REPORT TO CONGRESS

INNOVATIVE PRODUCTS AND TREATMENTS TO ACHIEVE ABSTINENCE FROM TOBACCO USE, REDUCTIONS IN CONSUMPTION OF TOBACCO, AND REDUCTIONS IN THE HARM ASSOCIATED WITH CONTINUED TOBACCO USE

REQUIRED BY SECTION 918 OF THE
FEDERAL FOOD, DRUG, AND COSMETIC ACT

AS AMENDED BY PUBLIC LAW 111-31

Department of Health and Human Services
Food and Drug Administration

I. Introduction and Summary

Section 918 of the Federal Food, Drug, and Cosmetic Act (FD&C Act)[1] requires that the Secretary of the Department of Health and Human Services (HHS) submit a report to Congress examining the best way to regulate, promote, and encourage the development of "innovative products and treatments," including both nicotine-based and non-nicotine-based products and treatments, to better achieve three goals: (A) total abstinence from tobacco use, (B) reductions in consumption of tobacco, and (C) reductions in the harm associated with continued tobacco use.

This examination primarily implicates the work of the Food and Drug Administration (FDA or the Agency). FDA is an agency within HHS charged with protecting the public health by ensuring the safety and effectiveness of a variety of products, including medical products such as drugs and devices. Since 2009, FDA's public health mission has also included the regulation of tobacco products. The regulation of "innovative products and treatments" to achieve the three goals identified in Section 918 will primarily involve products within the categories of drugs, devices (including drug/device combination products), and tobacco products. FDA is the agency charged with duties such as the review of drug, device, and tobacco products before marketing, the issuance of approvals or authorizations for marketing, and the continuing regulation of products once on the market.

An important way FDA can promote and encourage the development of "innovative products and treatments" to achieve abstinence, reductions in consumption, and reductions in harm is by providing open and working pathways for products to come to market. Although the development of new products is undertaken by industry, FDA is working actively to promote the development of new products and treatments for tobacco dependence on a variety of fronts. Most recently, FDA issued a notice of findings allowing the modification of certain warnings and directions for use in the labeling of existing over-the-counter nicotine replacement therapy (NRT) products. On December 17, 2012, FDA held a public hearing under 21 CFR Part 15 to obtain input on FDA's regulation of NRTs and the promotion of innovative approaches in the development of products and treatments for tobacco dependence. This report incorporates input received at the Part 15 hearing, including comments submitted to the associated docket, as well as the results of our consultations with various scientific, medical, and public health experts.

To achieve the three goals identified in Section 918, FDA is working to examine the regulation of existing and new products and treatments for tobacco dependence and will look at regulation comprehensively across all relevant product categories. This report describes the pathways to market that are available for products regulated under the drug,

[1] Section 918 was added to the FD&C Act by the Family Smoking Prevention and Tobacco Control Act of 2009 (Tobacco Control Act or TCA), Public Law 111-31 (June 22, 2009).

device, and tobacco-product authorities, along with FDA's ongoing efforts to regulate products and treatments in a way that will bring about abstinence, reductions in consumption, and reductions in harm.

In considering innovative approaches in all three of these areas, FDA also intends to consider potential countervailing effects, including the possibility that more people will maintain an addiction to nicotine; the possibility that more people will engage in "dual use" of cigarettes and other, alternative nicotine-containing products; and the possibility that existing and new products will be attractive to non-users, particularly youth. FDA will take account of these issues in the approval and authorization for marketing of innovative products and treatments for tobacco dependence.

II. Background: The Categories of Products at Issue in Section 918 and the Impact of *Sottera* on FDA's Regulatory Authority

A. The Provisions of Section 918

The specific terms of Section 918(b) require that the Secretary, after consultation with recognized scientific, medical, and public health experts, "submit to the Congress a report that examines how best to regulate, promote, and encourage the development of innovative products and treatments (including nicotine-based and non-nicotine-based products and treatments) to better achieve, in a manner that best protects and promotes the public health – (A) total abstinence from tobacco use; (B) reductions in consumption of tobacco; and (C) reductions in the harm associated with continued tobacco use." The statute further requires that the report "include the recommendations of the Secretary on how the [FDA] should coordinate and facilitate the exchange of information on such innovative products and treatments among relevant offices and centers within the Administration and within the National Institutes of Health [NIH], the Centers for Disease Control and Prevention [CDC], and other relevant agencies."

All three of the goals set forth in Section 918(b) highlight areas where further innovation is needed, and in each case there may be specific products or treatments that could help achieve a particular goal. But the evaluation of innovative approaches to abstinence, reductions in consumption, and reductions in harm also raises larger regulatory questions that call for FDA to develop a comprehensive regulatory approach across all products and treatments that target users of tobacco.

The concept of achieving "total abstinence from tobacco use," for example, encompasses the approval of medical products to bring about cessation (quitting) in individuals who currently use tobacco — but also raises the question of whether individuals should be encouraged to quit smoking while remaining addicted to nicotine. Similarly, in seeking to achieve "reductions in consumption of tobacco," it is possible to envision a product

designed to cause users to smoke fewer cigarettes or otherwise consume less tobacco. But it is also important to consider whether reduction in consumption confers a health benefit at either the individual or the population level, particularly given the possibility that users who reduce their cigarette consumption may engage in "dual use" with other tobacco- or nicotine-containing products. Finally, the goal of "reductions in the harm associated with continued tobacco use" might suggest a product such as a chemopreventive agent that is designed to reduce the harm associated with an individual's ongoing tobacco use. Some stakeholders have also argued, however, that certain tobacco products are potentially less toxic than cigarettes and that use of those products should be encouraged as a substitute for smoking. Complex questions remain about the impact of this and other so-called "harm-reduction" strategies on individual users, on initiation by current nonusers, and on the overall public health. These issues will be discussed further below in Section V.

In Section 918(a), a separate provision from the one requiring a report, Congress instructs the Secretary to (1) consider designating smoking-cessation products, including nicotine replacement therapies (NRTs), as fast track products benefiting from expedited approval; (2) consider approving the extended use of NRTs for the treatment of tobacco dependence; and (3) review and consider the evidence for additional indications for NRTs, "such as for craving relief or relapse prevention."

As the language of Section 918(b) makes clear, Congress intended this report to address a range of innovative products and treatments — both nicotine-based and non-nicotine-based — to the extent those products may have an impact on tobacco dependence and/or related harms. And as noted above, to address the three goals identified in Section 918(b), this report will examine the regulation of existing and new products and treatments for tobacco dependence. Therefore, this report will discuss FDA's regulation of NRT products (a number of which are already on the market) as well as new and "innovative" products and treatments.

B. Definitions of the Products at Issue: Drugs and Devices are Defined by Their Intended Use, While Tobacco Products Are Not

Drugs are defined under the FD&C Act to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease," as well as "articles (other than food) intended to affect the structure or any function of the body."[2] Medical devices are defined in very similar terms.[3] The so-called "intended use" of an item is therefore critical to FDA's ability to regulate drugs and devices. An article's intended use is determined by FDA based primarily on the claims that are made about the product.

[2] FD&C Act § 201(g)(1).
[3] FD&C Act § 201(h).

The term "tobacco product," by contrast, is defined to include "any product made or derived from tobacco that is intended for human consumption."[4] FDA's authority to regulate tobacco products, therefore, depends first on the product's physical makeup.[5]

The definition of "tobacco product" *excludes* any item that falls within the definition of a drug, a medical device, or a combination product[6] — for example, any item whose "intended use" involves the diagnosis, cure, mitigation, treatment, or prevention of disease.[7]

Products whose intended use makes them drugs or devices (or combination products) are subject to Chapter V of the FD&C Act (including section 505, which sets forth the approval standards for "new drugs"). These products are regulated by FDA through the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH).

Products that meet the definition of "tobacco product" are regulated by FDA through the Center for Tobacco Products (CTP). The FD&C Act gives FDA direct authority over cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco products. The FD&C Act also gives FDA authority to deem other products that fall within the "tobacco product" definition to be subject to FDA's tobacco authorities under Chapter IX of the FD&C Act.[8]

C. The Impact of Sottera on FDA's Regulatory Authority

As discussed above, the definition of "tobacco product" explicitly excludes products that meet the legal definition of "drugs" or "devices." In *Sottera, Inc. v. FDA*, the U.S. Court of Appeals for the D.C. Circuit took up the question of whether electronic cigarettes containing nicotine derived from tobacco fall within the definition of "tobacco product" (and are therefore regulated by CTP), or fall within the definition of "drugs" or "devices" (and are regulated by CDER/CDRH).[9]

The answer, the court ruled, depends upon the intended use of the product. Nicotine-containing products as "customarily marketed" (including traditional cigarettes) — provided they are not also marketed for what the court described as "therapeutic"

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[4] FD&C Act § 201(rr)(1).
[5] Tobacco products that claim to offer reduced risk or reduced exposure relative to other tobacco products do, however, become subject to additional regulatory requirements. These "modified risk tobacco products" are discussed in Section IV.
[6] A combination product is one that combines a drug, device, or biological product. Combination products are regulated according to whether the primary mode of action is that of the drug, the device, or the biological product. *See* FD&C Act § 503(g)(1).
[7] FD&C Act § 201(rr)(2).
[8] FD&C Act § 901(b).
[9] This case arose after FDA attempted to regulate electronic cigarettes under the drug/device authorities. *See Sottera, Inc. v. FDA*, 627 F.3d 891 (D.C. Cir. December 2010).

purposes — can be regulated by CTP. Nicotine-containing products that are marketed for "therapeutic" purposes cannot be regulated as tobacco products, but can be regulated by CDER/CDRH as drugs/devices. Because no evidence had been presented to the court that the electronic cigarettes at issue in the case had been marketed with "therapeutic" claims, the court held that they could not be regulated as medical products.

In the wake of *Sottera*, a product's intended use (e.g., as embodied in a product's marketing claims) determines whether it will be regulated as a drug or device, rather than a tobacco product. The classification of products into "medical product" and "tobacco product" categories has important implications for both industry and the public. The ruling in *Sottera* has therefore had a significant and complex impact on FDA's regulation of nicotine-containing products.

In Sections III and IV below, this report discusses the authorities that FDA is able to apply in regulating drugs/devices and tobacco products. As further set forth below, the standards that must be met before FDA can legally allow a product to reach the market are different for drugs/devices than for tobacco products. Generally speaking, drugs and devices must be approved for a particular intended use in individuals. New or modified tobacco products are subject to different criteria that take into account the product's impact on the health of the population as a whole.

Section V describes FDA's approach to developing a comprehensive regulatory strategy to encourage innovation and achieve abstinence, reductions in consumption, and reductions in harm. Section VI summarizes the consultations undertaken by FDA in preparing this report, and FDA's strategy for facilitating the exchange of information on innovative products and treatments within the relevant government agencies.

III. Drug/Device Authorities and Pathways to Market

Under the FD&C Act section 505, FDA is charged with ensuring that new drugs have been shown to be safe and effective for their intended use before they reach the market. CDER's mission, therefore, is to promote and protect the public health by ensuring the safety and efficacy of marketed drugs.

A. Drug and Drug/Device Approval Pathways

FDA has extensive premarket approval authority over "new" drugs — drugs that are not "generally recognized as safe and effective" (GRAS/E) and/or have not been used to a material extent or for a material time.[10] A product whose intended use falls within the definition of "drug" under FDCA section 201 and which is also a "new" drug must obtain premarket approval from FDA. This is done through submission of a new drug

[10] *See* FD&C Act § 201(p) (defining "new drug").

application (NDA) or an abbreviated new drug application (ANDA) by the product's "sponsor" (usually the manufacturer).

An NDA must establish safety and efficacy in individuals via "substantial evidence," which has typically been interpreted to mean two adequate and well-controlled clinical trials. The NDA applicant also proposes labeling for the product that reflects its intended use. If the benefit that can be expected from use of the drug outweighs the risks inherent in its use, FDA will approve the NDA and the drug can be legally marketed in accordance with its approved labeling.[11]

Many products approved under NDAs are classified as prescription drugs if a potential for harmful effect or other factors suggest that they are only safe for use under the supervision of a licensed practitioner.[12] A prescription drug approved under an NDA can later be "switched" to over-the-counter (OTC) status if it is determined that the product can be safely and effectively used by consumers without the supervision of a practitioner. A medication can also be approved directly as an OTC product through the NDA process.[13]

Products that combine "drug," "device" and/or "biologic" components are regulated as "combination products," with the pathway to market determined by the component that has the primary mode of action.[14] In general, a product that contains nicotine intended to be used as a "drug," along with a "device" component to deliver the nicotine, would be considered to have its primary mode of action through the drug component and would be regulated through the NDA process. As an example, the current prescription nicotine inhaler, which is intended for use in smoking cessation, was approved under an NDA.

FDA has significant postmarket authorities related to ensuring the continued safety and efficacy of drug products once they are on the market. For example, FDA continues to monitor drug safety through postmarket safety reports and can require changes in product labeling based on new information that comes to light after approval. FDA also has the authority to withdraw a drug from the market if it is determined that the product's risks outweigh its benefits.

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[11] Under certain circumstances, sponsors can pursue an ANDA application. The ANDA process reduces the time and effort needed for approval by, among other things, allowing the applicant to rely on FDA's previous finding of safety and effectiveness for a listed drug rather than having to repeat the studies conducted to support approval of the listed drug. To rely on such a finding, the ANDA applicant must show that, among other things, its proposed drug product is the same as the listed drug with respect to active ingredient, dosage form, strength, route of administration, and, with certain narrow exceptions, labeling, and that its product is bioequivalent to the listed drug. *See* FDCA § 505(j)(2). In this report, we focus primarily on the NDA pathway, which is the most likely pathway for a novel or innovative drug product.

[12] FDCA § 503(b)(1).

[13] Drugs can also be legally marketed if they conform to a final OTC monograph, but no monographs currently exist to cover treatments for tobacco dependence.

[14] *See* 21 CFR § 3.2(m).

Since the 1990s, accelerated approval and fast track processes have been available to facilitate the approval of new drug products under the NDA process.[15] These processes have been available on a case-by-case basis for drug candidates that are intended to treat a serious or life-threatening condition and that have the potential to fill an unmet medical need. Accelerated approvals permit sponsors to obtain approval in certain cases based on studies that rely on a surrogate endpoint, rather than a clinical outcome (or a clinical endpoint other than survival or irreversible morbidity). In such cases, postapproval studies are generally required to confirm the results submitted prior to approval.

Under the Food and Drug Administration Safety and Innovation Act (FDASIA),[16] expedited review processes are available to any product intended to treat "a serious or life-threatening disease or condition." The requirement that the product demonstrate the potential to meet an unmet medical need remains. FDASIA also provides a definition of "breakthrough therapy" — a product intended to treat a serious or life-threatening disease or condition and one that may, based on preliminary clinical evidence from one or more clinically significant endpoints, offer substantial improvement over existing therapies.

Products eligible for fast track have generally also been accorded priority review status. Priority review is a designation given to products that offer a major treatment advance or that supply a treatment option where none exists. Priority review products are accorded a six-month target period for NDA review.

Accelerated approval and fast track mechanisms have been and will remain fully available to sponsors of products targeting tobacco dependence and the associated harms. As discussed here, however, a number of NRT approvals were granted before these mechanisms came into existence.

B. Application of the Drug/Device Authorities to Treatments for Tobacco Dependence

The NDA approval processes described above apply to any product that aims to treat or cure tobacco dependence, or that otherwise falls within the "drug" definition. Currently, all products that are approved by FDA for tobacco dependence were approved as aids to smoking cessation.

There are currently five types of FDA-approved nicotine-based therapies on the market as stop-smoking aids: the nicotine patch, gum, lozenge, spray (prescription only), and inhaler (prescription only). There are also two FDA-approved non-nicotine-based therapies (both prescription only): bupropion (Zyban and generics) and varenicline (Chantix). All of these products were originally approved by CDER through the NDA

[15] The application of these processes to drug products for smoking cessation is discussed further below in Section III.B.
[16] Public Law 112–144 (July 9, 2012).

process, and were all found safe and effective (in conjunction with behavioral support) as aids to smoking cessation.

The current labeling of these products reflects the regimen that was used in the efficacy studies the sponsors originally submitted with their NDAs. For example, the currently labeled duration of use for OTC NRT products, which generally ranges from 8 to 12 weeks depending on the product, reflects the period of use that was associated with achievement of smoking cessation in the clinical trials that formed the basis for approval.

The original NDAs for the NRT gums and patches were approved between 1984 and 1992 (these products were all "switched" to OTC between 1996 and 2002). The spray and inhaler NDAs were approved in 1996-97, and the lozenge NDA (the only NDA in the group that was submitted for OTC use without prior prescription approval) in 2002.

Recognizing the importance of making treatments for tobacco dependence widely available, CDER worked to facilitate the "switch" of NRT products to OTC status. For example, the NRT patch was first approved as a prescription product in 1991 and was switched to OTC status in 1996.

The original accelerated approval pathway (21 CFR Subpart H), which allows for approval based on surrogate endpoints with a requirement for postmarket studies, did not become available until 1992. The fast track approval process, which provides more frequent meetings with and feedback from FDA, was created via statute in 1997 (that statute also "codified" the Subpart H process).[17] Priority review became available as an Agency procedure in 1996.

Even the earliest of these mechanisms, therefore — the Subpart H regulations — postdated the original NRT applications. All of the original gum and patch NDAs were filed and granted by 1992 (only the spray, inhaler, and lozenge came later).

Despite the lack of formal mechanisms for accelerating the early NRT approvals, CDER took a number of steps to facilitate and expedite the NDA process for these products. For example, CDER approved the NRTs' indication for smoking cessation based on an efficacy endpoint of one-month quit. This one-month quit endpoint was accepted in place of the ultimate clinical goal of permanent smoking cessation.

The NDAs for bupropion and varenicline were approved in 1997 and 2006, respectively. Both these applications also benefited from an efficacy endpoint of one-month abstinence from smoking. Varenicline received priority review. Both products are currently on the market and provide an additional option for smokers wishing to quit. Neither product contains nicotine; varenicline binds to nicotine receptors in the brain, while bupropion inhibits reuptake of dopamine, noradrenaline, and serotonin in the central nervous system. In 2009, based on adverse event reports suggesting an association of both

[17] *See* FD&C Act § 506.

products with serious neuropsychiatric symptoms, FDA required the addition of boxed warnings[18] to their labeling.

IV. Tobacco-Product Authorities and Pathways to Market

CTP was established in August 2009 and, since that time, has been working to protect public health in the United States by regulating the manufacture, distribution, marketing and sale of tobacco products under the Tobacco Control Act. CTP's mission is to prevent and reduce tobacco use harms in the United States.

Currently, only cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco products are subject to FDA's tobacco authorities under Chapter IX of the FD&C Act. The FD&C Act also gives FDA the authority to deem other products that fall within the "tobacco product" definition to be subject to FDA's tobacco authorities under Chapter IX of the FD&C Act.

As noted above in Section II, the definition of "tobacco product" specifically excludes drugs, devices, and combination products. Therefore, CTP does not regulate drug or device products used to treat tobacco dependence, or any other products or treatments made or derived from tobacco that are drugs or devices (e.g., NRTs or other smoking cessation aids).

A. "New" Tobacco Product Pathways

CTP does, however, have premarket review authority over "new" cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco products — which are defined to include any such tobacco products not commercially marketed in the United States as of February 15, 2007, and any modification of such a tobacco product where the modified product was commercially marketed after that date.[19] The FD&C Act gives FDA the authority to deem other products that fall within the "tobacco product" definition to be subject to FDA's tobacco authorities, including its premarket review authorities.

"New" tobacco products subject to FDA's tobacco-product jurisdiction must follow one of three pathways to market. First, a manufacturer may submit a report providing its basis for determining that its product is "substantially equivalent" (SE) to an appropriate predicate product.[20] If CTP determines that the product is substantially equivalent to an appropriate predicate product, CTP will issue a marketing authorization order. Such an order reflects a determination that the product either has the same characteristics as the

[18] *See* 21 CFR 201.57(c)(1).
[19] FD&C Act § 910(a)(1). The modification may include a change in "design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient."
[20] *See* FD&C Act § 905(j)(1)(A)(i).

predicate, or has different characteristics, but does not raise different questions of public health.[21] This pathway to market is often referred to as the "SE pathway."

Second, a legally marketed product with a minor modification of an additive may be granted an exemption from having to prove substantial equivalence.[22] This pathway is referred to as the "SE exemption pathway."

Finally, manufacturers of "new" tobacco products may apply for marketing authorization by submitting a premarket tobacco product application (PMTA).[23] The PMTA pathway requires applicants to demonstrate that permitting the new product on the market would be appropriate for the protection of the public health. In determining whether this demonstration has been made, CTP considers the risks and benefits to the U.S. population as a whole, including both tobacco users and nonusers,[24] and must deny the PMTA if the applicant fails to meet its burden.[25]

CTP also has several important postmarket authorities with regard to "new" tobacco products, including the authority to restrict the sale and distribution of the product,[26] or to temporarily suspend marketing of the product if CTP determines that there is a reasonable probability that the product poses a greater risk than other tobacco products on the market.[27] CTP may also withdraw a PMTA-based marketing order in certain cases, including when CTP finds that the order is no longer appropriate for the protection of public health; the application contained an untrue statement of material fact; or the applicant has failed to comply with certain requirements of the FD&C Act.[28]

Under the PMTA authorities, marketing authorization depends on a determination that the marketing of the product is appropriate for the protection of public health. Any time a manufacturer creates a new tobacco product or modifies an existing tobacco product in any way, FDA must review the product and consider data regarding its potential effects on public health. CTP must deny a PMTA if the applicant has failed to show that the product is appropriate for the protection of public health.

B. Modified Risk Tobacco Products

CTP has additional authorities with regard to tobacco products that make claims of reduced risk or reduced exposure relative to other tobacco products. These additional authorities over "modified risk tobacco products" (MRTPs) were designed in part to

[21] FD&C Act § 910(a)(3)(A).
[22] *See* FD&C Act §§ 905(j)(3), 905(j)(1)(A)(ii) and 21 CFR 1107.1.
[23] FD&C Act § 910(a)(2).
[24] FD&C Act § 910(c)(4). CTP considers both the increased or decreased likelihood that existing users of tobacco products will quit, and the increased or decreased likelihood that nonusers of tobacco products will start using such products.
[25] FD&C Act § 910(c)(2).
[26] FD&C Act § 910(c)(1)(B).
[27] FD&C Act § 910(d)(3).
[28] FD&C Act § 910(d)(1)(A)-(F).

avoid problems such as those associated with the marketing of so-called "light/low" and "mild" products. Cigarette makers started using "light," "low," and "mild" labels following the landmark 1964 Surgeon General's report on the health effects of smoking. Consumers believed that these products were less harmful.[29] However, these "light" and "low" cigarettes were found to be no safer than regular cigarettes,[30] and may even have contributed to smoking initiation among young people[31] and impeded cessation.[32]

A tobacco product is an MRTP if:

- It represents in its label, labeling, or advertising, either implicitly or explicitly, that:
    - the tobacco product presents a lower risk of tobacco-related disease or is less harmful than one or more other commercially marketed tobacco products;
    - the tobacco product or its smoke contains a reduced level of a substance or presents a reduced exposure to a substance; or
    - the tobacco product or its smoke does not contain or is free of a substance.

or

- It uses the descriptors "light," "mild," "low," or similar descriptors in its label, labeling, or advertising.

or

[29] *See* TCA§ 2(38). A nationwide 1987 survey found that 45.7% of "Ultra-Light" smokers, 32.2% of "Light" smokers, and 29.4% of "Regular" smokers said that low-tar cigarettes reduced the risk of cancers. *See* Giovino, G.A., et al., Attitudes, knowledge, and beliefs about low-yield cigarettes among adolescents and adults. In The FTC Cigarette Test Method for Determining Tar, Nicotine, and Carbon Monoxide Yields of U.S. Cigarettes, Report of the NCI Expert Committee, 49. Smoking and Tobacco Control Monograph No.7, U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute (1996). Yet studies have indicated that switching to "Light" cigarettes did not provide any better route towards quitting than simply staying with "Regular" cigarettes. *See* Weinstein, N, Public understanding of risk and reasons for smoking low-yield products. In Risks Associated with Smoking Cigarettes with Low Machine-measured Yields of Tar and Nicotine, 196. Smoking and Tobacco Control Monograph 13, U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute (2001).

[30] Studies have shown that changes in cigarette design have not lowered the risk of disease caused by cigarettes. *See* Benowitz, N and Burns, DM, Public Health Implications of Changes in Cigarette Design and Marketing, 10. Smoking and Tobacco Control Monograph 13.

[31] A national survey of adolescent and young adult smokers of "Light" or "Ultra-Light" cigarettes in 1993 found that they chose their brand of cigarettes because of taste (33%), because they were less irritating (29%), because they thought they were healthier than other brands (21%), and because they "just liked them" (19%). *See* Giovino, GA et al., 48. Smoking and Tobacco Control Monograph No.7. Studies have also indicated that children and adolescents believed "Light" cigarettes were not as risky or harmful to their health, and showed that adolescents believed they had a better chance of being able to quit smoking "Light" cigarettes than "Regular" cigarettes. *See* Kropp RY and Halpern-Felsher BL, 2004, Adolescents' beliefs about the risks involved in smoking "light" cigarettes, Pediatrics, 114(4):e445-451.

[32] *See* Smoking and Tobacco Control Monograph 13 at 10.

- The tobacco product manufacturer has taken any action directed to consumers through the media or otherwise, other than by means of the tobacco product's label, labeling, or advertising, that would be reasonably expected to result in consumers believing that the tobacco product or its smoke may present a lower risk of disease or is less harmful than one or more commercially marketed tobacco products, or presents a reduced exposure to a substance or substances.[33]

It is important to note that a product made or derived from tobacco that is intended to be used for the treatment of tobacco dependence is a drug or device and not a tobacco product, and consequently cannot qualify as an MRTP.[34]

Before any tobacco product can be marketed as an MRTP, an application must be filed with FDA and FDA must issue an order allowing that MRTP on the market.[35] If FDA determines that the product, as actually used, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and will benefit the health of the population as a whole (taking into account both users and nonusers), CTP may issue a "risk modification order."[36]

If the product's claims are limited to reduced exposure to a hazardous substance (as opposed to lower risk or reduced harm), the reduction is substantial and the available scientific evidence suggests that a measurable and substantial reduction in morbidity and mortality is reasonably likely to be demonstrated in future studies, CTP may issue an "exposure modification order."[37] These orders are limited to a term of five years, and may be renewed if applicable requirements are still met.[38]

In light of the risks known to have been associated with previously marketed "light/low" and "mild" products, and the substantial harm to the public health that would result from the marketing of "reduced risk" or "reduced exposure" products that did not in fact reduce risk or exposure, MRTPs must satisfy strict criteria before they can be marketed. In addition to the basic requirements described above for "risk modification orders" and "exposure modification orders," FDA must take into account in evaluating any MRTP additional factors including the relative health risks to individuals of the product; the increased or decreased likelihood that current users will switch to the product rather than quit; the increased or decreased likelihood that nonusers will start using the product; and the risks and benefits of the product as compared to the use of smoking cessation

[33] FD&C Act § 911(b)(2).
[34] FD&C Act § 911(c).
[35] If a product is a "new" tobacco product — i.e., was first marketed after February 15, 2007, or was modified after that date — and also makes modified-risk claims, the manufacturer must satisfy the criteria for both a new product and an MRTP application.
[36] FD&C Act § 911(g)(1).
[37] FD&C Act § 911(g)(2).
[38] FD&C Act § 911(g)(2)(C)).

products approved as drugs.[39] In addition, FDA must apply special safeguards to ensure that reduced exposure claims are not misunderstood by consumers.[40]

C. Tobacco Product Standards

In addition to the above authorities over "new" tobacco products and the additional requirements for tobacco products making modified risk claims, CTP can issue tobacco product standards to control certain characteristics of tobacco products such as nicotine yield or the level of particular constituents.[41] Tobacco product standards may be issued for protection of the public health, including based on evidence related to the likelihood that existing users of tobacco products will stop, or that non-users will start.[42] The process for issuance of a tobacco product standard includes notice-and-comment rulemaking, with the publication of a proposed standard followed by a comment period.[43]

V. Achieving Abstinence, Reductions in Consumption, and Reductions in Harm Through a Comprehensive Approach to Regulation

In working to achieve all three of the goals identified in Section 918(b) — total abstinence from tobacco use, reductions in consumption, and reductions in harm — FDA is working to develop a comprehensive strategy that incorporates the work of CDER and CDRH on medical products and CTP on tobacco products. FDA is also considering how to drive innovation towards these goals in the regulation of existing products as well as new ones, as the two categories are not fully exclusive of each other (e.g., a new indication for an existing medical product might represent a significant innovation). Finally, FDA and all interested stakeholders should remain aware that actions undertaken in pursuit of any one of the three goals set forth in Section 918(b) may have an impact on our ability to achieve the others. These issues are discussed more fully in the following sections.

A. Achieving Abstinence from Tobacco Use

[39] FD&C Act § 911(g)(4).
[40] For example, FDA must ensure that the labeling and advertising of an MRTP "enable the public to comprehend the information concerning modified risk and to understand the relative significance of such information in the context of total health and in relation to all of the diseases and health-related conditions associated with the use of tobacco products." FD&C Act § 911(h)(1).
[41] FD&C Act § 907(a)(4).
[42] FD&C Act § 907(a)(3). Note that there are limitations on FDA's authority with regard to tobacco product standards. For example, FDA cannot set a product's nicotine yield to zero. FD&C Act § 907(d)(3).
[43] *See* FD&C Act § 907(c)-(d).

To pursue the goal of abstinence from tobacco use, FDA is considering the best use of its authorities to regulate existing drug and device products (including NRTs) as well as other, more novel, treatments. As discussed below, FDA has responded to requests that the labeling of OTC NRT products be modified to ensure effective use of these products as aids to quitting smoking. FDA remains open to considering additional indications and accelerated approval options for NRTs and other medical products. These and other new developments raise the possibility that consumers will continue using nicotine in a longer term, *ad hoc* manner as a replacement for cigarettes, and likely remain addicted to nicotine. FDA remains aware of the public health implications of this approach, including the potential risks associated with "dual use" of nicotine-containing products and cigarettes.

1. Regulation of Existing Drug Products: Modifying Labeling Provisions Relating to the Use of NRTs for Smoking Cessation

Among products currently approved by FDA, one important category of products for achieving abstinence is nicotine replacement therapy (NRT). As noted above, there are currently a number of NRT products on the market, including several OTC products, such as a nicotine patch and gum as well as prescription-only options such as a nicotine inhaler. These products all came to market based on a showing of safety and effectiveness as aids to smoking cessation, in conjunction with behavioral support.

In three citizen petitions focused on the regulatory treatment of OTC NRTs,[44] and at our December 17, 2012, hearing, various stakeholders have argued that OTC NRT products are underused because certain statements in the labeling have caused consumers to overestimate the risks associated with these products. In particular, stakeholders have highlighted provisions relating to concomitant use of NRT (both with other NRT and with cigarettes) and use beyond the labeled period of up to 12 weeks (depending on the product). The argument has been made that the current warnings and directions relating to concomitant use and duration of use limit the effectiveness of OTC NRT products for some consumers, including very dependent smokers who may desire a higher dose of nicotine than that provided by current NRTs and individuals who may have difficulty adhering to the labeled regimen for use (e.g., individuals affected by mental illness). Participants in the December 17 hearing also argued that OTC NRTs are currently perceived by tobacco users as less appealing than other, more novel nicotine-containing

[44] All three petitions relate to the labeling and conditions of use of OTC NRT products. The State of New York's Commissioner of Health submitted a petition to FDA, dated January 22, 2008 (FDA Docket No. 2008-P-0116); the University of Maryland School of Law submitted a petition to FDA on behalf of the Society for Research on Nicotine and Tobacco (SRNT) and the Association for the Treatment of Tobacco Use and Dependence (ATTUD), dated February 11, 2010 (FDA Docket No. 2010-P-0089); and a group including the American Cancer Society Cancer Action Network, the American Lung Association, the Campaign for Tobacco-Free Kids and the American Legacy Foundation submitted a petition to FDA, dated August 26, 2010 (FDA Docket No. 2010-P-0454).

products (such as electronic cigarettes), in part because of the NRTs' specific directions for use and other statements set forth in the labeling.

In a Notice of Findings (NOF) accompanying our recent response to the three citizen petitions referenced above,[45] FDA has allowed the modification of certain provisions in the labeling of OTC NRT products relating to concomitant use and duration of use. Specifically, FDA is recommending modifications to certain warnings and directions for use relating to use of OTC NRT concomitantly with cigarettes or with other nicotine-containing products (including other NRTs) and relating to use of OTC NRT for longer than the labeled period of treatment.

As further detailed in the NOF, FDA's review of data that have become available since NRT products were originally approved has shown that these provisions relating to concomitant use and duration of use can be modified without raising significant safety concerns. It is FDA's hope that the modification of these provisions in the labeling will allow OTC NRT products to be used effectively for smoking cessation by all potential users.

We emphasize, however, that the modification of these labeling provisions is based solely on an evaluation of safety concerns. There is a significant legal and scientific distinction between these safety-based changes to product labeling, on the one hand, and the granting of a new indication, on the other.[46] The recent NOF did not change the labeled indication of these OTC NRT products; they are still intended for use as aids to smoking cessation. FDA cannot grant a new drug indication based solely on a determination that the product is safe for use under a new set of circumstances. As discussed above in Section III, the product must be shown both safe *and* effective for the new intended use. New indications for drug products generally require the submission of safety and efficacy data, as appropriate, by the product's sponsor.

2. Driving Innovation in New and Existing Products and Treatments

a) New drug indications and the use of fast track authorities for drug approval

Section 918(a) asks that FDA consider approving several new indications for NRT products. Specifically, Section 918 mentions the approval of extended use of NRTs for the treatment of tobacco dependence, and the approval of NRTs for "relapse prevention" and "craving relief."

[45] Because these three petitions made many of the same requests, FDA has issued a single response to all three petitions.

[46] The three citizen petitions referenced above requested several new indications for OTC NRT. These requests are discussed in FDA's response to those petitions.

FDA is aware that a number of stakeholders consider these new indications to be appropriate as additional indications for existing NRT products. FDA is considering whether these indications could be appropriate for an NRT product. Without deciding this issue, we provide the following comments on these potential indications.

An indication could be envisioned for extended use as a more effective way to achieve cessation. Under section 505 of the drug approval authorities, this new indication would require a showing that longer term use is an effective way to stop smoking. An indication for extended use could also be a "maintenance" indication — i.e., extended use of the product that is required in order to sustain abstinence. This type of indication would require a showing, for example, that patients who quit while using a particular product are more likely to remain abstinent if they continue using the product indefinitely.

An indication for "relapse prevention" might be better described as an indication for reduction of the *risk* of relapse in individuals who have quit smoking. This indication could be supported by evidence showing, for example, that individuals who have recently quit experience a lower rate of relapse when they receive a course of treatment with the product.

Cravings are a symptom of nicotine withdrawal. The mode of operation of currently approved NRT products is to mitigate the withdrawal symptoms experienced in the course of a quit attempt. In the clinical trials that supported NRT approval, the endpoint was smoking cessation, and NRTs were therefore proven effective in helping people quit. The data submitted to FDA were not sufficient to prove these products effective in relieving any particular withdrawal symptom. A number of stakeholders have argued that NRT products can be proven effective specifically for the relief of cravings, whether the craving relief is sought as part of a quit attempt or not. Many smokers, for example, may seek temporary relief from cravings in situations (such as in a non-smoking workplace, or on an airplane) in which they are unable to smoke. Such an indication would have to be supported by evidence showing that the NRT product is safe and effective under the FD&C Act section 505 for this intended use.

To the extent these indications have been submitted for review as additional indications for approved drug products, FDA has carefully considered them and has used available mechanisms to facilitate their development and evaluation. In submissions reviewed to date, evidence has not been sufficient to support any of these potential indications under the section 505 standard.

FDA remains open, however, to working with sponsors to develop these new indications. As further evidence is created and submitted by product sponsors, new indications for treating tobacco dependence, potentially including those described above, may be developed to meet the section 505 criteria and reach the market. To facilitate that process, FDA included detailed questions about new indications for extended use, relapse prevention, and craving relief in the notice announcing the December 17, 2012, hearing. These questions solicited input on a number of points, including the evidence currently

available to support these indications; how study endpoints should be defined; and how concepts such as "relapse" and "craving" should be defined and measured to satisfy the criteria for approval under section 505.[47] At the hearing and in comments submitted to the docket, we received a number of comments relating to these questions. Based on our review to date, it appears that additional work may be required to design and conduct studies adequate to demonstrate efficacy for any of the new tobacco-dependence indications discussed above. FDA remains committed to working with sponsors of NRT and other products in their efforts to support new indications and new product approvals.

Likewise, we are committed to using our fast track and accelerated approval authorities to facilitate the approval of new treatments for tobacco dependence. It is generally accepted that a product that helps people stop smoking will be addressing a serious or life-threatening condition. An additional criterion for fast track status, however, is that the product demonstrate the potential to address an "unmet medical need."

FDA solicited input on this issue at the December 17 hearing.[48] Specifically, we asked how a new product candidate might meet the "unmet medical need" criterion in light of the existing approved therapies for smoking cessation. Where there are existing therapies, filling an "unmet medical need" has been understood to mean showing a clear advantage over those available treatments, such as superior effectiveness or the avoidance of serious side effects.

As one stakeholder suggested, for example, a product that demonstrates a potential for efficacy in improved craving relief might have an advantage over existing products in helping smokers quit. FDA is ready to work with sponsors who wish to develop the evidence that their product candidate offers such an advantage and should therefore qualify for fast track status.

In addition, we have solicited comments on how a smoking-cessation product might offer preliminary clinical evidence, based on clinically significant endpoints, of substantial improvement over existing therapies and thereby qualify as a "breakthrough therapy."[49] We are open to working with sponsors of tobacco-dependence treatments who wish to obtain "breakthrough" status as well.

b) Broader regulatory challenges: complete abstinence vs. continued use of nicotine

FDA clearly encourages innovation in treatments for tobacco dependence, including the development of the new indications described above. However, these new uses raise significant public health questions. The currently marketed NRT products (along with bupropion and varenicline) are the only products that have been proven effective in

[47] *See* 77 Fed. Reg. 70955, 70957 (November 28, 2012).
[48] *See* 77 Fed. Reg. 70955, 70956-57 (November 28, 2012).
[49] *See* 77 Fed. Reg. 70955, 70957 (November 28, 2012).

promoting abstinence, and all were approved as aids to smoking cessation. They are intended to help the user quit smoking and, after a defined period of time, to stop use of the nicotine (or other therapy).

If any of the potential new NRT indications discussed above are approved, individuals might be encouraged to stop smoking, but continue to use nicotine on an *ad hoc,* or continuous, basis. For example, if NRTs are approved and marketed for relapse prevention, a user might continue using them indefinitely to keep from smoking. Other non-medical products containing nicotine, such as electronic cigarettes, also offer the option of *ad hoc* nicotine consumption, with different delivery mechanisms and a more recreational format.[50] As nicotine is an addictive substance, the potential for long-term nicotine use by former smokers is a real possibility.

Although smoking cessation is an important goal to pursue, with undeniable health benefits, the implications of continuing nicotine addiction after smoking cessation are not yet fully understood. Many stakeholders at the December 17 meeting told FDA that they had experienced benefits from the continued use of nicotine, ranging from increased focus to the reduction or elimination of cigarette smoking. Several of these stakeholders expressed frustration with a so-called "abolitionist" approach that calls for smokers to quit both cigarettes and nicotine. These stakeholders felt that addiction to nicotine was not necessarily harmful, and that individual consumers should be able to choose the duration and pattern of nicotine use that is most beneficial for them.

It remains unclear, however, whether individuals who quit smoking but continue to use nicotine (and likely remain addicted to nicotine) are at higher risk for returning to cigarettes, or initiating use of other tobacco products. These potential risks, including the risk of "dual use" of nicotine and cigarettes, raise important public health concerns over and above the specific health risks that may be associated with any particular tobacco product. FDA will take these issues into account while encouraging innovation in the development of new products and treatments to promote abstinence from tobacco use. The problem of dual use is discussed further in the following section.

B. Achieving Reductions in Consumption of Tobacco

In contrast to the variety of products currently marketed as aids to smoking cessation, there are currently no FDA-approved products for reduction in consumption of tobacco. A number of stakeholders have argued, however, that reducing consumption may be beneficial to some users.

Specifically, some stakeholders have argued that NRTs or other nicotine-containing products can be used to reduce consumption as a step towards quitting. A number of stakeholders at the December 17 hearing argued for a "flexible" approach to quitting in which NRT or other nicotine-containing products would be used to reduce tobacco

[50] We note that these products have not been evaluated by FDA either for their impact on public health, or on the health of an individual.

consumption as desired over a period of time to be determined by the user. These stakeholders argued that the currently labeled quit regimen for approved NRT products requires "abrupt" cessation, in that the user is instructed to pick a certain day to quit and use NRT for a limited period of time thereafter.

Evidence is currently insufficient to show whether a "flexible quit" approach actually leads to cessation of tobacco use. In practical terms, therefore, the "flexible quit" scenario — in which a user might use a nicotine-containing product to reduce or replace cigarette consumption over an undefined period of time — may essentially be an example of dual use, in which a user maintains an addiction to nicotine that he satisfies sometimes by smoking cigarettes and sometimes by using other tobacco- or nicotine-containing products.

Some stakeholders have argued that dual use does not have a negative impact on cessation; however, available evidence does not appear to rule out such an effect.

Meanwhile, many consumers may believe that reducing the number of cigarettes they smoke will lead to health benefits, and many companies seeking to market nicotine-containing products may be ready to encourage that belief. It is currently unclear, however, whether a smoker who reduces the number of cigarettes he consumes will necessarily reduce his risk of tobacco-related harms. The available evidence suggests, for example, that duration of tobacco use — the number of years a person continues to smoke or use tobacco — is a stronger predictor of lung cancer than level of consumption.[51] For these reasons, the prospect of widespread dual use is a real concern and one that FDA plans to take into account in any discussion of reduction in consumption.

A number of stakeholders have recognized this, including stakeholders present at our December 17 hearing, who argued that dual use should be discouraged unless it leads to cessation. Similarly, several stakeholders argued that reduction in consumption should not be pursued as a public health goal unless that reduction helps people to quit.

FDA encourages manufacturers to develop evidence on how products may reduce tobacco consumption and the health effects of such reductions. For example, it is possible to envision a medical product that is proven to reduce consumption of tobacco and thereby lead to cessation through a reduce-to-quit regimen. Some stakeholders have argued that non-medical products, including nicotine-containing products such as electronic cigarettes, could also be used to reduce consumption of traditional tobacco products.[52] For the reasons outlined above, FDA plans to use its authorities to carefully examine such uses, including the impact on health outcomes and the potential impact on initiation and continuation of tobacco use.

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[51] *See* Report of the Surgeon General, *How Tobacco Smoke Causes Disease* (2010) at 651-2.

[52] It is particularly problematic to evaluate the benefit of any reduction in consumption achieved with these products as they have not been evaluated by FDA either for their impact on public health, or on the health of an individual.

C. Achieving Reductions in the Harm Associated With Continued Tobacco Use

To date, no manufacturer of a drug or device product has demonstrated to FDA that its product is safe and effective for reducing the harm associated with continued tobacco use. Likewise, no manufacturer has demonstrated to FDA that its tobacco product significantly reduces the harm and the risk of tobacco-related disease to the individual tobacco user and that its product will benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products. FDA anticipates having additional discussions with stakeholders on issues related to reducing the harm associated with continued tobacco use.

A number of stakeholders, however, have argued for a so-called "harm-reduction" approach to tobacco use based on the idea that many currently available products that contain tobacco or nicotine may be less harmful to users than cigarettes. These stakeholders argue that if consumers are given appealing alternatives to smoking and adequate information about the related risks, consumers will shift to these alternative tobacco products and thus experience reduced harm. These stakeholders have also argued that presenting other tobacco products as harm-reducing alternatives is a potential tool for reducing cigarette smoking prevalence.[53]

Other stakeholders have countered that the strategy of moving users to purportedly "safer" sources of nicotine will simply serve to sustain and expand tobacco use and addiction. In addition, FDA cannot assume that all of these nicotine-addicted users would completely give up smoking, or that once "shifted" to alternative tobacco products, they would not subsequently switch back. Other potential concerns raised by this strategy of shifting to "safer" sources of nicotine include increased initiation, reductions in cessation rates, and an overall negative impact on the public health.

The so-called "harm-reduction" approach therefore raises issues similar to those discussed in connection with the continuation of nicotine addiction following smoking cessation (see Section V.A above), and the phenomenon of dual use (see Section V.B).

In seeking to encourage the development of innovative products for modified risk, while taking into account the issues of addictiveness, initiation effects, cessation effects, and dual use described above, FDA can apply several regulatory tools. Under its MRTP authorities, FDA can allow the marketing of products that establish reduced risk or reduced exposure to harmful constituents relative to other tobacco products. The MRTP pathway may provide an important mechanism for the development of innovative harm-reduction products, particularly if manufacturers can develop products that substantially reduce toxicity, addictiveness, or both. FDA has issued a detailed draft guidance on the

[53] FDA has not evaluated or authorized any tobacco products to make claims that they are less harmful than cigarettes or otherwise reduce tobacco-related harms. Such claims would generally require evaluation through the MRTP process described above in Section IV.

MRTP application process; has consulted with the Institute of Medicine (IOM) on the design of studies required to support MRTP applications; and, in August 2011, held a workshop on the "Scientific Evaluation of Modified Risk Tobacco Product Applications." The IOM issued a report on its findings in December 2011, and public comments were received in the docket following the August 2011 workshop on MRTPs. FDA intends to consider the IOM report and the comments submitted to the docket in preparing its final guidance on MRTP applications.

We note that to date no MRTP applications have been filed with FDA so that the products and claims could be evaluated for their impact on the health of an individual user and on overall public health.

FDA also has the authority to issue tobacco product standards, which can be used in a variety of ways, including to regulate nicotine (thereby reducing addictiveness); to regulate toxicant levels; or to require the reduction or elimination of an additive, constituent, or other component. By mandating product changes to reduce the harmful effects of tobacco use, tobacco product standards could provide an additional means to develop product changes to decrease the morbidity and mortality from tobacco use.

VI. Consultation With Experts and Ongoing Coordination of the Exchange of Information on Innovative Products and Treatments

As noted above in Section II, Congress required that this report be submitted "after consultation with recognized scientific, medical, and public health experts (including both Federal agencies and nongovernmental entities, the Institute of Medicine of the National Academy of Sciences [IOM], and the Society for Research on Nicotine and Tobacco [SRNT])."[54] Congress further required that the report include "the recommendations of the Secretary on how the [FDA] should coordinate and facilitate the exchange of information" on innovative products and treatments "among relevant offices and centers within the Administration and within the [NIH], the [CDC], and other relevant agencies."[55]

Our consultation with scientific, medical, and public health experts, including those affiliated with the organizations and agencies named above, has been critical to our work in preparing this report. The discussions we have had with Federal agencies in developing this report, including NIH, CDC, and others, will also provide the foundation for our ongoing exchange of information among government agencies on innovative products and treatments and on our pursuit of the goals of abstinence, reductions in consumption, and reductions in harm.

[54] FD&C Act § 918(b)(1).
[55] FD&C Act § 918(b)(2).

A. Consultation with Recognized Scientific, Medical, and Public Health Experts

A number of Federal agencies have significant expertise in the scientific, medical, and public health issues associated with tobacco dependence, and can provide valuable insights into the regulation and development of products and treatments to combat tobacco use. As part of our effort to draw on this expertise in our response to Section 918, representatives of FDA (including personnel from CDER and CTP) and of the Office of the Assistant Secretary for Health (OASH) within HHS held a half-day meeting on September 27, 2012, with representatives of a number of Federal agencies, including NIH, CDC, the Substance Abuse and Mental Health Services Administration (SAMHSA), the Health Resources and Services Administration (HRSA), the Agency for Healthcare Research and Quality (AHRQ), the Department of Defense (DoD), and the Veterans Administration (VA).

Representatives of CDER, CTP and OASH/HHS also conferred with a number of IOM members during an extended teleconference on November 19, 2012.[56] The discussion at both these meetings covered a wide range of topics relating to Section 918, including the regulation of NRTs and the development of products and treatments to achieve abstinence, reductions in consumption, and reductions in harm.

FDA has also had a number of meetings with experts from within the public health community to discuss their views on issues related to Section 918. These include a meeting between CDER and SRNT on March 9, 2012; a meeting between FDA's Deputy Commissioner for Tobacco and Medical Products, CDER, and SRNT on June 4, 2012; and a meeting between the Deputy Commissioner for Tobacco and Medical Products, CDER, CTP, and the Campaign for Tobacco-Free Kids (CTFK) on June 8, 2012.[57]

In addition, at the Part 15 hearing held December 17, 2012, to obtain input on FDA's regulation of NRTs and the development of innovative products and treatments for tobacco dependence, FDA received input from many scientific, medical, and public health experts, including SRNT; CTFK; the Association for the Treatment of Tobacco Use and Dependence (ATTUD); the American Cancer Society Cancer Action Network; the Schroeder Institute for Tobacco Research and Policy Studies at Legacy; the Legal Resource Center for Tobacco Regulation, Litigation and Advocacy at the University of Maryland School of Law; and the American Council on Science and Health. A

[56] Participants in this meeting included David Brian Abrams, Ph.D. (Legacy Schroeder Institute); Richard J. Bonnie (University of Virginia School of Law); Ellen R. Gritz, Ph.D. (The University of Texas MD Anderson Cancer Center); Bonnie Halpern-Felsher, Ph.D. (UCSF Helen Diller Family Comprehensive Cancer Center); Dorothy K. Hatsukami, Ph.D. (The University of Minnesota); Dr. Richard D. Hurt (Mayo Clinic); Dr. Rose Marie Martinez (IOM); Matthew L. Myers (Campaign for Tobacco-Free Kids); Richard J. O'Connor, Ph.D. (Roswell Park Cancer Institute); and Dr. Steven A. Schroeder (UCSF Smoking Cessation Leadership Institute).

[57] Note that SRNT is a petitioner on the citizen petition filed with FDA in February 2010, and the Campaign for Tobacco-Free Kids is a petitioner on the citizen petition filed in August 2010.

substantial number of additional comments from experts in the scientific, medical, and public health communities, as well as from industry, have been submitted to the docket created to accompany the hearing.

The Tobacco Control Implementation Steering Committee, which is coordinated by OASH/HHS and includes representatives from a number of agencies including NIH, CDC, HRSA, and SAMHSA (as well as FDA's CDER and CTP), has also provided significant input into the development of this report.

B. Coordinating and Facilitating the Exchange of Information Within FDA and Among Other Relevant Government Agencies

Within FDA, internal processes are being put in place across all relevant centers (CDER, CDRH and CTP) to build on our work so far in responding to Section 918 and ensure the continuation of a coordinated approach to our regulation of products and treatments related to tobacco dependence.

FDA also plans to maintain its communications with outside stakeholders, including those in the public health community and at the IOM who have contributed so much to our work to date in this area.

Finally, FDA will ensure that the expertise of other Federal agencies is taken into account as we regulate and seek to encourage the development of new products and treatments to achieve abstinence from tobacco use, reductions in consumption, and reductions in harm. This will be accomplished in part by continued consultation with the Tobacco Control Implementation Steering Committee in our work on the issues raised by Section 918.