

Written Testimony of
Jeffrey E. Harris, M.D., Ph.D.
concerning proposed regulations
to implement Massachusetts General Law 94, section 307A
before the
Massachusetts Department of Public Health
250 Washington Street, Boston, Massachusetts
January 30, 1997, 1:40 p.m.

- I am a primary-care doctor at the Massachusetts General Hospital, as well as a professor at M.I.T., where I have taught courses in health economics and toxicology and public policy.

- I have served as: a contributor and senior reviewer to several U.S. Surgeon General's Reports on smoking and health; a consultant to the U.S. Consumer Product Safety Commission concerning toxicity testing of cigarettes; and a consultant to the U.S. National Cancer Institute concerning the relationships between individual chemical components of cigarette smoke and human diseases.

- On August 30, 1985, I testified on the Tolman Tobacco Disclosure Bill (S. 1982) before the Joint Committee on Health Care of the Massachusetts Senate and House of Representatives.

- I have reviewed M.G.L., section 307C, and the proposed regulations entitled "Cigarette and Smokeless Tobacco Products: Reports of Added Constituents and Nicotine Ratings (105 CMR 660.000)."

- **The Food and Drug Administration's (FDA's) Generally Regarded as Safe (GRAS) standard cannot automatically be applied to cigarette additives. A substance that is regarded as GRAS in food may not be "generally regarded as safe when burned or inhaled," as defined in MGL ch. 94, s. 307C, or 105 CMR 660.004(2)(a).**

- Cigarette smoke is a complex aerosol containing thousands of distinct chemicals that are produced during the heating, burning, and chemical "cracking" of the cigarette. Most of the known carcinogens in cigarette smoke (such as polyaromatic hydrocarbons) are substances that are not present in an unlit cigarette, but are formed during the process of smoking. Hydrogen cyanide, formed during smoking, has toxic effects on the cilia that line the respiratory tract, and may cross the placenta in a pregnant smoker to harm the growing fetus. Oxidants and nitrogen oxides, formed during smoking, contribute to lung damage and the development of emphysema. Carbon monoxide, formed during smoking, reduces the oxygen-carrying capacity of red blood cells [1].

- A scientifically competent analysis of cigarette additives similarly requires consideration of their chemical byproducts during the heating, burning, and chemical “cracking” that occurs during smoking. Thus, some natural amino acids, which may be added to cigarette smoke, give rise to genotoxic and carcinogenic amino-heterocyclic compounds during heating. Certain plant extracts (e.g. licorice root extract, which contains 25% glycyrrhizin) can give rise to carcinogenic aromatic hydrocarbons during burning. Some tobacco additives may give rise to benzene (a known human carcinogen) during smoking [2].

- The FDA evaluates food additives (e.g., the new fat substitute Olestra) by reference to GRAS list. GRAS substances, however, are specifically recognized as safe in *foods*. Their safety is usually based upon a long history of safe use in *foods*, or their close similarity to other substances already in *foods*. When the GRAS status of any substance is unclear, FDA has specific procedures for companies to petition the Agency to review the substance. During such procedures, companies may supply data from their own testing laboratories. In such cases, the substance under scrutiny is not kept secret; instead, its identity and any studies conducted by the company are publicly aired for scientific review [3].

- When I, as a physician, consult my *Physician’s Desk Reference* to assess the safety of *inhaled* drugs that I might prescribe, I find that pharmaceutical companies submit data on animal studies by multiple routes of installation, including long-term inhalation, not just the oral route. Standard toxicological studies, such as *in vivo* and *in vitro* mutagenicity and genotoxicity studies and whole-animal reproductive studies, are routinely performed. In addition, all active and inactive components of the inhalant are disclosed, including propellants, pH adjusters, and other additives [4].

- **The toxicity testing of the chemical components of cigarette smoke follows procedures that are widely accepted in the scientific community and private industry [5], including the cigarette industry [6]. The same procedures could be used by the Department of Public Health to assess the safety of additives disclosed by manufacturers under 105 CMR 660.005(3).**

- In its toxicological testing of new cigarette prototypes that heat instead of burn tobacco, R.J. Reynolds Tobacco Company (RJR) conducted a comprehensive analytical and biological evaluation of each chemical component of the whole smoke emitted from such cigarettes [6, pp. 79ff]. Each smoke aerosol component was assessed for: the level of potential exposure to the consumer; the history of use in consumer products, including cigarettes; the quantity and quality of toxicological data available; and a battery of toxicity tests conducted by R.J. Reynolds. These tests included: bacterial mutagenicity (Ames test); *in vitro* and *in vivo* genetic toxicology (sister chromatid exchanges and chromosomal aberrations in CHO cells and bone marrow, unscheduled DNA synthesis in isolated rat hepatocytes,

micronucleus assay in bone marrow, urine mutagenicity); and both short-term and longer-term animal inhalation studies of whole smoke and smoke components [6, pp. 85-92].

- In its review of existing literature and standards, RJR consulted information on threshold limit values (TLV's) developed by the American Conference of Governmental Industrial Hygienists and the acceptable daily intakes (ADI's) developed by the Environmental Protection Agency [6, p.93 and Table 3.4.2-1]; as well as lists of carcinogens published by the U.S. Surgeon General's Reports and in the tobacco monograph of the International Agency for Research on Cancer (IARC) [6, p. 100].

- With respect to proprietary flavor ingredients used in the development of its new cigarette, RJR specifically consulted lists of flavoring substances determined by the Flavor Extract Manufacturers Association (FEMA) or the FDA to be GRAS in food. Nonetheless, all flavor mixtures (as well as smoke containing the flavorants) were tested in the Ames assay, and in acute (14-day) and sub-chronic (90-day) inhalation studies [6, pp. 578ff]. Extensive animal studies were conducted on glycerol, propylene glycol, and a humectant mixture.

- Appended to my testimony is a copy of Figure 3.2-1 from RJR's monograph [6, p. 80] illustrating the procedures used by the company to analyze smoke components.

References

1. Jeffrey E. Harris, "Cigarette Smoke Components and Disease: Cigarette Smoke is Far More Than a Triad of 'Tar,' Nicotine, and Carbon Monoxide," Chapter 5 in *The FTC Cigarette Test Method for Determining Tar, Nicotine, and Carbon Monoxide Yields of U.S. Cigarettes: Report of the NCI Expert Committee*. Smoking and Tobacco Control Monograph No. 7, Bethesda, MD: National Cancer Institute, 1996, pp. 59–70.
2. American Health Foundation, "Comments by the American Health Foundation" on the List of Additives in the 1988 Report of the Independent Scientific Committee on Smoking and Health. Valhalla, NY: American Health Foundation, March 30, 1990.
3. Food and Drug Administration. "'Low Calorie' Fat Substitute," FDA Bulletin Board, Questions and Answers, Washington, DC: Food and Drug Administration, January 27, 1988.

4. Physician's Desk Reference. Monograph on Maxair Autohaler and Maxair Inhaler (pirbuterol acetate inhalation aerosol), 3M Pharmaceuticals. Montvale, NJ: Medical Economics Data Production Company, 1985: 1382-85.

5. Jeffrey E. Harris, "Overview and Major Considerations in the Toxicity Testing of Low Ignition-Potential Cigarettes," Chapter B in: *Toxicity Testing Plan for Low Ignition-Potential Cigarettes. Vol. 5 of Final Report: Fire Safe Cigarette Act of 1990* (Washington D.C.: U.S. Consumer Product Safety Commission, August 1993).

6. R.J. Reynolds Tobacco Company. *New Cigarette Prototypes That Heat Instead of Burn Tobacco*. Winston-Salem, NC: R.J. Reynolds Tobacco Company, 1988.