RESEARCH TO INFORM FDA REGULATORY ACTIONS

CAREER AWARD WEBINAR

RFA-OD-18-005, -006, -007, -008

NATIONAL INSTITUTES OF HEALTH

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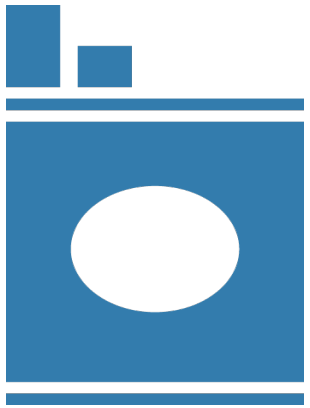
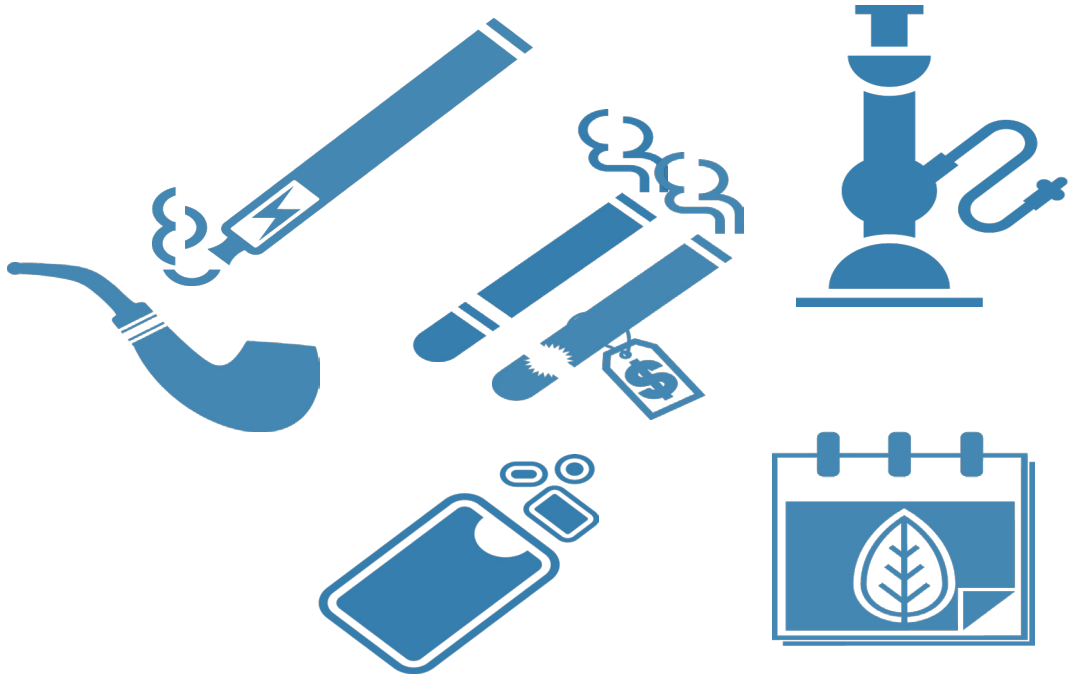
CARRYING OUT HISTORIC LEGISLATION

- Since 2009, CTP had authority to regulate tobacco products intended for human consumption to reduce harm across the population
- Initially regulated the manufacture, marketing, and distribution of cigarettes, cigarette tobacco, roll-your-own, and smokeless



NEW REGULATION

- 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



POPULATION HEALTH STANDARD

- 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




TOBACCO REGULATORY SCIENCE

- Tobacco regulatory science involves the application of the best available science to specific regulatory questions
- Tobacco regulatory research translates general scientific knowledge into the specific scientific findings which serve as actionable information for regulatory decisions and actions
- To do this, tobacco regulatory science evaluates distinct situations to determine the effect on public health

SELECT CTP REGULATORY ACTIVITIES

- Product standards
- Product review
- Compliance and enforcement
- Public education

PRODUCT STANDARDS

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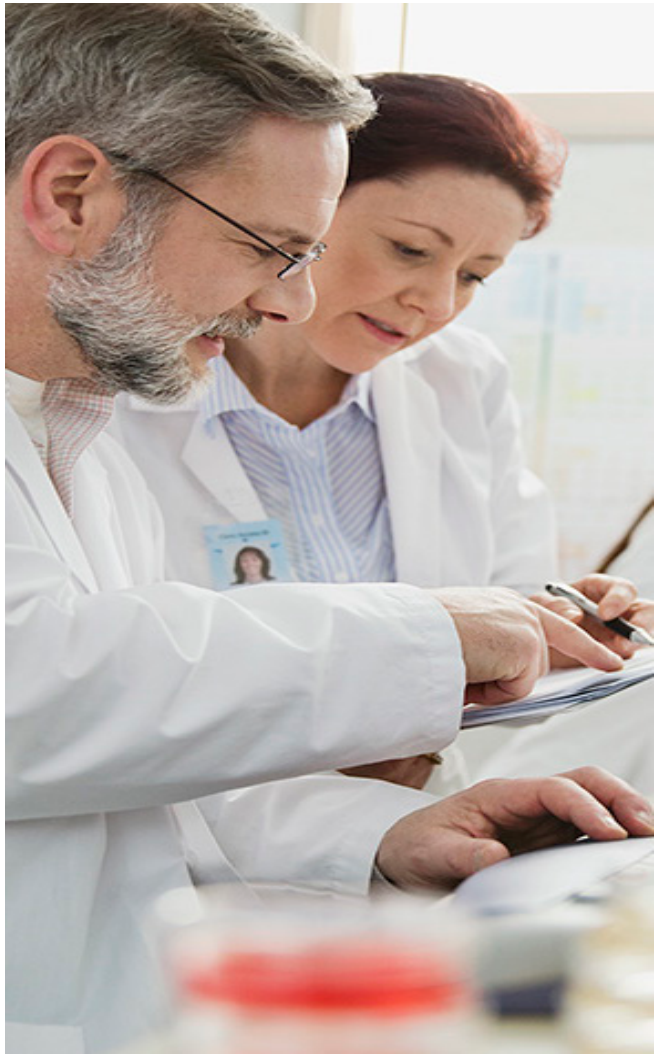
- Product standards are one example of tobacco product regulation
- Through rulemaking, the Tobacco Control Act allows adoption of "…tobacco product standards… appropriate for the protection of public health." Sec 907.
- Examples of Potential Product Standards
  - Nicotine yields
  - Reduction or elimination 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?



PRODUCT STANDARDS – OTHER POTENTIAL QUESTIONS

- Does a specific marketed product meet the standard?

- To answer this question, the standard should be:
  - Justifiable
  - Appropriate
  - Unambiguous
  - Measureable

PRODUCT STANDARDS – RESEARCH

- Research should:
  - Be specific
  - Be directly relevant to the situation
  - Could measure alternatives above and below the standard

PRODUCT REVIEW

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

PRODUCT REVIEW – STATUTORY QUESTIONS

- 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?

PRODUCT REVIEW – RESEARCH

Information

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

Impact

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

Public health

- Morbidity
- Mortality

COMPLIANCE AND ENFORCEMENT

COMPLIANCE AND ENFORCEMENT

- FDA is responsible for implementing and enforcing the provisions of the TCA and regulations that restrict the manufacturing, sale, distribution, and marketing of tobacco products.

- FDA monitors for industry compliance through surveillance, inspections, and investigations of tobacco product retailers, distributors, importers, and manufacturers

- FDA issues enforcement actions when violations are found

COMPLIANCE – ADULTERATED PRODUCTS

- Under section 902 of the FD&C Act, a product is adulterated if, among other things:
  - It has an added poisonous or deleterious substance that renders the product injurious to health
  - Manufacturer did not pay user fees
  - It is not in conformity to product standards
  - It does not have a marketing order, if required
  - It does not meet Tobacco Product Manufacturing Practices, if required
  - It is in violation of Modified Risk claim restrictions

COMPLIANCE – MISBRANDED PRODUCTS

- A product is misbranded if:
  - It has false or misleading labeling or advertising
  - Is missing required information on labeling
  - It does not include directions for use as required by the Secretary
  - It was manufactured in an establishment not in compliance with registration requirements
  - The manufacturer has not reported the components, ingredients and constituents as required by the Secretary
  - It does not bear labeling required by a product standard

COMPLIANCE AND ENFORCEMENT RESEARCH

- Data that supports compliance actions are strongest if they are specific to that case
- Generalized research can supplement evidence collected during surveillance, inspections, and investigations to enable the agency to determine whether there has been a violation of the law

PUBLIC EDUCATION

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.

PUBLIC EDUCATION – RESEARCH

- Scientific research can:
  - 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
  - help understand the messages that can be used to reach vulnerable groups
  - help guide the creation of messages that resonate with the audience and promote behavior change
  - show how information can be provided in a format that is understandable and not misleading to a lay person

CTP SCIENTIFIC INTEREST AREAS

As outlined in the RFAs*

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

*RFA-OD-18-005, -006, -007, -008

NON-RESPONSIVE RESEARCH TOPICS TO RFA-OD-18-005, -006, -007, -008

Although the following research topics may be within FDA CTP's regulatory authorities to fund, they are not included in these RFAs and grant applications will be deemed nonresponsive:

- Studies of short term health effects and/or acute topography/clinical pharmacology testing of early generation ENDS products
- Mechanistic studies/basic science of disease development unless biomarkers of harm with predictive value for disease development associated with tobacco product use is an outcome
- Short-term studies of the acute effects of reduced nicotine content cigarettes
- When addressing chronic toxicity, short-term studies (i.e., 90 days or less) of acute or subchronic toxicity without a rationale explaining how shorter studies are relevant to long-term effects
- Graphic health warnings for cigarette packages and advertisements
- Communicating harmful and potentially harmful constituents to the public
- Impacts of marketing restrictions on adults
- Descriptive studies of demographics and/or risk perceptions that describe only exposure to advertising without linking exposure to tobacco use behaviors

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

THANK YOU