authorities. The agency proposes to make these products subject to regulation pursuant to the act's device authorities. The remainder of this discussion explains the regulatory framework for combination products; why nicotine-containing cigarettes, loose tobacco, and smokeless tobacco products are drug/device combination products; and why the agency can exercise its discretion to regulate them only under the act's device provisions. Finally, this section discusses a number of other legal issues raised by the provisions of the proposed rule.

1. The Federal Food, Drug, and Cosmetic Act and Combination Products

As part of the Medical Device Amendments of 1976, Congress established, for the first time, a premarket approval mechanism for certain devices. Congress also expanded the act's device definition to expressly include items such as implements, machines, implants, and in vitro reagents. "Device" was defined as:

an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

(1) recognized in the official National Formulary, or the United States

Pharmacopeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

(3) intended to affect the structure of any function of the body of man or other animals, and which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes.

Pub. L. No. 94-295 (1976).

The act was amended by the Safe Medical Devices Act of 1990, among other reasons, to recognize and provide for the regulation of products that constitute a combination of a drug, device, or biological product (21 U.S.C. 353(g)). The Safe Medical Devices Act also modified the act's drug and device definitions to conform them to the new section regarding primary jurisdiction over combination products. (See S. Rep. 101–513). Among these modifications is that the definition of "drug" no longer excludes devices or their components, thereby eliminating the notion that "drug" and "device" are mutually exclusive terms.

In light of the act's public health protection purposes, the agency has consistently construed the device definition broadly, and courts have upheld this interpretation. *United States* v. An Undetermined Number of Unlabeled Cases, 21 F.3rd 1026, 1028 (10th Cir. 1994); United States v. 22 Rectangular Devices, 714 F. Supp. 1159, 1162 n.7 (listing additional examples), 1164–65 (D. Utah 1989); see, e.g., United States v. 23, More or Less, Articles, etc. 192 F.2d 308, 309 (2d Cir. 1951) (phonograph records used in treating insomnia).

Because the act's definition of device is a statutory term of art, it encompasses a very wide assortment of items. Obvious examples of devices are simple medical implements such as thermometers or tongue depressors and more complicated electronic products such as X-ray machines or cardiac pacemakers. Less obvious examples of devices include in vitro reagents and other products used for diagnostic purposes, such as culture media made from snake venom (21 CFR 864.8100, 864.8950) and animal and human sera (21 CFR 864.2800). FDA also regulates many organic substances as devices. For example, a simple plant product that consists of nothing more than coagulated tree sap, gutta percha, which is used to fill the root canal in a tooth, is a device (21 CFR 872.3850). All of these articles are devices because they are instruments, apparatuses, implements, machines, contrivances, implants, in vitro reagents, or another similar or related article with uses or effects encompassed by the act. Therefore, understanding what can properly be regarded as a device for purposes of the act requires a statutory, not a lay, understanding of the term. The following discussion identifies the parts of cigarettes, loose cigarette tobacco, and smokeless tobacco that are devices, and explains why these products are drug delivery systems.

2. Cigarettes, Smokeless Tobacco Products, and Loose Tobacco Are Drug Delivery Systems

Because drugs cannot be administered in pure chemical form, drug delivery systems are designed and used to deliver drugs into the body's circulatory system or to specific target sites in the body at predetermined, controlled rates.1 FDA considers articles such as instruments, machines, contrivances, implants, or other similar or related articles, whose primary purpose is the delivery of a drug, and that are distributed with a drug product to be drug delivery systems. Intercenter Agreement Between the Center for Drug Evaluation and Research and the Center for Devices and Radiological Health, Section VII.A.1.(b) (October 31, 1991). These articles are often called "prefilled delivery systems." Examples of

these combination products include contrivances containing drugs, such as pre-filled syringes, transdermal patches, and metered-dose inhalers. *Id.* CDER has primary jurisdiction over the regulation of such products, and has the authority to use drug provisions, device provisions, or a combination of drug and device provisions to regulate particular drug delivery systems. *Id.*

Cigarettes and smokeless tobacco products function like drug delivery systems in that they contain a drug, nicotine; are used to deliver the drug to the site at which the drug will be absorbed into the body, the mouth or lungs; and after the drug has been delivered, the delivery system, the cigarette butt or smokeless tobacco material, depleted of nicotine, remains and must be discarded. Only the nicotine delivered by these products achieves its primary intended purpose by chemical action in or on the body. The subsections below explain in greater detail why these products are drug delivery systems.

a. *Cigarettes.* Cigarettes are drug delivery systems consisting of a drug, nicotine, and device components that include the tobacco itself, the paper the tobacco is rolled in and, in the case of filter cigarettes, the filter. A cigarette is analogous to a metered-dose inhaler, an instrument that converts a drug into an aerosolized form for inhalation and delivery to the lungs for absorption into the bloodstream.

Although lighting a cigarette appears to be a simple action, there is, in fact, a complex process taking place within the cigarette. A cigarette consists of carefully blended and treated nicotinecontaining rolled tobacco. The blended and treated tobacco is wrapped in paper that is precisely treated so that the entire tobacco rod burns in a controlled manner. Attached to the tobacco rod (in 95 percent of U.S. cigarettes) is a filter with many possible design features, including vents and chambers. The primary purpose of parts of the cigarette, and the cigarette itself, a consciously engineered and, in the industry's own words, "highlyengineered"² product, is to effectuate the delivery of a carefully controlled amount of the nicotine to a site in the human body where it can be absorbed. The drug, nicotine, is generally contained within the treated rolled tobacco. The delivery system, the nicotine-containing cigarette, must be lit to have its intended effect on the structure or function of the body and, once lit and used, is discarded.

In this manner, an average American cigarette yields approximately 1.0 mg of nicotine, although the smoker can adjust