The FDA "Deeming Rule" and Tobacco Regulatory Research

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In May 2016, the Food and Drug Administration extended its tobacco regulatory authorities to other products meeting the definition of a tobacco product (Deeming Rule). This authority now includes, but is not limited to, electronic nicotine delivery systems (ENDS), such as electronic cigarettes, as well as all cigars, pipes, and hookahs (waterpipes). The FDA's Center for Tobacco Products has been able to fund research projects addressing these newly deemed tobacco products through a variety of mechanisms, including partnership with the Tobacco Regulatory Science Program, National Institutes of Health. In building the evidence base to inform the regulation of and communications about new and emerging tobacco products, it is important for investigators to be mindful of the goals of tobacco regulatory science, ie, scientific inquiry specifically to inform potential regulatory decisions and actions to protect the public's health. Having solid scientific evidence will allow the FDA to make the most appropriate regulatory decisions regarding newly deemed products.

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When the Food and Drug Administration (FDA) issued its final rule in May 2016 to extend its tobacco regulatory authorities to other products meeting the definition of a tobacco product (Deeming Rule), it expanded its jurisdiction. This authority now includes, but is not limited to, electronic nicotine delivery systems (ENDS), such as electronic cigarettes, as well as all cigars, pipes, and hookahs (waterpipes).[1] The Deeming Rule is meant to be foundational in that it brings these newly deemed tobacco products under the provisions of the 2009 Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act).[2] For example, covered products will not be allowed to be sold to persons under 18 years of age or sold in vending machines, except in adult-only facilities; moreover, the dispensing of free samples is disallowed. In addition, manufacturers of these tobacco products must register and provide product listings to the FDA, report ingredients and harmful and potentially harmful constituents, submit applications for pre-market review and authorization for new and products modified after February 15, 2007, place health warnings on product packages and advertisements, and not sell modified risk products unless authorized by the FDA. Beyond these foundational aspects that are automatically in force based on the Tobacco Control Act, there are additional areas where the FDA can take further regulatory action through notice and comment rulemaking. These actions may include development of product standards that would be appropriate for the protection of public health, such as changing the nicotine yields of a product, reducing or eliminating other constituents, and restricting the sale and distribution of a product.

What does the Deeming Rule mean for tobacco regulatory research? In principle, tobacco regula-

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tory science translates general scientific knowledge and specific findings to inform regulatory decisions and actions.[3] As such, the FDA uses the best available scientific data to support its regulatory actions. When strong science is available, the FDA can be certain that its regulatory actions will be effective in accomplishing its mission of reducing disease and death that result from tobacco use. The good news is that the FDA is already "ahead of the game" in developing the science related to newly deemed products. Through its Center for Tobacco Products (CTP), the FDA has been funding projects addressing these newly deemed tobacco products via National Institutes of Health (NIH) grants, research contracts, and work with the Centers for Disease Control and Prevention, the FDA's National Center for Toxicological Research, and other Federal partners.[4] For example, in fiscal year 2015, the CTP funded 59 active research projects addressing electronic cigarettes, 25 projects addressing cigars, and 15 projects addressing hookah smoking (projects not mutually exclusive).

Since 2011, the CTP has been partnering with NIH to foster tobacco regulatory research within the framework of the Tobacco Control Act. The NIH infrastructure for solicitation, review, and management of scientific research provides the CTP with the ability to fund a robust regulatory research grant program that builds upon and complements decades of NIH investment in tobacco-related research. The partnership's organizational unit, the Tobacco Regulatory Science Program (TRSP), works to coordinate research across NIH centers and institutes that may inform the FDA's regulatory authorities with respect to manufacture, marketing, and distribution of tobacco products.[5]

In anticipation of the FDA's ability to assert eventual jurisdiction over previously unregulated tobacco products, and to improve understanding of the potential public health impact of such regulation, the TRSP has been overseeing a large portfolio of biomedical, behavioral, and social sciences research to generate data on a variety of topics (eg, ENDS, cigars, waterpipes, tobacco flavors and flavorings, communication about tobacco products).[6]

In building the evidence base to inform the regulation of, and communications about new and emerging tobacco products, it is important for investigators to be mindful of the goals of tobacco regulatory science (ie, scientific inquiry specifically to inform potential regulatory decisions and actions to protect the public's health) compared to the goals of traditional NIH-supported science (ie, scientific inquiry that seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health). Though it is relevant to regulation of newly deemed tobacco products, NIH research aimed at understanding the etiology of disease or disease progression associated with tobacco products, improving diagnosis or treatment of associated disease/addiction, or testing interventions to improve clinical practice, is generally not within the scope of tobacco regulatory research as mandated by the Tobacco Control Act. On the other hand, there are lines of inquiry on addiction, appeal, and toxicity of newly deemed tobacco products that are not as clearly distinct, and fall within overlapping CTP and NIH interests. For example, use of ENDS for substances other than tobacco (eg, marijuana or alcohol) is relevant to understanding use and potential harm of these products (and appropriate for NIH), but is not useful for informing potential regulatory actions on ENDS within the FDA's tobacco regulatory authorities. Likewise, applying approaches used to study cigarettes to investigate newly deemed combusted tobacco products may not meet NIH criteria for novelty and innovation, but may provide evidence needed to build a scientific foundation for new tobacco product regulation. Though the FDA and the NIH research priorities may differ, together they are needed to implement evidence-based policy and practice to improve public health.

In addition to the research projects already funded on newly deemed tobacco products, there is further work that will be valuable to informing future regulatory actions and activities related to products that were already under the FDA's regulatory authority and the newly deemed products. When considering research that would be useful to inform the FDA, a helpful guideline is to articulate which specific rule, regulatory decision, or activity could potentially be made based on the results of a research study. Examples of tobacco regulatory action decisions include determining whether a tobacco product submitted for pre-market review meets the criteria for marketing, evaluating whether a product would benefit public health if it were

allowed to make modified risk claims, determining the most appropriate regulations and guidance including product standards that would be appropriate for the protection of public health, and considering how best to educate the public regarding the health risks associated with tobacco product use. If thinking about a potential specific rule, investigators should consider what would be most impactful in helping the CTP meet its mission to reduce morbidity and mortality caused by tobacco use. CTP Director Mitch Zeller has stated publicly that the CTP is exploring potential product standards in the areas of addiction, toxicity, and appeal. Investigators should explore both the TRSP and CTP websites to see research that has been funded.[4, 6] When designing studies, researchers should consider the population health standard, given that the FDA needs to take into account the impact on the population as a whole, including both users and nonusers of tobacco products, when making regulatory decisions. For studies focusing on a vulnerable population, investigators should think how the CTP would use results to inform a regulatory activity or action as not all vulnerable populations are relevant to all research questions. For example, understanding how best to communicate to the LGBT community regarding the health effects of tobacco products is appropriate given that the LGBT community has a higher smoking prevalence compared with the general population. Studying the LGBT community regarding the varying nicotine content of tobacco products and dependence, however, may not be justified given that there is no evidence that this population responds any differently than the general population.

The following points are examples of some areas of tobacco regulatory research that would directly inform the FDA in developing the most effective regulations. These examples are not meant to be comprehensive and are only provided for illustrative purposes:

- data that fully characterize a public health concern and evidence that this concern leads to an adverse impact on public health;
- data that describe the current situation such as levels of ingredients or harmful/potentially harmful constituents, user behavior, or harm perceptions;
- evidence of causality or association of the item proposed to be regulated with the adverse impact;
- evidence that the proposed (quantitative) requirement would end or ameliorate the impact;
- viability of technical means of meeting the requirement;
- quantitative estimate of the benefit resulting from the requirement;
- costs associated with complying with the requirement; and
- quantitative impact of other related changes that may limit the benefit of the requirement.

For researchers interested in modifying a newly deemed product for investigational purposes, the FDA does not yet have regulations that require the submission of information on investigational tobacco products (ITPs) used in studies and investigations. Whether or not it is a newly regulated product, a sponsor may submit information to the CTP for review regarding its proposed use of an investigational tobacco product before enrolling subjects in the planned study or investigation. Although not a requirement, the FDA encourages this voluntary submission because it allows the FDA to work with sponsors to help ensure that there are adequate controls on how and to whom the investigational tobacco products are distributed. The FDA released a draft guidance document entitled *Use of Investigational Tobacco Products: Guidance for Industry and Investigators* in September 2015.[7] When final, the guidance will reflect the FDA's most detailed recommendations on the use of investigational tobacco products. If the main objective of the proposed study is to evaluate the proposed product for therapeutic purposes (eg, smoking cessation), the product would not fall under the CTP's jurisdiction, but rather, the FDA's Center for Drug Evaluation and Research, and it would need an Investigational New Drug Application (IND).[8]

Through research to inform evidence-based policies and practices, the United States has made substantial and meaningful progress in tobacco control over the past 5 decades. With the tobacco landscape continuing to shift, the FDA Deeming Rule

provides unprecedented opportunity for reducing the morbidity and mortality caused from tobacco product use. Having solid scientific evidence will allow the FDA to make the most appropriate regulatory decisions regarding newly deemed products.

Disclaimer

This publication represents the views of the authors and does not represent the FDA/CTP or the NIH position or policy.

Conflict of interest disclosure

The authors have no competing interests to declare.

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