accept these modified products.

#### Diversity of Tobacco Products Demands Similar Diversity of MRTPs

Although accumulating evidence suggests that potential MRTPs, such as Swedish-style snus products, electronic cigarettes and novel aerosol delivery systems, may replace traditional cigarettes for some smokers, a substantial percentage of continuing smokers have not adopted the available alternative products that differ markedly from traditional cigarettes. Continuing smokers who are unwilling to switch to a product radically different from traditional cigarettes should be given the choice of potentially reducing their risk by the availability of combustible MRTPs that provide even modest or incremental reductions in harmful smoke constituent exposures.

The concept of a substantial public health benefit derived from the wide acceptance of even a modestly reduced exposure product was recognized many years ago by Ernst Wynder, who stated at the 1979 Banbury Conference on Safer Cigarettes:

*"...as a practical matter, it is important to appreciate that a virtually harmless cigarette smoked by only 1% of the population will have a lesser impact on the reduction of tobacco-related diseases than a somewhat more harmful cigarette smoked by 80% of the total smoking population. Research on the less harmful cigarette should therefore be directed toward developing a cigarette containing the lowest possible amount of harmful elements for all*

*tobacco-related diseases, but one that has sufficient acceptability for the largest segment of smokers.*<sup>8</sup>

MRTPs that reduce exposure may be acceptable to smokers if they are similar enough to traditional cigarettes to support initial trial by smokers.

Filter cigarettes serve as an example of a reduced yield/reduced exposure product that achieved acceptance from smokers who had previously smoked only unfiltered cigarettes. The development of filter cigarettes in the 1950s led to their eventual domination of the U.S. marketplace. Epidemiology studies have confirmed that smoking filtered cigarettes has conveyed reduced disease risks compared to smoking unfiltered cigarettes.<sup>9</sup>

#### Communication to Smokers

Accurate and understandable information communicating the advantages and limitations of MRTPs that may provide minor, moderate or major potential benefits to smokers will be critical in order to maximize the potential for MRTPs to reduce the health effects of continued smoking. The magnitude of the potential risk reduction for any given MRTP product or product class must be communicated clearly and accurately to the consumer, based upon the best scientific data available. A significant new component of product appeal in the case of MRTPs will be the provision of factual scientific information on the reduced exposures that are actually delivered under real-world conditions of their use and, to the extent that it may be measurable with the best available assessments, their potential to result in reductions in biomedical changes associated with tobacco use. The ability of contemporary science to measure those changes is certainly imperfect, but a considerable understanding of disease mechanisms is available to broadly identify at least some indices of potentially meaningful risk reductions.<sup>10</sup> Any and all MRTP claims should be held to a single, rigorous scientific standard founded in the best current capabilities of the analytical chemistry, toxicological and biomedical sciences. Modest reductions in exposure should justify modest MTRP claims, just as extensively reduced exposures should justify more significant MRTP claims.

#### Conclusion

As FDA considers approval of potential MRTPs, Lorillard urges it to consider the full spectrum of potentially less harmful products, including combustible MRTPs. The potential reductions in risk from a combustible MRTP product design would appear to be modest relative to those for a radically different noncombustible product. Nevertheless, in light of the well-established and

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<sup>8</sup>A safe cigarette?, Proceedings of a meeting held at the Banbury Center, Cold Spring Harbor, N.Y., Oct. 14-16, 1979, eds. G. B. Gori, and F. G. Bock, Banbury Report 3. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory.

<sup>9</sup> Lee, PN & Saunders E. 2004. Does increased cigarette consumption nullify any reduction in lung cancer risk associated with low-tar filter cigarettes? *Inhalation Toxicology*, 16:817-833; Harris, JE, Thun MJ, et al. 2004. Cigarette tar yields in relation to mortality from lung cancer in the cancer prevention study II prospective cohort, 1982-8. *BMJ* 328; 72-76.

<sup>10</sup> U.S. Department of Health and Human Services, How Tobacco Smoke Causes Disease, a Report of the Surgeon General (2010).

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considerable risks that accompany traditional cigarette use, even a modest reduction in exposure and risk for such a product that is broadly accepted by consumers may in the final analysis offer the greatest benefit to the public health.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Neil L. Wilcox". The signature is written in a cursive, flowing style with some loops and flourishes.

Neil L. Wilcox, D.V.M., M.P.H