E-CIGARETTES: KEY POLICY AND RESEARCH QUESTIONS

Mitch Zeller, Retired Director
U.S. Food and Drug Administration, Center for Tobacco Products
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OUTLINE

- Setting the Stage
- Harm Reduction and the Reality of Premarket Review in the U.S.
- U.S. Food and Drug Administration's 2017 Framework and Comprehensive Plan
- The State of the Harm Reduction Debate Today
- Reframing the Debate
- Closing Thoughts

SETTING THE STAGE

KEY CHARACTERISTICS OF E-CIGARETTES

- Pulmonary delivery of nicotine
- No combustion
- No tobacco

YES…THERE IS A CONTINUUM OF RISK

One Representation of the Continuum of Risk

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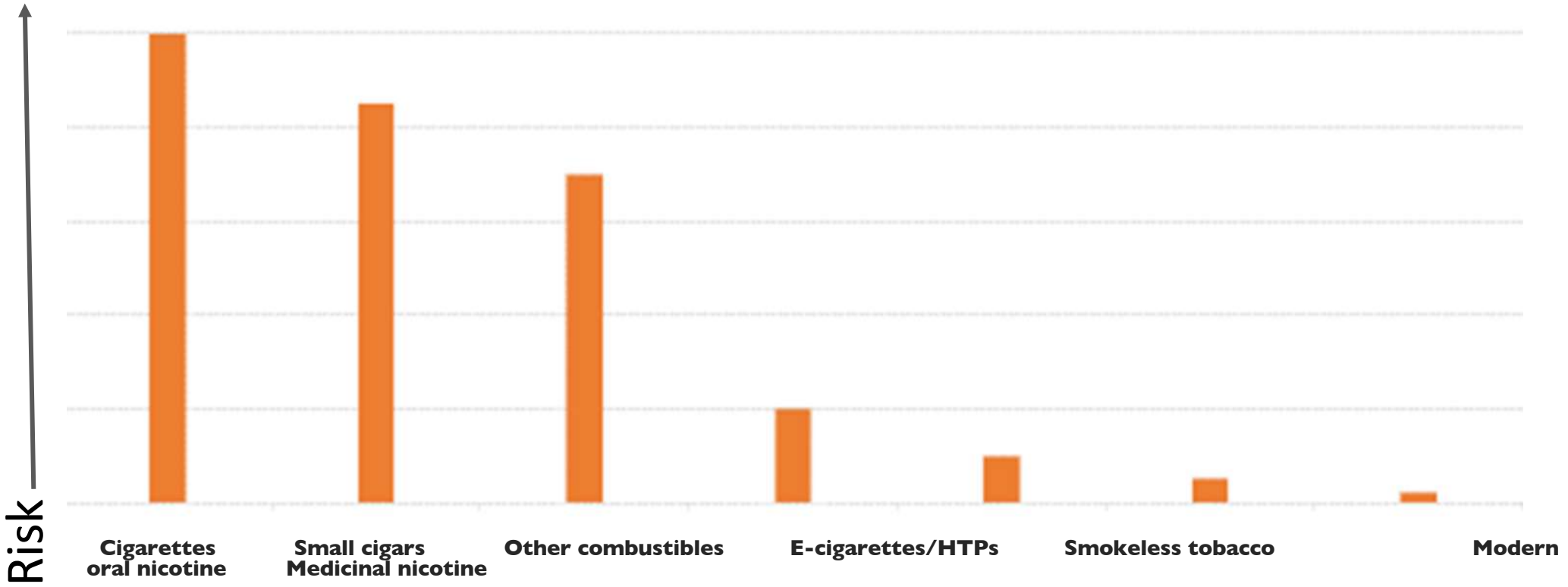

Source: Created by Ken Warner

YES…WE NEED TO THINK ABOUT NICOTINE DIFFERENTLY

- The continuum of risk is an important framing
- Smokers smoke for the nicotine but die from the tar
- Public health opportunity to move smokers down the continuum of risk

BUT…HOW DOES THIS ALL APPLY TO REGULATORY POLICY KEYED TO HARM REDUCTION?

- Policy not made in the abstract
- In the U.S. this means case-by-case determinations
- Under U.S. law, must account for intended and unintended impacts
- In any country, need to assess "net" population-level effects

KEY *REAL WORLD* QUESTIONS

- The "two central areas" of this conference:
  - Health effects
  - User trajectories
- Leave the world of the abstract and the categorical
- When making regulatory policy, ask two key questions about the real world:
  - **Who** is using the products?
  - **How** are the products being used?

HARM REDUCTION AND THE REALITY OF PREMARKET REVIEW IN THE U.S.

PREMARKET REVIEW

- Family Smoking Prevention and Tobacco Control Act
- Key provisions include premarket review of new tobacco products and any health claims:
  - Legal standard for marketing e-cigarettes and other Electronic Nicotine Delivery Systems: "appropriate for the protection of the public health" (APPH)
  - Case-by-case decisions based upon evidence submitted in each application

PREMARKET REVIEW

- Key provisions include premarket review of new tobacco products and any health claims (continued):
  - Benefits to adults need to be demonstrated to outweigh risks to kids, especially for flavored products
  - Not categorical
  - Legal and evidentiary burden squarely on each company

THE MARKETPLACE FOR NICOTINE

- With e-cigarettes the nicotine can be delivered without having to burn tobacco leaves and inhale the smoke
- And the nicotine doesn't directly cause cancer, lung disease and heart disease
- But, concerns surrounding nicotine addiction, flavors and kids

HARM REDUCTION AND THE REALITY OF PREMARKET REVIEW

- The continuum of risk is real; more harmful and less harmful ways to deliver nicotine
- A pack-a-day smoker who completely switches to e-cigarettes will reduce their risk
- But…marketing authorization decisions are not made on an abstract and categorical basis
- The U.S. premarket review provisions clearly place the burden on each company to demonstrate benefits outweigh risks on a case-by-case basis

U.S. FOOD AND DRUG ADMINISTRATION'S 2017 FRAMEWORK AND COMPREHENSIVE PLAN

"AT A CROSSROADS"

- When the 2017 framework was announced, then-FDA Commissioner Scott Gottlieb said:
  - "We truly find ourselves at a crossroads when it comes to efforts to reduce tobacco use. But if we're going to meaningfully improve the public health, we need to be willing to take a hard look at our entire approach."

FOCUS ON THE GREATEST RISK

- Commissioner Gottlieb also said:
  - "Nicotine, while highly addictive, is delivered through products on a continuum of risk…[and] the combustible cigarette is where nicotine's delivery leads to incredible amounts of disease and death."

THE FDA VISION

- A world where the cigarette was no longer capable of creating or sustaining addiction
- A world where adults who would still seek nicotine, for whatever reason, could get it from alternative and less harmful sources

THE FDA VISION

- A strategic regulatory framework designed to:
  - Decrease the potential that future generations of kids become addicted to cigarettes
  - Increase the number of addicted smokers who successfully quit
  - Provide access to less harmful products for adults needing them
  - Encourage innovations in medicinal nicotine and other therapeutic products aimed at cessation

KEY ELEMENTS OF THE 2017 PLAN

- Regulatory policies focused on addiction, appeal and cessation
- A 3-pronged youth tobacco prevention plan:
  - Access
  - Marketing
  - Education
- A science-based review of new products under the APPH standard for potential marketing authorization and exposure and risk reduction claims

KEY ELEMENTS OF THE 2017 PLAN

- Encourage a national dialogue on nicotine
  - Correct misperceptions about nicotine safety
  - Explain the continuum of risk
  - Account for adverse impacts on youth
- Provide more time for industry applications and creation of "foundational" rules
  - Applications originally due in 2018 would not have been due until 2022

AND THEN 2018 HAPPENED

- JUUL
- Explosion in youth use of e-cigarettes following a two-year decline and leveling off
- Public health groups sued to shorten the application deadline
- A year later, a court ruled that the applications were due in 10 months, rather than in 3 more years

THE STATE OF THE HARM REDUCTION DEBATE TODAY

THE DEBATE

- An incredibly divisive debate within tobacco control and public health circles…domestically in the U.S. and globally
- Both sides prefer the debate to remain focused on the pros and cons of e-cigarettes and harm reduction
- The result…anger and stalemate

INCONVENIENT TRUTHS IN THE U.S.

- Inconvenient truths for both sides of the debate and certain members of Congress
- Certain heated, smokeless and e-cigarette products meet the APPH standard and deserve their marketing authorization; also includes a "Very Low Nicotine" cigarette
  - Some of these products have also passed the test to get exposure and harm reduction claims authorized
  - More marketing authorizations are certain to follow

INCONVENIENT TRUTHS IN THE U.S.

- Flavored e-cigarette products so far have failed, on a case-by-case basis, to pass the APPH test
  - Case for benefits not made
  - Proposed marketing and youth access restrictions, to date, insufficient to overcome deficiencies in proving benefit
  - 3 of the 4 Federal appellate courts who have ruled have sided with FDA; the fourth was a split decision

INDUSTRY BEHAVIOR

E-Cigarette

Toy

E-Cigarette

Toy

REFRAMING THE DEBATE

A POLICY COMMON GROUND?

- What if combustible products could no longer create or sustain addiction?
- In the U.S., FDA has the authority to do this and the regulatory science supports it

NICOTINE REDUCTION IN COMBUSTIBLE PRODUCTS

The New York Times

"F.D.A. Aims to Cut Down on Smoking by Slashing Nicotine Levels in Cigarettes"
June 21, 2022

"Nicotine is powerfully addictive," said FDA Commissioner Robert M. Califf, M.D…"Lowering nicotine levels to minimally addictive or non-addictive levels would decrease the likelihood that future generations of young people become addicted to cigarettes and help more currently addicted smokers to quit."

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NICOTINE REDUCTION IN COMBUSTIBLE PRODUCTS

- Published modeling projects through end of century:
  - Over 33 million Americans won't become regular smokers
  - Adult smoking rate will plummet to less than 1.5%
  - More than 8 million tobacco-caused deaths will be avoided…from one FDA rulemaking

NICOTINE REDUCTION IN COMBUSTIBLE PRODUCTS

- But many of the 30+ million current smokers will still seek nicotine
- So, what are the implications for alternative and potentially less harmful nicotine-delivering products that would not be affected by such a policy?

THE 6 QUESTIONS

"The Future of Nicotine Regulation: Key Questions and Challenges," Nicotine & Tobacco Research (2019)

The Questions:

1. How comfortable are we with long-term, or possibly permanent, use of less harmful nicotine delivery mechanisms by adults, if they help keep currently addicted smokers from relapsing to combustible tobacco products?

2. How much weight should be placed on diminished interest in quitting nicotine altogether?

3. Given the potential health impacts of dual use of tobacco, how acceptable is a short period of dual use while transitioning to less harmful nicotine-containing products?

THE 6 QUESTIONS

The Questions:

4. What if many current smokers engage in dual use on a long-term or permanent basis?

5. Can we revise labeling and indications for medicinal nicotine to increase quitting?

6. How might youth initiation be affected by the availability of different nicotine-containing products and how should we account for youth uptake of these products?

CLOSING THOUGHTS

CLOSING THOUGHTS

- Inconvenient truths abound, on both sides
- On the one hand, there is a role for certain heated, smokeless and e-cigarette products; and, maybe one day, flavored e-cigarettes
    - Some people may need to stay on less harmful forms of nicotine for a long time, possibly forever
- On the other hand, companies must bear the burden of proof
    - Kids like flavors, nicotine can be addictive, and marketing practices continue to target young people

CLOSING THOUGHTS

- When was the last time any of those truths were acknowledged by those who find either set of them inconvenient?
- No apparent interest from the loudest mouths on both sides in seeking common ground, even on principles
- As a result, the noise being generated, especially on social media, is an echo chamber

CLOSING THOUGHTS

- I still believe in the FDA 2017 framework
  - A world where kids cannot become addicted to combustible products
  - A world where addicted adults have access to less harmful forms of nicotine and improved medicinal products
- This remains an achievable vision that will save countless lives

CLOSING THOUGHTS

- But are we ready to ask the tough questions about nicotine, starting with the need for long-term or permanent use of less harmful products for those who need to?
- What about extended periods of dual use if there is demonstrable evidence of benefit?
- Is there any level of unintended consequences (e. g. kids' use, relapse) that is acceptable?
- The areas of focus of this conference (health effects and user trajectories) are critical to getting us the evidence we will need to answer these questions

MERCI!