FDA
CENTER FOR TOBACCO PRODUCTS

Presented by
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Office of Science, CTP

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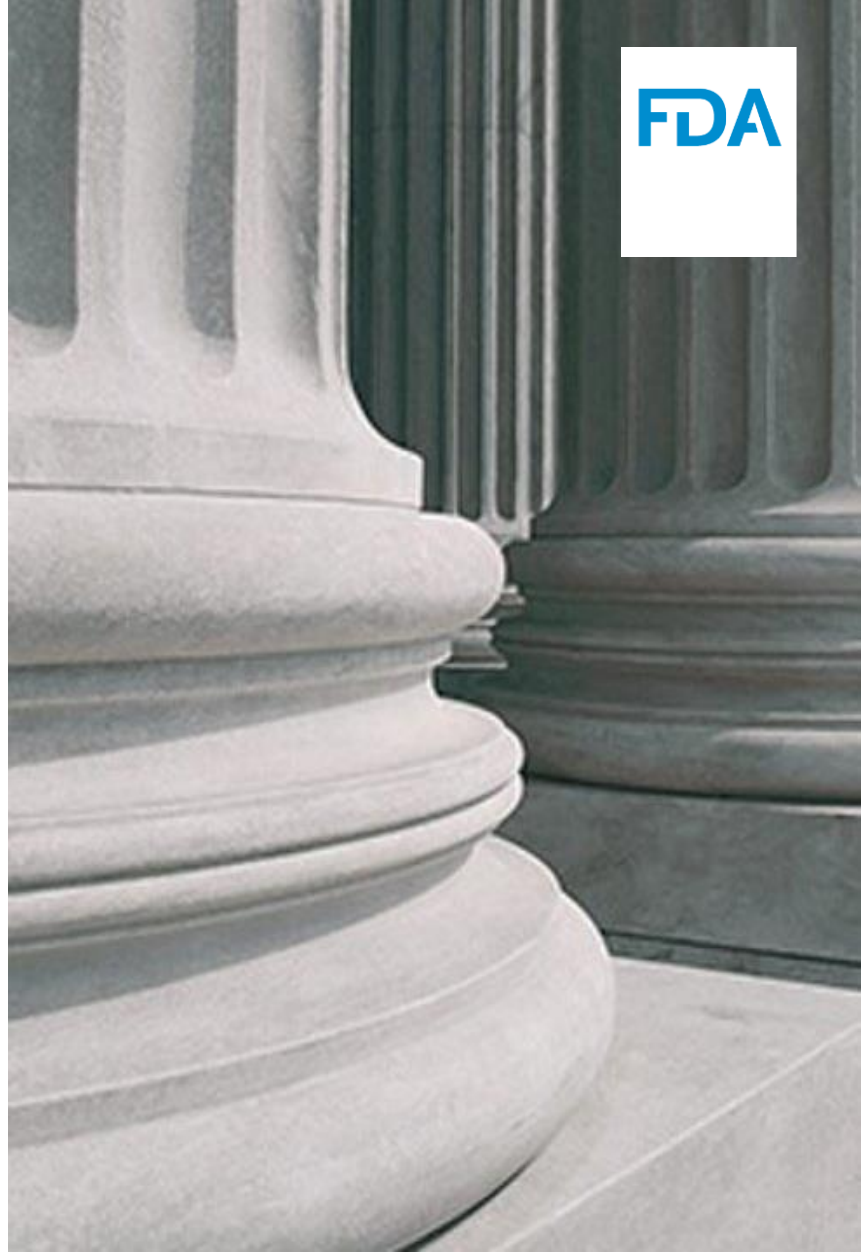
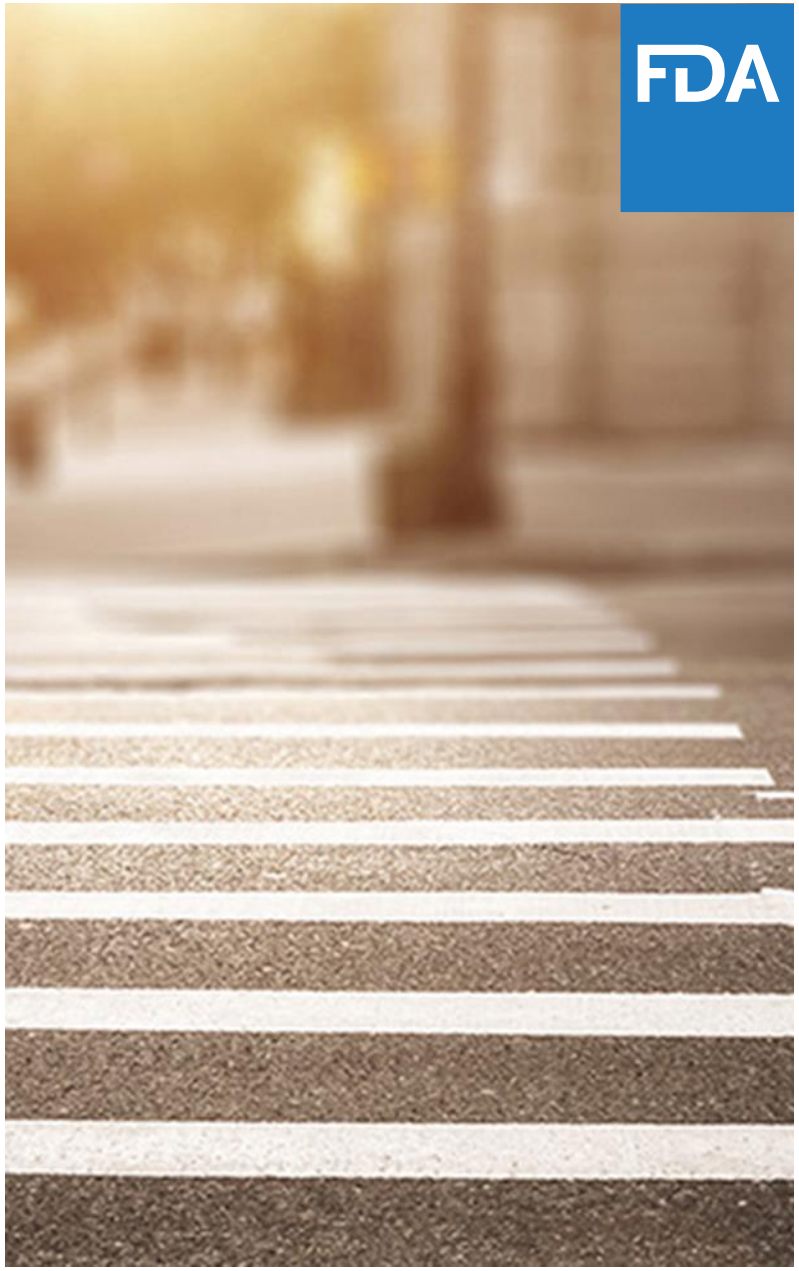


DISCLAIMER

This presentation is not a formal dissemination of information and the views and opinions expressed in this presentation are those of the author and do not necessarily represent the views, official policy or position of the U.S. Food and Drug Administration.

TOPIC AREAS

- New Leadership
- The Work of CTP's Office of Science
  - Research
  - Application Review
  - Rule-making
- Communications and Transparency



NEW LEADERSHIP

Brian A. King, Ph.D., M.P.H.
CTP Director
(July 2022)

Matthew Farrelly, Ph.D.
Office of Science Director
(March 2023)

Research

WHY RESEARCH?

- Science-based approach crucial to CTP's regulatory programs and mission
- Tobacco regulatory science research critical to understanding impact of manufacturing, marketing, and distribution of tobacco products on public health
- Research informs policy development, product standards, and review of tobacco product applications

CTP RESEARCH PROGRAM

Over 600
CTP-funded research projects from FY10 - FY22

More than 60%
of these projects were funded through the NIH

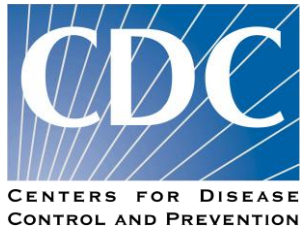
Other partners include, CDC, US DOE, RTI International, Genway and Battelle

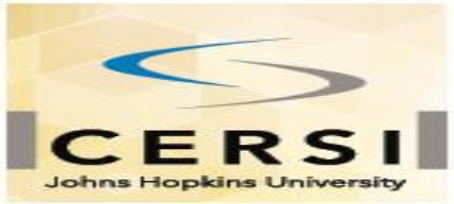
Have resulted in more than
3,600 publications
from FY10 - FY22

Of those publications almost
400 publications
were published in FY22

CTP RESEARCH PARTNERS

- CTP funds research through collaboration with federal agencies and contracts with non-HHS organizations that have particular expertise



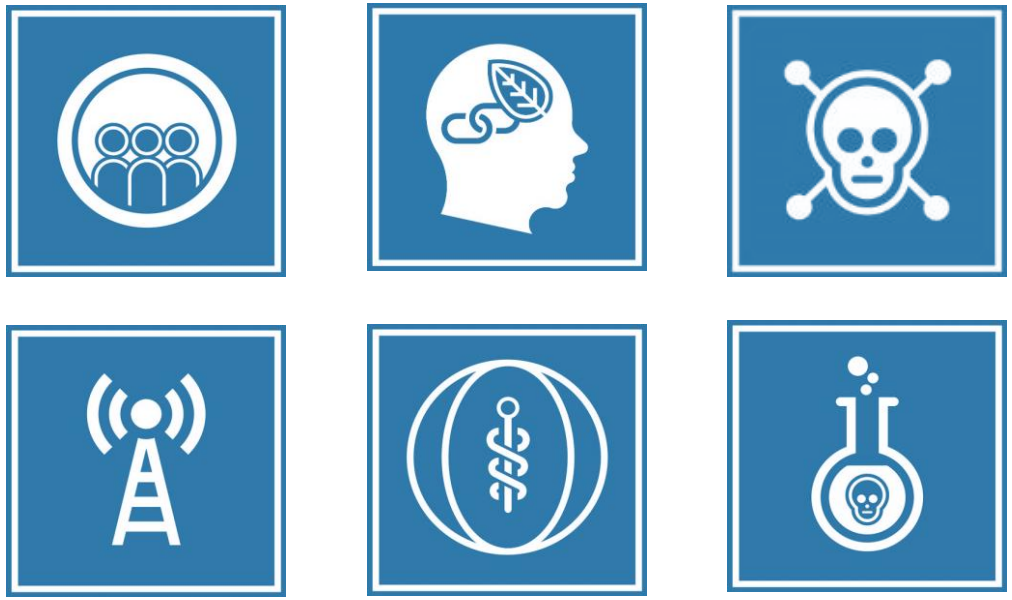


TOBACCO REGULATORY SCIENCE PROGRAM (TRSP)

- FDA and NIH Partnership
- CTP collaborates with NIH to fund grants through an Intra-Departmental Delegation of Authority (IDDA)
- The Tobacco Regulatory Science Program (TRSP) is the team responsible for the management of our portfolio at the NIH
  - CTP-TRSP portfolio includes more than 117 active projects as of FY21, with more than 425 projects over the past 11 years
  - Find a list of active Funding Opportunity Announcements here

CTP OS RESEARCH PRIORITIES

- Addiction
- Behavior
- Communications
- Health Effects
- Impact Analysis
- Marketing Influences
- Product Composition and Design
- Toxicity



https://www.fda.gov/tobacco-products/research/research-priorities

TOBACCO CENTERS OF REGULATORY SCIENCE (TCORS)

- Helps inform and assess FDA's prior, ongoing, and potential regulatory activities
- Flexibility and capacity to respond to FDA's research needs as issues are raised in today's rapidly evolving tobacco marketplace
- Our Role:
  - CTP staff serve as FDA liaisons to the 9 TCORS

POPULATION ASSESSMENT OF TOBACCO AND HEALTH (PATH) STUDY

By monitoring and assessing behaviors, attitudes, biomarkers, and health outcomes associated with tobacco use in the United States, the PATH Study helps enhance the evidence base available to inform FDA's regulatory activities related to tobacco.

PATH

Population Assessment of Tobacco and Health

A collaboration between the NIH and FDA

PATH STUDY

- Longitudinal cohort study of tobacco use, its determinants, and its impacts
- Nationally representative of U.S. civilian, non-institutionalized population ages 12 years +
- Data and biospecimen collection began in September 2013; ~46,000 persons participated in Wave 1
- Completed six waves of data collection with full cohort
- Wave 7 currently in field with both data and biospecimen collection
- Additional three special collections conducted with large subsamples of cohort to respond to priority topics; Wave 4.5 (youth), Wave 5.5 (youth and young adults), and the Adult Tobacco Survey or PATH-ATS
- FDA scientists authored over 100 PATH Study papers published in peer-reviewed journals including more than 30 papers led by FDA
- More than 600 papers published by federal and non-federal authors using PATH Study data
- In addition to papers, PATH Study released hundreds of tables and figures with analyses from Wave 1 – Wave 5 (publicly available online)

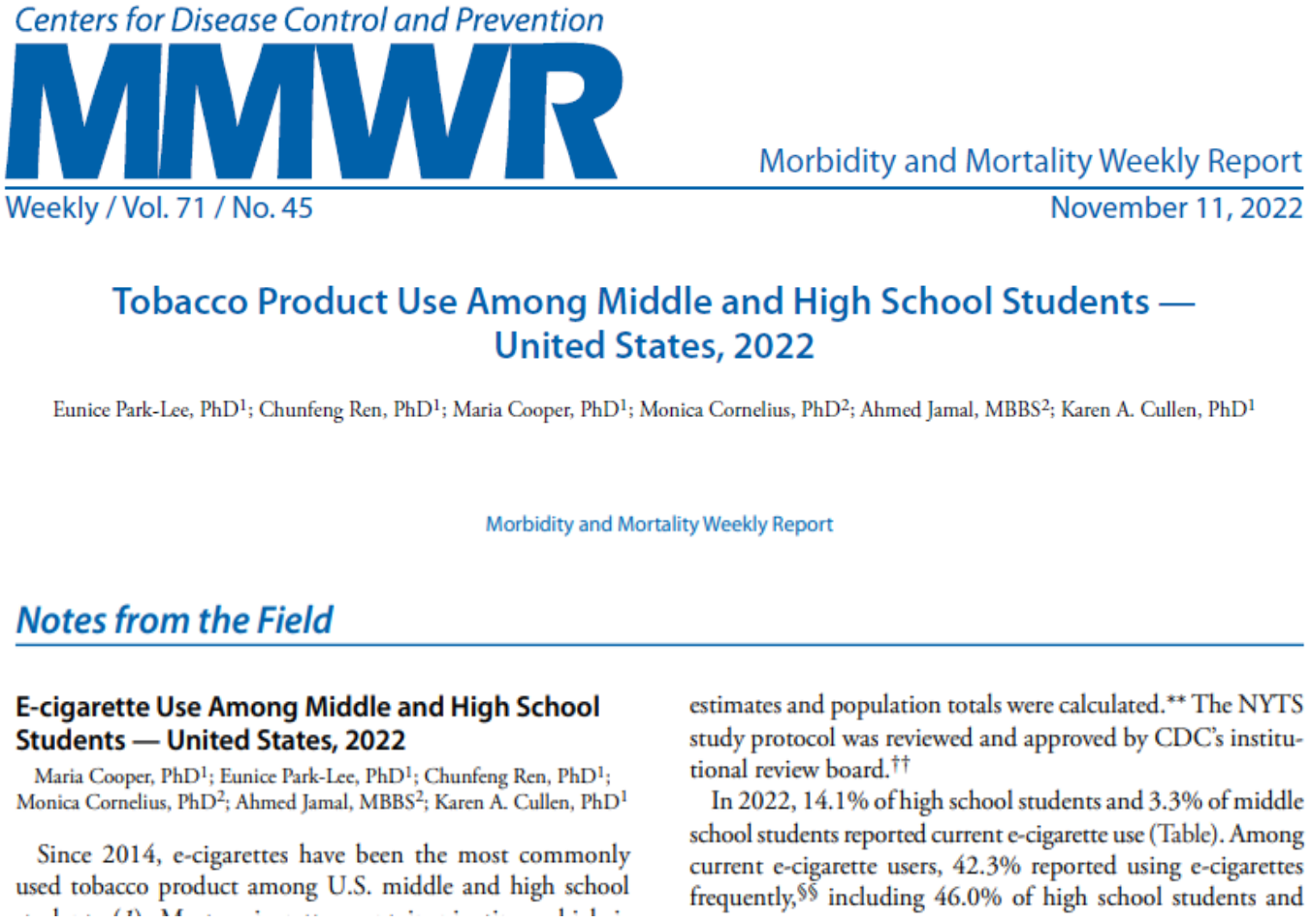
NATIONAL YOUTH TOBACCO SURVEY (NYTS)

- National, cross-sectional survey of U.S. middle (grades 6-8) and high (grades 9-12) school students enrolled in public and private schools
  - School-based, self-administered, voluntary
  - Mode of data collection changed over the years:
    - 1999 – 2018: Paper-and-pencil instrument
    - 2019 – 2020: Electronic tablet data collection
    - 2021 – present: Web-based data collection

- Since 2012, FDA co-sponsored with CDC to collect the NYTS data annually
  - Collaboration on areas, such as questionnaire updates, data analyses, and publications

NATIONAL YOUTH TOBACCO SURVEY 2022

- Data collected between January 18 and May 31, 2022
  - 28,291 students from 341 schools participated
  - Response rate = 45.2%
- Included additional samples of Asian and American Indian or Alaska Native students
- Ability to compare results between 2022 and previous survey waves is limited due to methodological changes
- FDA and CDC collaborated to publish reports using the 2022 data



Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 71 / No. 45

November 11, 2022

Tobacco Product Use Among Middle and High School Students — United States, 2022

Eunice Park-Lee, PhD[1]; Chunfeng Ren, PhD[1]; Maria Cooper, PhD[1]; Monica Cornelius, PhD[2]; Ahmed Jamal, MBBS[2]; Karen A. Cullen, PhD[1]

Morbidity and Mortality Weekly Report

Notes from the Field

E-cigarette Use Among Middle and High School Students — United States, 2022

Maria Cooper, PhD[1]; Eunice Park-Lee, PhD[1]; Chunfeng Ren, PhD[1]; Monica Cornelius, PhD[2]; Ahmed Jamal, MBBS[2]; Karen A. Cullen, PhD[1]

Since 2014, e-cigarettes have been the most commonly used tobacco product among U.S. middle and high school

estimates and population totals were calculated.** The NYTS study protocol was reviewed and approved by CDC's institutional review board.††

In 2022, 14.1% of high school students and 3.3% of middle school students reported current e-cigarette use (Table). Among current e-cigarette users, 42.3% reported using e-cigarettes frequently,§§ including 46.0% of high school students and

Application Review

APPLICATION REVIEW STATUS TOTAL: PMTA FY20-23

Applications received for about

26 million

products, mostly e-cigarettes

Action taken on 99% of the applications, including

Marketing authorizations for

23

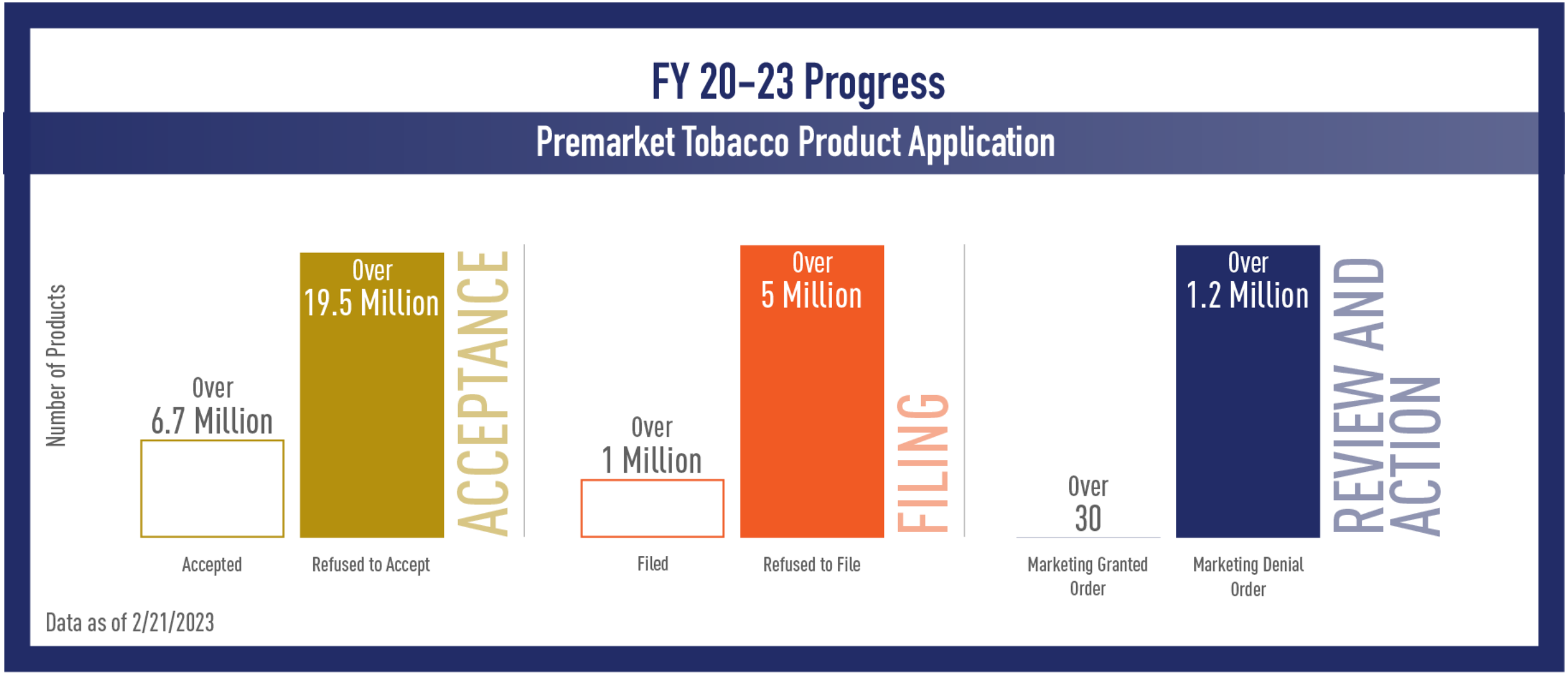
e-cigarette products

Refuse to accept letters, Refuse to file letters, or Marketing denial orders for

Millions

of products

APPLICATION REVIEW STATUS TOTAL: PMTA FY20-23



APPROACH TO FLAVORED E-CIGARETTES (FE) IN PMTA REVIEW

- Determined risk to youth posed by flavored e-cigarettes is substantial and well-established by existing scientific literature
- Could only be overcome by robust and reliable evidence demonstrating that new flavored products provided added benefit, relative to tobacco-flavored e-cigarettes, to adult smokers in terms of complete switching or significant reduction in cigarette use
- Two types of evidence most likely able to demonstrate this added benefit to adult smokers:
  - Randomized Controlled Trial (RCT)
  - Longitudinal Cohort Study
- Because evidence demonstrating this added benefit to adult smokers was determined necessary for marketing of a FE product to be found APPH, in absence of such evidence, there would be no justification to authorize such products (i.e., Marketing Denial Order (MDO))
- Streamlined review of FE PMTAs: Focuses on presence/absence of types of evidence deemed necessary to demonstrate added benefit to adult smokers of flavored e-cigarettes products

PROGRESS ON PMTAS FOR NON-TOBACCO NICOTINE PRODUCTS

FDA

MORE THAN

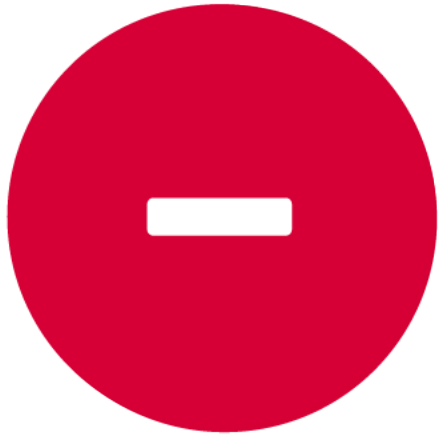
8,600

products accepted for review

MORE THAN

925,000

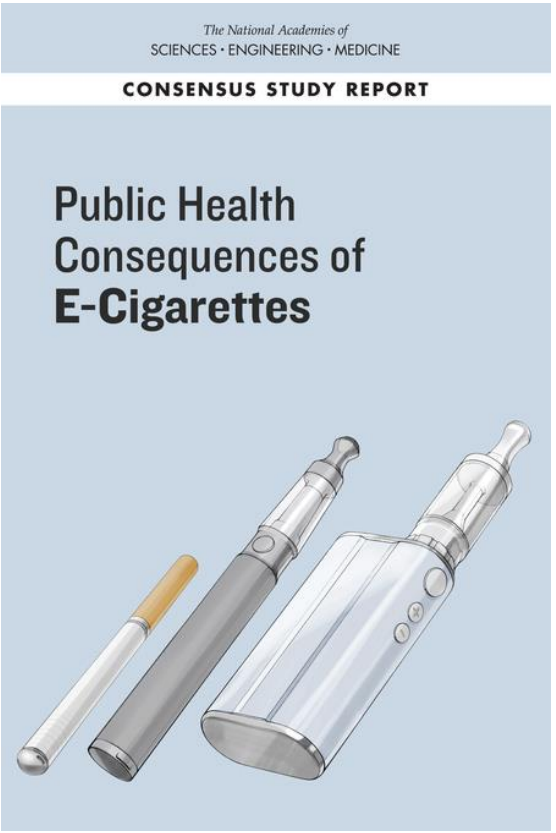
products not accepted for review



*As of Jan 20, 2023

THE E-CIGARETTES STATE OF THE SCIENCE

- OS stays abreast of e-cigarette literature
- In 2018, the National Academies of Science, Engineering, and Medicine (NASEM) released a report compiling available knowledge on the Public Health Consequences of E-cigarettes
  - Reviewed e-cigarettes literature from before August 31, 2017
- Since publication of NASEM report, e-cigarettes products have rapidly evolved and risen in popularity among users
- Up-to-date knowledge of e-cigarettes literature needed to maintain current understanding of e-cigarettes products, their use, and associated potential effects on individual and public health



EFFECT OF LITERATURE ON TOXICOLOGICAL RISK ASSESSMENT IN REVIEW

- Literature is used to provide information for decisions regarding:
  - Problem formulation
  - Hazard identification/assessment
  - Questions of exposure
  - Dose response
  - Quantification
  - Risk Characterization

- **Hazard does not equal Risk**
  - *Hazard* is a potential source of harm or danger
  - *Risk* is the probability or likelihood of adverse outcomes (e.g., cancer, respiratory effects)

Important Literature Reference:
National Academies of Science: Science and Decisions
Discusses the steps of risk assessment and the need to look at the totality of information available

EFFECT OF LITERATURE ON TOXICOLOGICAL RISK ASSESSMENT IN REVIEW

Hazard Identification/Assessment

- Determine what chemicals are present and the amount of potential exposure
  - Product ingredients
  - Potential indirect hazards (e.g., leachables or extractables from storage containers)
  - Constituents that may be formed through transformation (e.g., pyrolysis, degradation)
- Use available literature to determine if the chemicals may cause harm, such as:
  - Established HPHC list with cancer and non-cancer toxicities (respiratory, cardiovascular, reproductive and developmental)
  - IARC carcinogen classifications
  - EPA assessments
  - Published scientific articles

EFFECT OF LITERATURE ON POPULATION HEALTH

- Researchers have used a variety of data sources to supplement or complement other information in PMTA such as:
  - Published, peer-reviewed literature
  - Analyses of existing national datasets
  - Original scientific investigations
- Literature reviews typically include:
  - Purpose of Review
  - Evaluation of Methods
  - Review of Results
  - Bibliography
- Literature reviews may be acceptable to support a PMTA, but generally considered less robust
- Conducting independent analysis of published studies can support a PMTA; useful if study details included

COMMON ISSUES

- Incomplete Information: we presume that at the time of application, you have collected all information and provided that information
- Incomplete ingredient listing
- Lack of chemical breakdown for complex ingredients
- Not providing function, CAS #, and content in mass (not %) for each ingredient
- Incomplete stability studies
  - Full stability studies not needed at submission but we need enough to understand potential risks on stability
- Incomplete HPHC evaluation: HPHCs should be collected at non-intense and intense conditions
  - For e-cigarettes, an intense condition may be a longer puff, but may also be at a higher temperature (these are sometimes linked)

COMMON ERRORS

- Inadequate demonstration of battery safety
- Contamination with toxic or genotoxic leachables
- Use of toxic or genotoxic ingredients
- Issues with TPMF contents
- Incomplete detail on quality systems, SOPs, certifications, and manufacturing
- Inadequate bridging data between products and between product and literature
- Inadequate or absent product specific benefit data

DEFICIENCY LETTERS (DL)

- Complete responses to all deficiencies needed
- Incomplete responses may lead to negative orders
- Late responses may result in administrative withdrawal of applications
- Extension requests considered with adequate justification on case-by-case basis, but few accepted
- Data provided in response to DL will be considered as additional information and not replacement information unless indicated and justified

MODIFIED RISK TOBACCO PRODUCT (MRTP)

- Copenhagen Classic Snuff reduced risk claim authorized March 16, 2023
  - Allows product to be marketed with claim: “IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer.”
  - Based on rigorous review of available evidence, including TPSAC recommendations, public comments, and other available scientific information, FDA concluded:
    - the specific claim related to lung cancer risk is scientifically accurate;
    - if current smokers switch completely from cigarettes to this MRTP, it would benefit population-level health by reducing overall tobacco-related disease and death;
    - those public health gains are not expected to be offset by nonusers starting to use this MRTP
- The US Smokeless Tobacco Company (USSTC) must monitor consumer impact; FDA may withdraw authorization as needed to protect public health

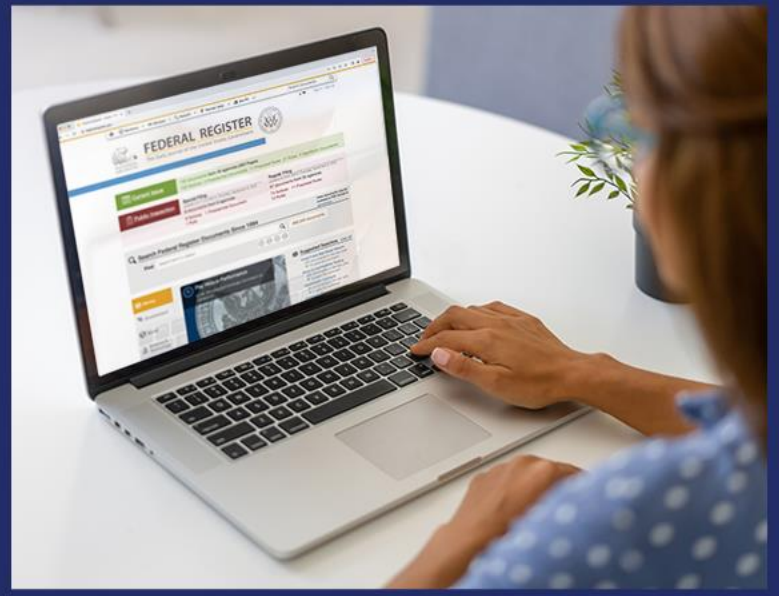
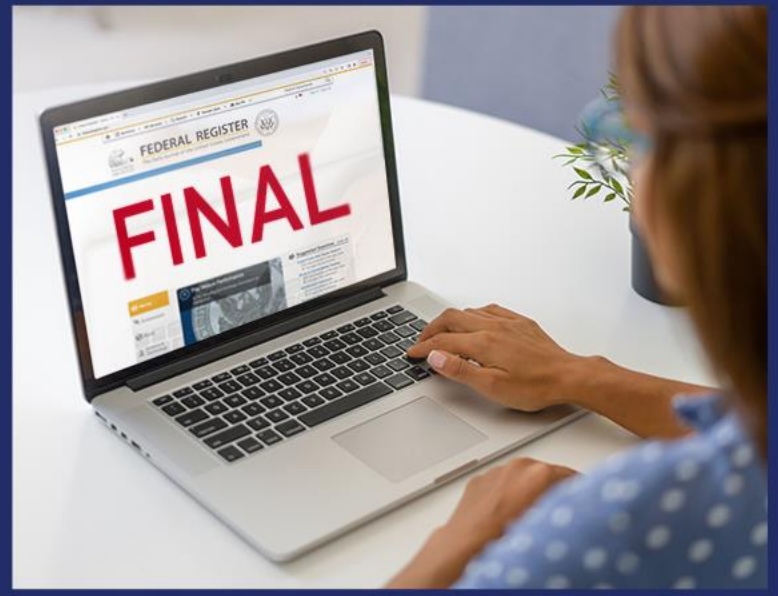
RESEARCH TO SUPPORT MRTPA

- OS led research to develop recommended items to assess e-cigarette risk perceptions for use in Tobacco Product Perception and Intention Studies (TPPIS)
  - Systematic literature review found there were no measures of e-cigarette risk perceptions that were completely consistent with tobacco researcher recommendations (O'Brien, Persoskie, & Tam, 2019)
  - OS scientists developed and validated brief measures to assess seven types of e-cigarette risk perceptions (O'Brien, Baig, & Persoskie, 2022)
    - Absolute health and addiction risks
    - Health and addiction risks relative to cigarettes
    - Pregnancy health risks relative to cigarettes
    - Health risks relative to NRT
    - Risks relative to all nicotine cessation

- Measures underwent rigorous measurement development process, follow recommendations from tobacco researchers (publicly available)

Rule-making

RULEMAKING PROCESS

Rule/Regulation Proposed	Public Comments Considered	Final Rule Issued
		

RESEARCH IN ACTION

Over a quarter of citations referenced in two recent proposed rules were CTP-funded publications

26%

Product Standard for Characterizing Flavors in Cigars:

- 254 peer-reviewed publications cited, of which 73 (29%) were CTP-funded

Tobacco Product Standard for Menthol in Cigarettes

- 250 peer-reviewed publications cited. Of these, 58 (23%) were CTP-funded

PROPOSED RULE: TOBACCO PRODUCT MANUFACTURING PRACTICES (TPMP)

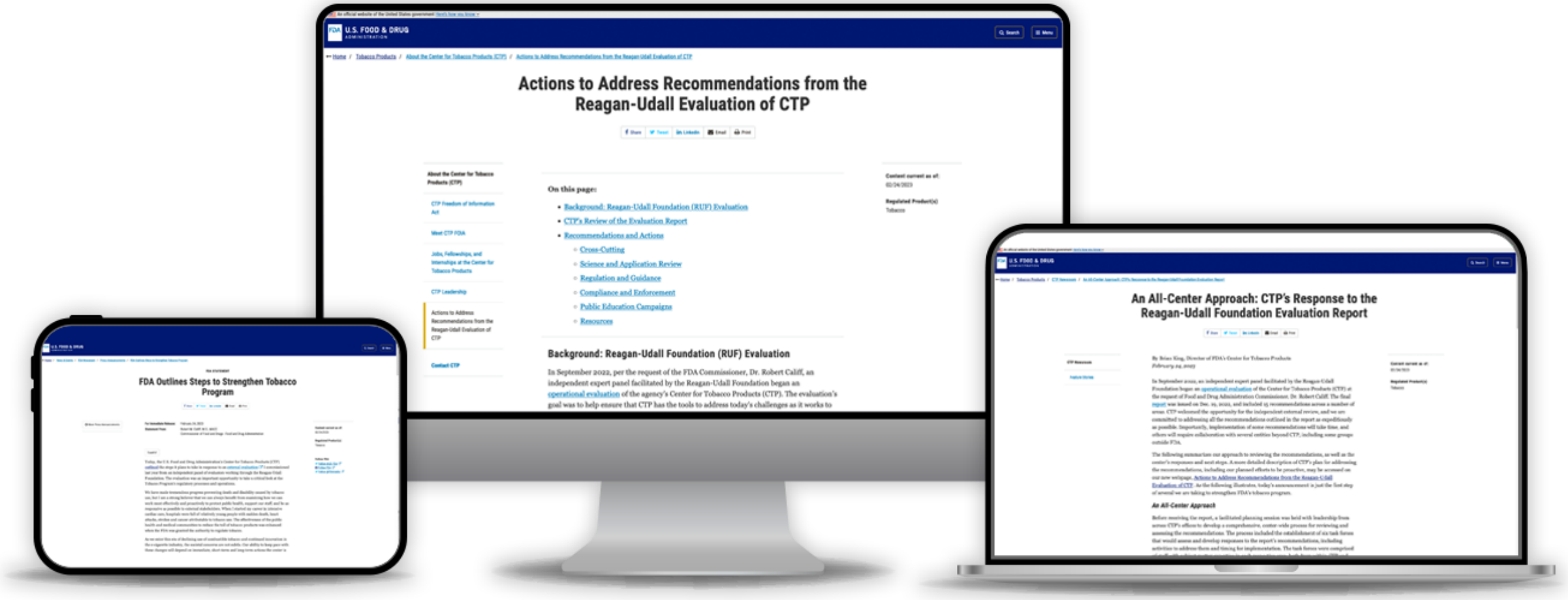
- March 8, 2023: FDA proposed new requirements for manufacturing, designing, packing and storage
  - Help protect public health by minimizing or preventing contamination; limit additional risks by ensuring product consistency
  - Apply to manufacturers of finished and bulk tobacco products, including component or part, sealed in final packaging
- Proposed rule establishes framework to adhere to, such as:
  - Establishing product design and development controls;
  - Ensuring that products are manufactured according to established specifications;
  - Minimizing manufacture and distribution of products that don't meet specifications;
  - Requiring appropriate measures to prevent product contamination;
  - Requiring investigation and identification of products that don't meet specifications;
  - Establishing ability to trace all components or parts, ingredients, additives and materials.

Communications & Transparency

REAGAN-UDALL FOUNDATION (RUF) EVALUATION

- Review RUF commitments/recommendations
  - Transparency of process
  - Transparency of standards
  - Transparency of practices
  - Transparency of decision making
- Increase Use of Tobacco Products Scientific Advisory Committee (TPSAC) Public Meetings
- Further Engagement with the public
  - Conferences
  - Public Meetings
  - Webinars

CTP'S RESPONSE



SCIENCE AND APPLICATION REVIEW

- Increase Use of Tobacco Products Scientific Advisory Committee (TPSAC)
- Develop Clear and Predictable Framework for Application Reviews
- Clarify Substantive Review Processes

CLOSING THOUGHTS

FDA remains committed to using our regulatory authorities to protect public health