The Food and Drug Administration's Regulation of Tobacco

The Center for Tobacco Products' Office of Science

David L. Ashley, PhD, Cathy L. Backinger, PhD, MPH

Background

The Family Smoking Prevention and Tobacco Control Act (TCA) was signed into law on June 22, 2009, and provided the Food and Drug Administration (FDA) broad regulatory authority with respect to the manufacture, marketing, and distribution of tobacco products. The three public health goals of the Center for Tobacco Products (CTP), FDA, are to prevent youth initiation of tobacco use, decrease harm and/or addictiveness of tobacco products, and encourage tobacco use cessation. The CTP has established an Office of Science to ensure that sound science exists with which to develop regulatory actions. Although there is a vast and sound science base with regard to numerous provisions within the TCA, new research will not only help assess the impact of FDA regulatory authority over tobacco products but will inform future regulatory activities. In order to meet the broad science demands within the TCA, the CTP developed seven research priority areas:

1. understanding the diversity of tobacco products;
2. reducing addiction to tobacco products;
3. reducing toxicity and carcinogenicity of tobacco products and smoke;
4. understanding adverse health consequences of tobacco use;
5. understanding communications about tobacco products;
6. understanding tobacco product marketing; and
7. understanding economics and policies on tobacco use and perceptions.

These seven priority research areas are discussed in relation to the TCA, including current scientific activities and future research plans of the CTP's Office of Science.

From the Office of Science, Center for Tobacco Products, Food and Drug Administration, Rockville, Maryland

Address correspondence to: David L. Ashley, PhD, Food and Drug Administration, Center for Tobacco Products, Office of Science, 9200 Corporate Blvd, Rockville MD 20850. E-mail: David.Ashley@fda.hhs.gov.

0749-3797/$36.00

http://dx.doi.org/10.1016/j.amepre.2012.08.004

Introduction

The addictive and toxic properties of tobacco products have been clearly known and widely accepted for decades by the scientific community and even fully acknowledged more recently by the tobacco industry. The dangers of tobacco use were known even before the Surgeon General's report in 1964 concluded that "cigarette smoking is a health hazard of sufficient importance in the U.S. to warrant appropriate remedial action."[1] This call to action helped fuel educational, policy, public health, and clinical advances that resulted in smoking prevalence among adults aged ≥18 years in the U.S. decreasing from 42.4% in 1965 to 19.6% in 2010.[2] But there is also clear evidence that this downward trend has slowed considerably during the past 5 years.[2] Smoking among youth has also flattened in recent years, with 19.5% of high school students reporting current smoking.[3] In addition, the use of smokeless tobacco products is increasing; for example, 11% of high school boys reported smokeless tobacco use in 2009[4] and dual use of cigarettes and smokeless tobacco products is common in many states.[5] Because of findings such as these, Congress recognized the importance of comprehensive federal regulatory authority over tobacco products and passed the TCA, which was signed into law by President Obama on June 22, 2009.

The TCA gave the FDA broad regulatory authority with respect to the manufacture, marketing, and distribution of tobacco products. Tobacco products are any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product.[6] Excluded from this new tobacco regulatory authority are products that meet the definition of tobacco products but were already being regulated as drugs, devices, or combination products. The FDA was given immediate jurisdiction over cigarettes, smokeless tobacco, cigarette tobacco, and roll-your-own tobacco and provided the authority for the Secretary of Health and Human Services to deem by regulation other tobacco products not within this immediate jurisdiction.

The TCA established a new standard for the FDA to regulate tobacco products according to their effect on overall population health. This public health mandate is

critically important to achieving the goals of the TCA. When evaluating tobacco product regulatory decisions, the FDA was directed by the TCA to examine the impact of the decision on the risk and benefits to the population as a whole, including users and nonusers of tobacco products, and taking into account the increased or decreased likelihood that existing users of tobacco products will stop using such products and the increased or decreased likelihood that those who do not use tobacco products will start using such products. This new standard directs the FDA not only to consider the impact of its decisions on the relative toxicity of these products but also to consider other influences on those who might start using tobacco products and those who might or might not quit their use.

The nature of this standard is critical for evaluating the overall effect of widely available and easily accessible tobacco products, but it also considerably raises the complexity of the scientific information used by FDA to make its determinations. The rather straightforward and well-established system of evaluating safety and efficacy that has been widely used in other areas by the FDA, such as for drugs and medical devices, was not appropriate for tobacco products. Instead, a more complex set of considerations evaluating a wider set of issues and criteria is necessary.

The regulatory authorities of the TCA can be subdivided in many ways. In order to better understand how the authorities given under the TCA can affect public health, it is possible to identify those authorities aimed to (1) prevent youth initiation of tobacco use; (2) decrease harm and/or addictiveness of tobacco products; and (3) encourage tobacco use cessation.

Preventing Youth Initiation

To accomplish the goal of preventing youth tobacco use, the FDA has been given the authority to decrease the access and attractiveness of tobacco products to children. These authorities include eliminating youth retail access (currently for cigarettes, smokeless, and roll-your-own); prohibiting the manufacture, distribution, and sale of cigarettes with fruit and candy flavors; removing false or misleading claims such as *light*, *low*, and *mild*; developing product standards to make initiation difficult and decrease the chances of youth becoming addicted; and educating on the dangers of tobacco use in order to change social norms to discourage youth from initiating tobacco use.[6] Section 201 of the TCA also gives the FDA authority to adjust and require health warnings and issue regulations requiring graphic health warnings that depict the negative health consequences of smoking.[6]

Decreasing Harm and/or Addictiveness

Because many adults are already tobacco users, eliminating youth access is not sufficient to fulfilling the public health goals of the TCA. The products themselves must be addressed so that they do not continue to cause death and disease in those who use them. To alter the impact of the product itself on the morbidity and mortality resulting from tobacco use, the TCA gives FDA tools aimed at decreasing the harm and/or addictiveness of tobacco products. These provisions include review of the characteristics and the effect on public health of new products that claim to be substantially equivalent to "grandfathered" tobacco products (those on the market as of February 15, 2007). It also includes the authority to evaluate whether the marketing of new products would be appropriate for the protection of public health. In addition, the FDA has the regulatory authority to issue an order allowing the marketing of a product as modified risk if the evidence shows that marketing a product as such will substantially benefit the health of the population as a whole and reduce the risk of tobacco-related disease associated with commercial tobacco products. Product standards could have a meaningful influence on the harm caused by tobacco products, and the FDA is given broad authority to develop tobacco product standards that, where appropriate for the protection of public health, include reducing or eliminating constituents (including smoke constituents) and provisions related to the construction, components, ingredients, additives, constituents, and properties of the tobacco product.

Specifically, the TCA gives the FDA the authority to reduce, but not eliminate, levels of nicotine in tobacco products. In addition, the TCA requires that tobacco product manufacturers test and report ingredients, additives, and harmful/potentially harmful constituents; submit all health, toxicologic, behavioral, or physiologic documents to the FDA; and provide information related to research carried out by the manufacturers. Finally, the FDA is given authority to apply regulations that address the methods, facilities, and controls used for manufacturing, packing, and storing tobacco products.

Encouraging Tobacco Use Cessation

The most immediate benefit to health from tobacco regulatory action would be to increase the number of current users who successfully end their use completely. To accomplish this, the FDA has been given the authority to apply advertising and marketing restrictions; remove false or misleading claims such as *light*, *low*, and *mild*; issue larger smokeless health warnings and graphic cigarette health warnings to promote cessation; communicate the hazards of tobacco product use and encourage cessation through new public education campaigns; carry out

expedited review of new/novel tobacco cessation drugs (this authority is with the Center for Drug Evaluation and Research, FDA); and educate the general public about the hazardous constituents and consequences of tobacco use. These provisions also include restricting sales and distribution of a tobacco product, including restrictions on the access to, and the advertising and promotion of, the tobacco products if it is determined that the regulation would be appropriate for the protection of public health.

The appropriate steps to reduce death and disability from tobacco use are necessarily based on the best available science. More accurate and actionable information can be used by the FDA to develop and define more specific regulatory action. The Office of Science was created within the CTP and tasked with using both the science that is currently available and developing new regulatory science that will drive regulatory action. To accomplish this mission, the FDA has begun to implement an extensive research program to inform regulatory decisions. This research will cover the entire breadth of scientific subject matter that will affect tobacco regulatory decisions including chemistry, engineering, toxicology, clinical medicine, addiction, behavior, epidemiology, social science, surveillance, and statistics.

Office of Science Research Priorities of the Center for Tobacco Products

Although there is a vast and sound science base supporting the numerous provisions of the TCA, new research will both help assess the impact of FDA regulatory authority over tobacco products and inform future regulatory activities. Specifically, research is highlighted in numerous sections of the TCA, including the need for consumer research, marketing research, product research and testing, and assessment of the impact of tobacco product use on public health.[5] Because of the importance of FDA research, the U.S. DHHS Tobacco Control Strategic Plan, *Ending the Tobacco Epidemic*, published in November 2010, included as one of its key strategic objectives, to "develop and implement a Department-wide research plan to support FDA's regulatory authority over tobacco."[7] Consequently, the CTP developed a research plan designed to address the broad range of scientific questions that will inform future regulatory options. Relevant scientific literature was reviewed including the January 2012 themed section of the journal *Nicotine and Tobacco Research* to identify research gaps related to the regulation of tobacco products, as well as eliciting priority research questions from stakeholders.[8–14]

The 56 identified research questions were categorized into seven areas, outlined in Table 1. Underscored within these research areas is the importance of addressing vulnerable populations. Both the use of tobacco products and adverse health outcomes caused by its use may have differential effects on different populations. Given the public health standard of the TCA, in making its determinations, the FDA will take into account the range of vulnerable populations including but not limited to age, gender, race, ethnicity, income, occupation, geographic location, people with mental health or medical comorbidities, the military/veterans, the lesbian, gay, bisexual, transgendered, questioning (LGBTQ) community, and pregnant women/women of reproductive age.

Diversity of Tobacco Products

As previously mentioned, the FDA currently does not have jurisdiction over all tobacco products. In 2010, the FDA asserted jurisdiction over electronic cigarettes (e-cigarettes) as drug-delivery devices; however, one e-cigarette company filed a lawsuit against FDA asking the court to determine

> . . . whether Congress has authorized (FDA) to regulate e-cigarettes under the drug/device provisions of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 351 *et seq.,* or under the Family Smoking Prevention and Tobacco Control Act of 2009 (the "Tobacco Act"), Pub. L. 111-31, 123 Stat. 1776.[15]

In December 2010, the court determined that e-cigarettes and other nicotine-containing products are not drugs or devices unless they are marketed for therapeutic purposes. The court went on to state that e-cigarettes and other nicotine-containing products can be regulated as tobacco products under the TCA if they meet the definition of tobacco product and fall under FDA's tobacco regulatory jurisdiction.[15] Consequently, the FDA announced its intent to assert jurisdiction over tobacco products for which it currently does not have jurisdiction.[16] Given the wide variety of tobacco products, including little cigars, cigarillos, large cigars, hookah tobacco, and e-cigarettes, research will help FDA understand the constituents, components, ingredients, additives, and design features of these products, as well as actual use behaviors and perceptions, attitudes, and beliefs about these products.

Reducing Addiction

One regulatory option to reduce the harm of tobacco use is to reduce the addictiveness of the product. Nicotine plays the primary role in addiction to tobacco through increasing levels of dopamine in the brain, which in turn affect reward and reinforcement.[17] Because most tobacco users are addicted to tobacco, reducing tobacco's addictive properties would mean fewer youth would start using

Table 1. FDA's Center for Tobacco Products research priorities

Understanding the diversity of tobacco products	
1	What are the constituents, components, and design features of new and emerging tobacco products (e.g., dissolvable tobacco products, e-cigarettes, hookah tobacco), and how do these features differ within the same class of products?
2	How do components and design features of new and emerging tobacco products affect the bioavailability of nicotine, other addictive substances, and harmful tobacco constituents?
3	What are the tobacco use behaviors of individuals using new and emerging tobacco products, including the multiple tobacco use behaviors?
4	What are the cognitive and affective factors (e.g., perceptions, attitudes, beliefs) associated with use of new and emerging tobacco products; how does product labeling and marketing influence behaviors related to tobacco product use?
5	What biomarkers of exposure should be used to measure exposure to new and emerging tobacco products?
6	What are the cognitive and affective factors (e.g., perceptions, attitudes, beliefs) influencing use of potential modified-risk tobacco products; how does labeling and marketing to different subpopulations, such as current smokers, former tobacco users, and youth, influence behaviors related to modified-risk tobacco products?
7	What are the factors, including menthol and other flavorings, that influence the appeal of tobacco products to both users and non-users, including youth and other vulnerable populations? What is the impact of these factors on experimentation, initiation, cessation, switching tobacco products, and multiple use?
8	What are individual cognitive and affective factors (e.g., perceptions, attitudes, beliefs) associated with use of smokeless tobacco products; how does product labeling and marketing influence behaviors related to use of tobacco products?
9	What are individual cognitive and affective factors (e.g., perceptions, attitudes, beliefs) associated with use of little cigars; how does product labeling and marketing influence behaviors related to use of little cigars? How do cognitive and affective factors differ among those who smoke little cigars compared to cigarettes?
10	What impact does potential modified-risk tobacco product claims on labels and in advertising have on tobacco use, initiation, and relapse? How do modified risk claims affect perceptions, attitudes, beliefs, and behaviors of consumers, including those in specific populations, such as nonsmokers, new users, current smokers, and former smokers, and youth and other vulnerable populations?
11	At what level do changes to constituent exposure, as well as tobacco product components and design features, affect consumer perceptions of the product?
Reducing addiction to tobacco products	
12	Beyond nicotine, what other constituents, components, and design features of tobacco products enhance the addictive properties?
13	What is the potential impact of modifying nicotine levels and other addictive substances in tobacco on the prevalence of tobacco use, including rates of initiation, progression to dependence, and cessation, as well as patterns of switching of products and use of multiple tobacco products?
14	How do reductions of nicotine in tobacco products affect consumer perceptions of their ability to quit tobacco product use? How do these perceptions influence product initiation, relapse, and cessation?
15	What high-throughput screens can be developed and/or used to evaluate compounds in tobacco products and smoke that may affect addiction (e.g., act on nicotinic or dopaminergic receptors, impact release and/or removal of nicotine or dopamine)?
16	How does genetic variation in sensitivity to flavorings and taste influence tobacco addiction?
17	What level of nicotine and other addictive substances in tobacco is associated with progression to dependence among cigar smokers, including users of little and large cigars and cigarillos?
18	What level of nicotine and other addictive substances in tobacco is associated with progression to dependence among smokeless tobacco smokers, including users of chewing tobacco, snuff, snus, and dissolvable tobacco products?
19	In animal models of dependence, what are the appropriate dosing and administration procedures for evaluating smokeless tobacco products?
Reducing toxicity and carcinogenicity of tobacco products and smoke	
20	How may reductions in the toxicity of tobacco products affect consumer perceptions of the risks and harms related to tobacco product use? How may these perceptions influence product initiation, relapse, and cessation?

(continued on next page)

Table 1. (*continued*)

Reducing toxicity and carcinogenicity of tobacco products and smoke	
21	What methods and measures best assess biologically relevant changes in harmful and potentially harmful constituents in tobacco products and smoke in both nonclinical models and humans?
22	What in vitro and in vivo assays are capable of comparative toxicity between two different tobacco products—with special attention to cardiotoxicity, respiratory toxicity, carcinogenicity, and developmental/reproductive toxicity?
23	What constituents, compounds, design features, and tobacco use behaviors impact toxicity and carcinogenicity of tobacco products and smoke?
24	How should the impact of reduced levels of harmful and potentially harmful constituents of tobacco products on toxicity and carcinogenicity be measured?
25	What level of reduction in harmful and potentially harmful constituents results in decreased disease risk?
26	In animal models, what smoke inhalation methods best mimic human exposure?
27	How does reduced toxicity/carcinogenicity in tobacco products affect consumer perceptions of risk/harm and influence behaviors?
Understanding adverse health consequences of tobacco use	
28	What are the biomarkers of disease (e.g., cancer, cardiovascular disease, pulmonary disease, reproductive and developmental effects) that can be associated with specific measures of tobacco exposure?
29	What magnitude of changes in biomarkers translates into clinically meaningful impacts on human health outcomes?
30	What novel biological and physiological markers (including genetic and epigenetic markers) are predictive of smoking-related and smokeless tobacco–related adverse health outcomes?
31	What animal models can be validated to establish standard toxicity changes and what magnitude observed within in vivo assays would correlate with changes in human health outcomes?
32	What are predictive models for adverse health impacts of tobacco products other than cigarettes on vulnerable populations?
33	What are the health risks of use of multiple tobacco product types, and how do these risks compare with single tobacco product use?
34	What is the potential impact on public health of potential modified-risk tobacco products, decreasing nicotine and other addictive substances and reducing harmful and potentially harmful constituents in tobacco products?
Understanding communications about tobacco products	
35	What the most effective messages regarding the FDA's regulatory authority over tobacco products and what are the best communication avenues to convey those messages to the public?
36	What factors influence the public perception of the FDA as a credible source of information related to tobacco products?
37	How should information regarding tobacco products and tobacco use, including risk, harmful and potentially harmful constituents, new and emerging tobacco products, and potential modified-risk tobacco products, be conveyed to the public so that it is understandable and not misleading?
38	What is the impact of health warnings on quit attempts and cessation among vulnerable populations?
39	What is the nature and extent of tobacco product discussions and communications in nontraditional venues such as social networking sites, online videos, blogs, and smartphone applications? Do certain subpopulations engage in certain types of nontraditional communication venues involving tobacco products? How do these modes of communication impact tobacco use?
40	What communication channels do vulnerable populations use to seek information and communicate about tobacco and health issues?
41	What is the impact of various factors such as font size, placement, attribution, text, context, or image type on warning effectiveness, including consumer risk perception and tobacco use behavior, among youth, young adults, adults, and vulnerable populations?
42	How do tobacco control brands and branding designed to promote health impact tobacco initiation and use, particularly among vulnerable populations; and how can these impacts best be measured?

(continued on next page)

Table 1. FDA's Center for Tobacco Products research priorities (*continued*)

Understanding tobacco product marketing	
43	What is the impact of tobacco industry marketing through social media campaigns and other nontraditional communication strategies on tobacco use behavior among vulnerable populations?
44	What is the impact of tobacco industry marketing of different types of smokeless tobacco products on vulnerable populations, such as youth and women?
45	What is the impact of tobacco industry marketing practices of mentholated cigarettes and other flavored tobacco products, as well as new and emerging tobacco products on tobacco use behavior, particularly among youth and other vulnerable populations?
46	What role do tobacco product advertising displays at the retail point-of-sale (POS) have on youth initiation, usage, and cessation? What is the relative impact of various ad features (e.g., size, number, location, color, images, and themes) on tobacco use behaviors?
47	What is the impact of tobacco advertising around schools, parks, and playgrounds on youth attitudes, beliefs, perceptions, and tobacco use?
48	How do factors related to the packaging, labeling, and advertising of tobacco products (e.g., colors, descriptors, market claims, branding) influence consumer perceptions about the risks of tobacco products and product use?
49	What is the impact of price promotions (including free samples and discounted products) on consumer behavior for various tobacco products, including the impact on non-users starting to use, and on individuals in various stages of quitting or contemplating quitting?
Understanding economics and policies on tobacco use and perceptions	
50	What is the trajectory of youth and/or young adult tobacco use (including use of tobacco products other than cigarettes, multiple use, and switching behavior) and how is it changing in response to FDA regulatory actions?
51	Among vulnerable populations, what are the knowledge, attitudes, and beliefs about tobacco products and FDA tobacco product regulatory authority?
52	To what extent do findings from regulatory actions on cigarettes generalize to other tobacco products in altering consumer behavior?
53	How does one measure changes in consumer surplus that result from public education initiatives or marketing restrictions to smokers who intend to quit? For example, how does one measure the potential gains to smokers from point-of-sale restrictions that may enhance self-control and efforts to quit smoking, as well as the potential losses that may be associated with quitting?
54	What is the impact of minimum package size (e.g., 20 little cigars, carton-only sales, five nonpremium cigars) and maximum purchase amount (e.g., maximum purchase of one pack, two packs, one carton, five cartons) on consumer behavior and illicit trade?
55	What are the best methods and models for estimating the magnitude and breadth of illicit trade activities related to tobacco products?
56	What is the impact of state, local, and tribal policies, as well as international policies, addressing tobacco product manufacturing, marketing, and distribution that may inform FDA tobacco product regulatory authority?

FDA, Food and Drug Administration

tobacco and more current tobacco users would find it easier to quit. The addictiveness of tobacco products has a direct influence on whether they increase initiation or decrease cessation of their use. These aspects are expressly described in the TCA as critical factors in evaluating the impact of tobacco products on public health. As mentioned, the FDA has the authority to regulate the levels of nicotine in tobacco products but is prohibited from reducing the nicotine yields of a tobacco product to zero. Section 907 of the TCA states that the FDA has authority for setting product standards for nicotine yields of tobacco products that are appropriate for the protection of public health.[6] Research to understand dependence in relation to nicotine level, how reductions in nicotine affect tobacco use behaviors, and other constituents and components beyond nicotine that affect addiction of both combustible and noncombustible tobacco products will inform the FDA's authority in this area.

Reducing Toxicity and Carcinogenicity

In determining the influence of tobacco products on population health, the FDA examines the influence on both users and non-users of these products. Data on the toxicity and carcinogenicity of tobacco products will inform the FDA's regulatory decisions specifically related to the health risk from using these products. The TCA describes the importance of the FDA evaluating the impact of new and modified-risk tobacco products on health and the

authority of the FDA to develop product standards to reduce the toxicity and carcinogenicity of tobacco products. Section 910 of the TCA provides the FDA the authority to review new tobacco products to determine whether authorizing them to be marketed would be appropriate for the protection of public health.[6] Section 911 defines modified risk products as "any tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products."[6] Section 907 states that the FDA can develop product standards appropriate for the protection of public health including "the reduction or elimination of other constituents, including smoke constituents, or harmful components of the products," or "the construction, components, ingredients, additives, constituents, including smoke constituents, and properties of the tobacco product."[6] Consequently, research will inform FDA concerning how reductions in the toxicity of tobacco products affect use behaviors and how the perceptions of products translate into overall reduction in harm. Research will also show what level of reduction in harmful and potentially harmful constituents will result in decreased disease risk and which assays can best compare toxicity between different tobacco products.

Adverse Health Consequences

Within the TCA, several sections address the importance of understanding the adverse health consequences of using tobacco products. Sections 904 and 915 describe ingredient and constituent reporting and testing. Part of Section 904 states that all documents related to the "health, toxicological, behavioral, or physiologic effects of current or future tobacco products, their constituents (including smoke constituents) ingredients, and components and additives" shall be submitted to the FDA at the request of the HHS Secretary from tobacco product manufacturers or importers of tobacco products.[6] In addition, testing and reporting of tobacco product constituents, ingredients, and additives, including smoke constituents by brand and subbrand for the protection of public health, are required.[6] In order to decrease the harms of tobacco use and its resultant morbidity and mortality, it is critical to understand the health risks of the broad range of tobacco products. Other research examples include identifying biomarkers of disease risk that can be associated with measures of tobacco exposure of different tobacco products and identifying novel biological and physiological markers that are predictive of tobacco-caused adverse health outcomes.

Communications

Several sections within the TCA address the importance of communicating factual information to the public.[6] For example, to develop the nine graphics to accompany the health warnings mandated in the TCA, the CTP conducted an online panel experimental study via contract of more than 18,000 adult, young adult, and youth smokers, as well as youth susceptible to smoking initiation, to assess a number of outcomes related to a single exposure to one of the proposed graphic health warnings. Outcomes included relative levels of emotional and cognitive reactions, recall of images and statements, influences on beliefs about the health risks of smoking and secondhand smoke, and quit intentions among smokers and perceived likelihood of smoking 1 year from when youth saw the graphic warnings compared to those exposed to a text-only warning statement.[18] When these graphic health warnings are implemented on cigarette packages and advertisements, it will be important to assess their effect on tobacco product knowledge, attitudes, beliefs, and use. In section 904 of the TCA, the HHS Secretary is directed to "publish in a format that is understandable and not misleading to a lay person" harmful and potentially harmful constituents and to place the list on public display. In addition, Section 904 of the TCA directs that periodic consumer research be conducted to ensure that the list is "not misleading to lay persons."[6] Examples of additional research questions addressing communications include how to effectively convey information regarding risks associated with tobacco products and use, particularly among vulnerable populations, and how to effectively convey FDA's regulatory authority over tobacco products.

Marketing of Tobacco Products

The manner by which tobacco products are marketed can markedly affect their use.[19] This is especially true for adolescents who have been shown to be vulnerable to tobacco marketing.[20] Several sections of the TCA give the FDA the authority to address the impact of the marketing of tobacco products on public health. Section 102 which is also known as the "1996 Rule" finalized regulations set forth by the HHS Secretary in 1996 aimed at preventing youth tobacco initiation and regular use. Examples include prohibiting distribution of free samples of tobacco products to those under age 18, banning candy and fruit flavorings in cigarettes, and the ability to limit color and design of packaging and advertising. In Section 104, the TCA directs FDA to conduct a study on the "public health implications of raising the minimum age to purchase tobacco products."[6] Consequently, it is important to conduct research to understand the influence, particularly among youth, of the range of the types and kind of tobacco product marketing on use behaviors, perceptions, attitudes, and beliefs. This research will inform further FDA regulatory actions to reduce the morbidity and mortality of tobacco products.

Economics and Policies

One of the most clearly documented influences on tobacco products use is the cost of the products. This cost can be monetary or it can be the effort required to overcoming barriers to obtain the product. As costs rise, use decreases.[21] Thus, economic factors are important in overall tobacco product use and the subsequent death and disease resulting from their use. To more completely understand both the costs and benefits of FDA regulatory actions on tobacco use and public health, research will inform several economic and policy questions. As part of any rulemaking process, the government provides an analysis of the impact of its proposed regulations.[22] Consequently, to best understand the risks and benefits of any proposed action, robust economic analyses need to identify the benefits of a rule, including demand and consumer surplus associated with the rule; gained life-years; improved health status; medical cost reductions; other financial effects; and reduced fire-related losses. As the FDA implements regulatory actions, research will assess tobacco use by the overall population and critical subgroups and vulnerable populations, as well as the effect on morbidity and mortality and the statistical modeling of outcomes.

Research Collaboration and Funding

To inform the FDA's regulatory activities, the CTP has already embarked on collaborations and awarded contracts in order to fund research with other government agencies, nongovernment science research organizations, and academic institutions. In Fiscal Year 2011, the CTP funded more than $30 million for research. As research moves forward, it will also be important to offer research training opportunities for new and emerging scientists across a wide variety of disciplines. Among Federal partners, the CTP is collaborating with the CDC on laboratory research of tobacco products, as well as national cross-sectional surveys. The CTP is also collaborating with the FDA's National Center for Toxicological Research on inhalation toxicology and carcinogenicity studies. Along with the NIH, several research initiatives designed to address the scientific research questions have been announced. To accelerate the pace of research, the NIH announced three funding opportunity announcements, including competitive revision applications, administrative supplements to NIH-funded Program Projects and Center grants, and Tobacco Research Centers of Excellence.[23] In this year and in the future, the CTP and its Office of Science expects to provide substantially increased funding to implement these and other research initiatives to ensure a comprehensive research portfolio relevant to the CTP's regulatory authorities.

One critical NIH research collaboration is the Population Assessment of Tobacco and Health (PATH) Study. PATH is a national longitudinal cohort study that will follow about 58,000 users of tobacco products and those at risk for tobacco use aged 12 years and older. Investigators will examine what makes people susceptible to tobacco use; evaluate use patterns and resulting health problems; study patterns of tobacco cessation and relapse in the era of tobacco regulation; evaluate the effects of regulatory changes on risk perceptions and other tobacco-related attitudes; and assess differences in attitudes, behaviors, and key health outcomes in racial/ethnic, gender, and age subgroups. PATH is scheduled to begin data collection in the fall of 2013 and results will help assess the impact of FDA regulatory authority and inform future regulatory activities.

Summary

The provisions within the TCA provide numerous opportunities to support research that builds on the existing science base that the FDA will use as it considers regulatory activities. Importantly, these authorities do not cover all the public health research and program areas that decrease the morbidity and mortality of tobacco use in this country. Several areas are outside of the CTP's purview, including regulating tobacco farming, changing taxes on tobacco, implementing tobacco-free and clean indoor air policies, and developing therapeutics for tobacco cessation. Even with these limitations, there is a role for all Federal partners, state and local government and nonprofit agencies, and other tobacco control partners, to address all facets of tobacco prevention, cessation, and control research, with the goal of improving the public's health by dramatically decreasing the morbidity and mortality caused by tobacco use.

The CTP was created in FDA and tasked with the responsibility for enforcing the TCA. This new responsibility placed an immediate opportunity and challenge for the Center. With more than 440,000 deaths each year from tobacco products, maintaining the status quo and just ensuring that things don't get any worse is not an acceptable solution. To fulfill its mandate of protecting the public health, the CTP is faced with the responsibility of quickly taking necessary and critical steps to meet its vision "to make tobacco-related death and disease part of America's past, not America's future and, by doing so, ensure a healthier life for every family." Additional research will inform the actions of FDA, and the Office of Science within the CTP is charged with overseeing that research. Every delay in fulfilling the mandates of the TCA results in more death and disease from tobacco product use. It is critical that FDA act in the most effective way to meet the public health challenges and opportunities of the TCA as quickly as possible.

The authors acknowledge members of the FDA's Center for Tobacco Products who provided critical input into the research priorities: Tesfa Alexander, Bridget Ambrose, Ben Apelberg, Kimberly Benson, April Brubach, Ii-Lun Chen, Conrad Choiniere, Chris Colburn, Larry Corder, Shawn Fultz, Allison Hoffman, Matt Holman, Corinne Husten, Ele Ibarra-Pratt, Jean Makie, Erik Mettler, Cindy Miner, Gail Schmerfeld, Brian Trent, Dana Van Bemmel, Emil Wang, and Marcella White. The authors also acknowledge Jonathan Kwan, CTP, for his assistance in organizing this article.

The printing of this journal supplement, including this article, was supported by ClearWay Minnesota[SM]. The information in this article is not a formal dissemination of information by FDA and does not represent agency position or policy. The contents are the responsibility of the authors alone.

No financial disclosures were reported by the authors of this paper.

References

1. U.S. Department of Health, Education, and Welfare. Smoking and health: report of the Advisory Committee of the Surgeon General of the Public Health Service. Rockville MD: Public Health Service, 1964.
2. Syamlal G, Mazurek JM, Malarcher AM. Current cigarette smoking prevalence among working adults—U.S., 2004–2010. MMWR Morb Mortal Wkly Rep 2011;60:1305–9.
3. CDC, Office on Smoking and Health. Cigarette use among high school students—U.S., 1991–2009. MMWR Morb Mortal Wkly Rep 2010;59:797–801.
4. Eaton DK, Kann L, Kinchen S, et al. Youth risk behavior surveillance—U.S., 2009. MMWR Morb Mortal Wkly Rep Surveill Summ 2010;59:1–142.
5. CDC, Office on Smoking and Health. State-specific prevalence of cigarette smoking and smokeless tobacco use among adults—U.S., 2009. MMWR Morb Mortal Wkly Rep 2010; 59(43):1400–6.
6. Family Smoking Prevention and Tobacco Control Act, Pub. L. No.111-31, 123 Stat 1776, 2009. www.gpo.gov/fdsys/pkg/PLAW-111publ31/pdf/PLAW-111publ31.pdf.
7. DHHS. Ending the tobacco epidemic: a tobacco control strategic action plan for the U.S. Department of Health and Human Services. Washington DC: Office of the Assistant Secretary for Health, November 2010. www.hhs.gov/ash/initiatives/tobacco/tobaccostrategicplan2010.pdf.
8. Leischow SJ, Zeller M, Backinger CL. Research priorities and infrastructure needs of the Family Smoking Prevention and Tobacco Control Act: science to inform FDA policy. Nicotine Tob Res 2012;14:1–6.
9. Hatsukami DK, Biener L, Leischow SJ, Zeller M. Tobacco and nicotine product testing. Nicotine Tob Res 2012;14:7–17.
10. Hecht SS. Researching opportunities related to establishing standards for tobacco products under the Family Smoking Prevention and Tobacco Control Act. Nicotine Tob Res 2012;14:18–28.
11. O'Connor RJ. Postmarketing surveillance for modified risk tobacco products. Nicotine Tob Res 2012;14:29–42.
12. Ribisl KM. Research gaps related to tobacco product marketing and sales in the Family Smoking Prevention and Tobacco Control Act. Nicotine Tob Res 2012;14:43–53.
13. DiFranza JR. Research opportunities concerning youth and the Family Smoking Prevention and Tobacco Control Act. Nicotine Tob Res 2012;14:54–61.
14. Hammond D. Tobacco packaging and labeling policies under the U.S. Tobacco Control Act: research needs and priorities. Nicotine Tob Res 2012;14:62–74.
15. Sottera Inc v US Food and Drug Administration, 627 F3d 891 (DC Cir 2010). www.cadc.uscourts.gov/internet/opinions.nsf/D02F9D2CA50299F0852577F20070BCC2/$file/10-5032-1281606.pdf.
16. Tobacco Products subject to the Federal Food, Drug, and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act; Notice of proposed rulemaking. 76 Federal Register 130(7 July 2011):40061–2. www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM263819.pdf.
17. Brody AL, Mandelkern MA, Olmstead RE, et al. Ventral striatal dopamine release in response to smoking a regular vs a denicotinized cigarette. Neuropsychopharmacology 2009; 34(2):282–9.
18. Nonnemaker J, Farrelly M, Kamyab K, Busey A, Mann N. Experimental study of graphic cigarette warning labels: final results report prepared for Center for Tobacco Products, Food and Drug Administration. Contract No. HHSF-223-2009-10135G. December 2010. www.regulations.gov/#!documentDetail;D=FDA-2010-N-0568-0008;oldLink=false.
19. National Cancer Institute. The role of the media in promoting and reducing tobacco use. Tobacco Control Monograph No. 19. Bethesda MD: DHHS, NIH, National Cancer Institute. NIH Pub. No. 07-6242, June 2008.
20. Cummings KM, Hyland A, Pechacek TF, Orlandi M, Lynn WR. Comparison of recent trends in adolescent and adult cigarette smoking behaviour and brand preferences. Tob Control 1997;6(S2):S31–S37.
21. DHHS. Reducing tobacco use: a report of the Surgeon General. Atlanta GA: DHHS, CDC, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2000.
22. The Regulatory Flexibility Act (5 USC Sec. 601–612) 1980. www.archives.gov/federal-register/laws/regulatory-flexibility/.
23. Notice of Intent to Publish a Request for Application for Centers of Excellence for Research Relevant to the Family Smoking Prevention and Tobacco Control Act. Notice No.: NOT-DA-12-007. grants.nih.gov/grants/guide/notice-files/NOT-DA-12-007.html.