UPDATE FROM THE FDA CENTER FOR TOBACCO PRODUCTS

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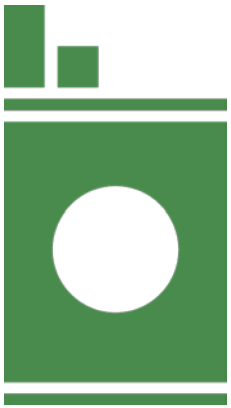
IMPLEMENTING THE TOBACCO CONTROL ACT

Since 2009, CTP had authority to regulate tobacco products intended for human consumption to reduce harm across the population

- Regulate 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 meeting the statutory definition of a tobacco product , 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

CTP‘S MISSION

To protect Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products and by educating the public, especially young people, about tobacco products and the dangers their use poses to themselves and others.

CTP STRATEGIC PRIORITIES

- **Product standards –** advancing product standards that yield strong standards to improve public health
- **Comprehensive FDA Nicotine Policy –** establishing an integrated, FDA-wide policy on nicotine-containing products that is public health based
- **Pre- & Post-Market Controls: Regulation and Product Reviews –** developing rules and guidance's for product review, manufacturing practices, and analytical test method validation
- **Compliance and Enforcement –** inspection, investigation, monitoring and review activities
- **Public Education –** educating at risk audiences on tobacco

DEFINING A PUBLIC HEALTH STANDARD

- Pursue a “public health” standard as tobacco cannot be regulated using FDA’s traditional “safe and effective” standard
- Take into account the benefits and the risks to both users and non-users of tobacco products
- Assess the “net” population-level health impacts of tobacco products

REGULATORY SCIENCE DECISION MAKING

Product Science

- Chemistry
- Engineering
- Microbiology

Nonclinical Science

- Toxicology
- Pharmacology
- Biology
- Environmental Science

Health Science

- Medicine
- Behavioral Pharmacology
- Psychology
- Neuroscience

Population Science

- Epidemiology
- Social science
- Statistics, modeling
- Evaluation

CTP STRATEGIC PRIORITIES

- **PRODUCT STANDARDS**
- COMPREHENSIVE FDA NICOTINE REGULATORY POLICY
- **PRE- & POST-MARKET CONTROLS: REGULATIONS & PRODUCT REVIEWS**
- COMPLIANCE AND ENFORCEMENT
- PUBLIC EDUCATION

EXAMPLES OF TOBACCO REGULATORY ACTIONS

***NOTE**: The potential research scenarios shown in the following slides are presented as a means for illustrating types of studies FDA would find useful. These should **not** be construed as regulatory actions or research under the consideration of FDA at this time.*

PRODUCT REVIEW

PRODUCT REVIEW

- Includes:
  - Investigational tobacco products
  - Pre-market tobacco applications (PMTA)
  - Substantial equivalence (SE)
  - Exemption from SE
  - Modified risk tobacco products (MRTPs)

- 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 CONSIDERATIONS

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

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

Public health
- Morbidity
- Mortality

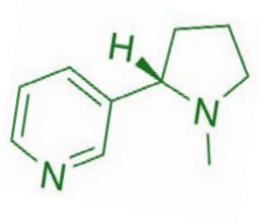
REGULATION AND GUIDANCE

IMPLEMENTING ONE OF THE LAW'S MOST POWERFUL TOOLS

- Advancing a product standard strategy that yields strong standards to improve public health

- Exploring potential standards for:
  - Addictiveness
  - Toxicity
  - Appeal

PRODUCT STANDARDS – REGULATION AND GUIDANCE



Product standards FDA could consider include:

- 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

CTP FUNDED RESEARCH IN TOBACCO REGULATORY SCIENCE

CTP RESEARCH PORTFOLIO

FDA/CTP collaborating with Federal agencies:

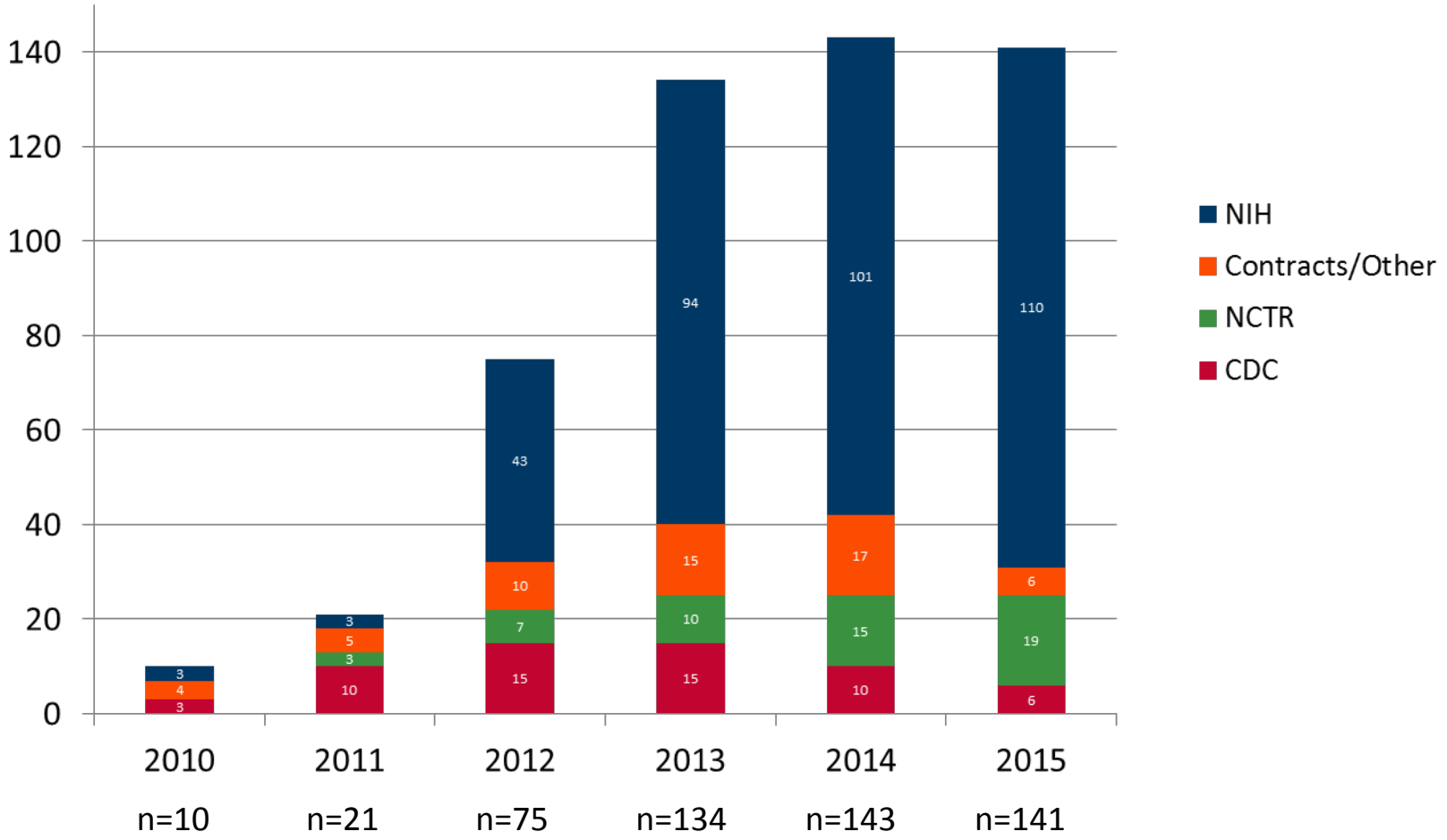
- National Institutes of Health
- Centers for Disease Control and Prevention
- FDA National Center for Toxicological Research

FDA/CTP is also contracting with non-HHS organizations that have particular expertise in scientific areas of interest

PATH
Population Assessment of Tobacco and Health

CENIC Center for the Evaluation of Nicotine in Cigarettes

OS RESEARCH FUNDING SUMMARY, FY10-15



NOTICE OF INTENT TO PUBLISH (NOT-OD-16-151)

Scientific Domains

1. Toxicity
2. Addiction
3. Health Effects
4. Behavior
5. Communication
6. Marketing Influences
7. Impact Analysis

A TCORS application must propose a program of multidisciplinary research around two to four of the seven research domains outlined below that will aid the development and evaluation of tobacco product regulations. Applications that choose fewer than two or more than four scientific domains will be deemed non-responsive.

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-151.html

1. TOXICITY

Understanding how tobacco products and changes to tobacco product characteristics affect their potential to cause morbidity and mortality, including animal and cell culture models as well as novel alternative toxicology approaches that test the toxicity of tobacco smoke, aerosols, or specific constituents in tobacco.

Priorities include:

- Toxicological assays (in vivo and in vitro) to compare toxicity across different types of tobacco products within the same class including electronic nicotine delivery systems (ENDS), cigars, waterpipes and smokeless tobacco
- How product design characteristics (and changes in those characteristics) impact constituent exposure and toxicity from tobacco products; biomarkers to assess exposure, as well as biomarkers to assess harm or toxicity of non-cigarette tobacco products, including ENDS

RESEARCH AREAS OF INTEREST

Toxicology studies of constituents that are present in and result from the combustion of tobacco products, including cigarettes, RYO, and smokeless products.

- Constituents include identified harmful and potentially harmful constituents (HPHCs), ingredients (e.g. flavors), and product material components
- In particular, focus on constituents that have scientific evidence of toxicity but limited dose-response data AND potential for high exposure with product use

RESEARCH AREAS OF INTEREST

Toxicology studies of constituents that are present in and result from the use of newly deemed tobacco products.

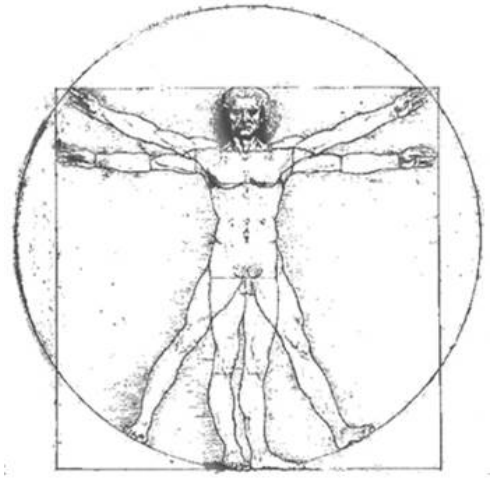
- In particular, focus on understanding the potential toxicity associated with chronic use of electronic nicotine delivery systems (ENDS) and cigars, given lack of data.
- Priority constituents include the components of e-liquids (e.g., glycerol, propylene glycol), other ingredients (e.g., flavors), and product material components that may have potential for high exposure with product use or scientific evidence of toxicity.

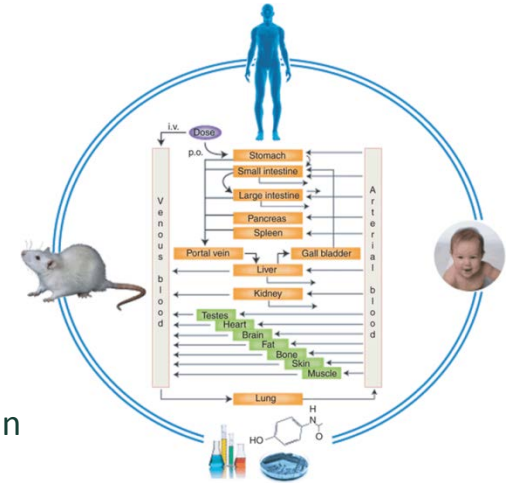



RESEARCH AREAS OF INTEREST

Computational modeling tools that can inform tobacco regulatory science efforts.

- Effective tools for integrating diverse dose-response and mechanistic data in order to more accurately predict human risk*
  - Sophisticated dosimetry models that offer flexibility in modeling exposure scenarios for which there are limited data.
  - Particularly relevant to assessing human exposure to toxicants, which often requires extrapolations across species, route, or dose levels.
- *In vitro* to *in vivo* extrapolation (IVIVE) approaches.





*Chiu, W.A. et al. Evaluation of physiologically based pharmacokinetic models for use in risk assessment. *Journal of Applied Toxicology*. 2007; 27(3): 218-37.

INFORMING STRATEGIC PRIORITIES-NCTR*

Product Standard

- E07549.01 - Evaluating the Toxicity and Inflammation Produced by Cigarette Smoke Using Human In Vitro Airway Models (Cao, X; Healy, S; Chemerynski, S)
- E07568.01 - Microbial Populations and the Development of Tobacco Specific Nitrosamines in Moist Snuff Products (Foley, S; Koenig, M)
- E07531.01 - 13-Week Nose-Only Inhalation Toxicity Study of NNK in Rats (Hu, S; Yeager, R; Rosenfeldt, H)

Informing Comprehensive Nicotine Policy

- E07537.01 - Aspects of Nicotine Self-Administration in the Nonhuman Primate (Goodwin, A; Jackson, K)

Pre- & Post-Marketing Review

- E07535.01 - CTP Scientific Enclave, TCKB, and Topic Modeling for Tobacco Industry Documents (Perkins, R; Aaronson, W; Sholtes, D)

**highlighted research examples-not exhaustive*

THANK YOU

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NCTR

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