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# RESEARCH TO INFORM FDA REGULATORY ACTIONS

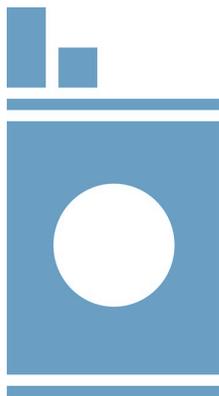
## R21 WEBINAR RFA-OD-19-021, RFA-OD-19-022 NATIONAL INSTITUTES OF HEALTH

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- Since 2009, CTP had authority to regulate tobacco products intended for human consumption to reduce harm across the population
  - Reducing the number of people who start to use tobacco products
  - Encouraging more people to stop using these products
  - Reducing the adverse health impact for those who continue to use these products
- Initially regulated the manufacture, marketing, and distribution of cigarettes, cigarette tobacco, roll-your-own, and smokeless



- FDA finalized a rule effective August 8, 2016 to regulate all tobacco products, including components or parts (but excluding accessories), subject to FDA's tobacco product authorities, including:
  - ENDS (e-cigarettes, e-cigars, vape pens, etc.)
  - All cigars
  - Pipe tobacco
  - Nicotine gels
  - Waterpipe (hookah)
  - Dissolvables not already under the FDA's authority
  - Future tobacco products



# THE TOBACCO CONTROL ACT'S AUTHORITIES



- The Tobacco Control Act amended the Food, Drug, and Cosmetic Act to provide FDA authority for:
  - Premarket review of new and modified risk tobacco products
  - Post-market surveillance
  - Product standards
  - Reporting of ingredients
  - Reporting of harmful and potentially harmful constituents
  - Adverse event reporting
  - Health warnings
  - Advertising and promotion restrictions
  - User fees

# NOT WITHIN CTP AUTHORITY



- In general, CTP's regulatory authorities do **not** extend to:
  - Setting tax rates for tobacco products
  - Regulating therapeutic products, such as those marketed to treat tobacco dependence (regulated by other parts of FDA)
  - Setting clean indoor air policies
  - Regulating tobacco growing
  - Requiring the reduction of nicotine yields to zero
  - Providing cessation services
  - Banning all cigarettes, smokeless tobacco products, little cigars, other cigars, pipe tobacco, or roll-your-own tobacco products
  - Changing the minimum age to purchase tobacco products

- FDA/CTP regulates tobacco based on a population health model
  - Tobacco **cannot** be regulated using FDA’s traditional “safe and effective” standard
- Regulatory actions are based on the risks and benefits to the population as a whole, including both users and nonusers of the product



# HOW FDA IS USING ITS TOBACCO AUTHORITIES



- Understand the regulated products
- Review new products before they can be marketed
- Review proposed modified risk products that state/imply reduced exposure or risk before they can be marketed
- Restrict marketing and distribution to protect public health
- Decrease the harms of tobacco products
- Ensure industry compliance with FDA regulation through education, inspections, and enforcement
- Educate the public about FDA's regulatory actions
- Expand the science base for regulatory action and evaluation



## REGULATORY SCIENCE

- Scientific discipline with independent goals and measures not found in either the basic or applied sciences
- Ensures that scientifically valid techniques, tools, and models are available to evaluate products
- Informs regulatory actions that promote optimal public health outcomes

## TOBACCO REGULATORY SCIENCE

- Informs FDA's regulatory authority
- Recognizes that tobacco products cannot be regulated using FDA's traditional "safe and effective" standard
- Enables FDA to best assess the "net" population-level health impacts

Uchiyama M. (1995). Regulatory science. *PDA Journal of Pharmaceutical Science and Technology*, 49, 185–187.

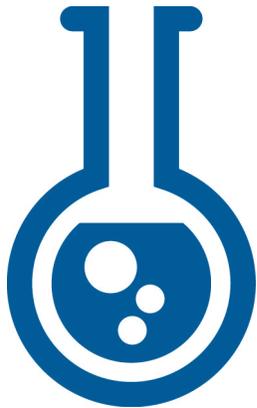
Hamburg M. A. (2010). Shattuck lecture: Innovation, regulation, and the FDA. *New England Journal of Medicine*, 363, 2228–2232.

Norman B. (2012). The Food and Drug Administration gets new tools to spur regulatory science. *Health Affairs (Millwood)*, 31, 1919–1922.

# THE SCIENCE OF TOBACCO REGULATION



- Product
  - Chemistry
  - Engineering
  - Microbiology
- Tobacco Product User
  - Toxicology
  - Pharmacology
  - Clinical medicine
  - Addiction
  - Product use behavior
- Population as a Whole
  - Environmental assessment
  - Epidemiology
  - Consumer perception
  - Statistical analysis
  - Evaluation



# SELECT CTP REGULATORY ACTIVITIES



- Product standards
- Product review
- Public education



# PRODUCT STANDARDS

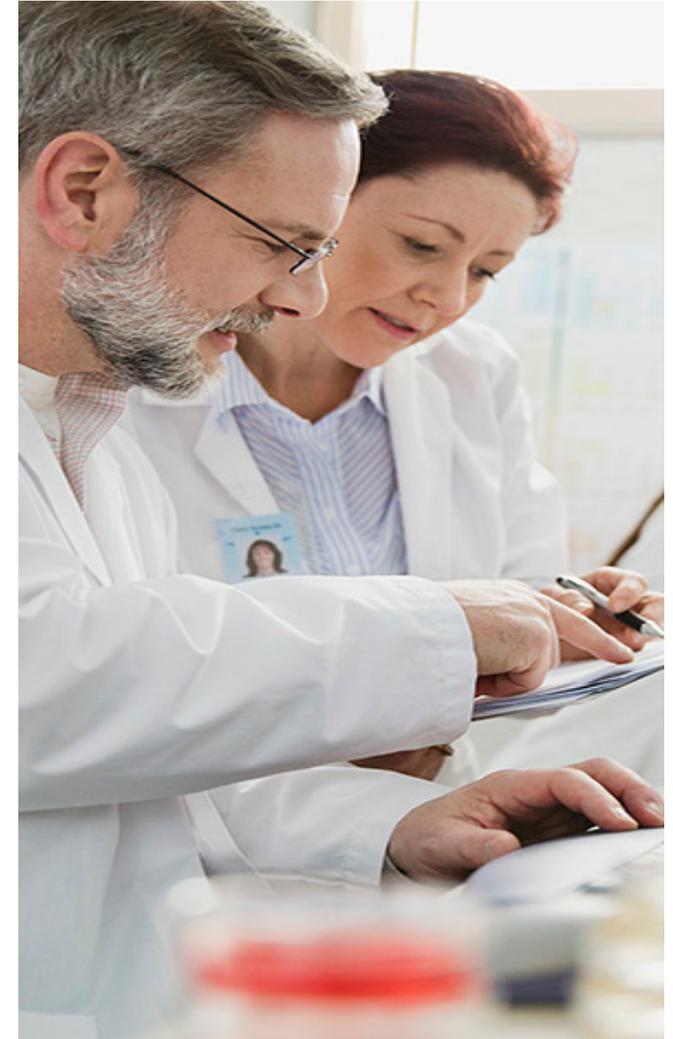


- Product standards are one example of tobacco product regulation
- Through rulemaking, the Tobacco Control Act allows adoption of “...tobacco product standards... appropriate for the protection of public health.” Sec 907.
- Examples of Potential Product Standards
  - Nicotine yields
  - Reduction or elimination of constituents, including smoke constituents
  - Construction, components, ingredients, additives, constituents, and properties of the tobacco product
  - Provisions for testing or measuring product characteristics
  - Restrictions on sale and distribution
  - Form and content of labeling for the proper use of the tobacco product

# PRODUCT STANDARDS – STATUTORY QUESTION



- Is a product standard appropriate for the protection of public health, considering:
  - The risks and benefits to the population as a whole
  - The increased or decreased likelihood that existing users of tobacco products will stop using such products
  - The increased or decreased likelihood that those who do not use tobacco products will start using such products?



# EXAMPLES OF PRODUCT STANDARD ACTIVITIES



## Notice of Proposed Rule Making (Published January 2017)

- Tobacco Product Standard for N-Nitrosornicotine Level in Finished Smokeless Tobacco Products
  - Proposing a tobacco product standard that would establish a limit of N-nitrosornicotine (NNN) in finished smokeless tobacco products



## Advance Notices of Proposed Rule Making (Published March 2019)

- Tobacco Product Standards for Nicotine Level of Combusted Cigarettes
  - To obtain information for consideration in developing a tobacco product standard to set the maximum nicotine level for cigarettes.
- Regulation of Flavors in Tobacco Products
  - To obtain information related to the role that flavors play in tobacco products.
- Regulation of Premium Cigars
  - To obtain scientific data related to the patterns of use and resulting public health impacts from premium cigars.



<https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/rules-and-regulations>



# PRODUCT REVIEW

- Includes:
  - Investigational tobacco products
  - New product review
  - Substantial equivalence (SE)
  - Exemption from SE
  - Modified risk tobacco products
- Applicant must provide adequate evidence for FDA to make a finding
- FDA uses scientific research to evaluate the evidence provided by the applicant





- Premarket Tobacco Applications (PMTA) - Is the marketing of a new product appropriate for the protection of public health?
- Substantial Equivalence (SE) - Do differences between a new product and a predicate product raise different questions of public health?
- Modified Risk Tobacco Products (MRTP) - Will the product as it is actually used by consumers significantly reduce the harm and risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole?



## Information

- Materials
- Ingredients
- Design
- Composition
- Constituents
- Other features
- Marketing

## Impact

- Appeal
- Addictiveness
- Behavior/use
- Exposure
- Pharmacokinetics
- Toxicity
- Perception
- Initiation
- Cessation

## Public health

- Morbidity
- Mortality



# PUBLIC EDUCATION

- FDA maximizes its impact on public health by focusing public education efforts on at-risk audiences such as:
  - general market youth who are already experimenting with cigarettes or open to it,
  - multicultural including African American, Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native youth,
  - rural youth, and
  - lesbian, gay, bisexual, and transgender (LGBT) young adults.



- *Every Try Counts* launched in January 2018
- Campaign Objective: Drive an **increase in motivation to quit among adult smokers** (ages 25-54) who want to quit but were recently unsuccessful, utilizing paid media tactics in and around where tobacco is sold to:
  - Get smokers to try again by **reframing what it means to quit**
  - Get smokers to try quitting more often by **practicing the quit**

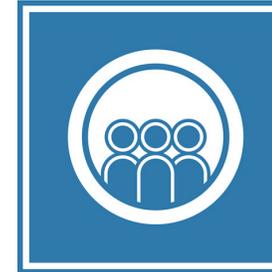


# CTP SCIENTIFIC INTEREST AREAS



## As outlined in the RFAs\*

- Toxicity
- Addiction
- Health Effects
- Behavior
- Communication
- Marketing Influences
- Impact Analysis



\*RFA-OD-19-021, -022



- Scientific research can:
  - understand the impact of changes in tobacco product characteristics (such as flavors or product design) on dependence
  - develop innovative methods and measures to assess tobacco use behaviors, including perceptions, susceptibility, experimentation, adoption, switching, and use (including dual use)
  - understand how product design characteristics (and changes in those characteristics) impact constituent exposure and toxicity from tobacco products
  - develop biomarkers to assess exposure, as well as biomarkers to assess harm or toxicity of non-cigarette tobacco products, including ENDS
  - help identify misperceptions among users and non-users of tobacco products
  - demonstrate new approaches to communication which would promote greater public understanding of the risks associated with the use of tobacco products



Thank You