OVERVIEW OF FDA REGULATORY FRAMEWORK FOR VERY LOW NICOTINE CIGARETTES

MITCH ZELLER

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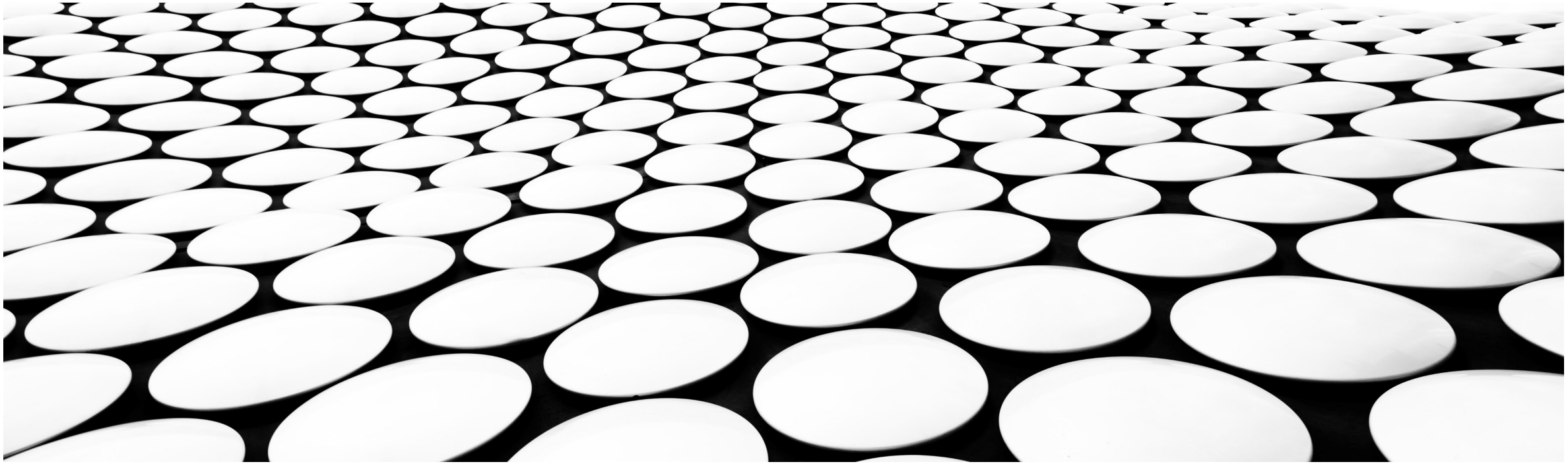

DISCLOSURE

- I recently joined Qnovia, Inc. as an advisor
- Qnovia is a start-up pharmaceutical company developing an inhaled smoking cessation product that it intends to seek FDA authorization for marketing

TOPICS TO COVER

- What the tobacco industry said about nicotine and when
- What the tobacco industry knew about nicotine and cigarette design in 1959
- Key provisions of the Tobacco Control Act related to product standards
- “Notice and Comment” rulemaking
- “Final agency action” and potential litigation

WHAT THE TOBACCO INDUSTRY SAID ABOUT NICOTINE AND WHEN

- “Nicotine is addictive. We are, then, in the business of selling nicotine – an addictive drug.” (Brown and Williamson, 1963)

WHAT THE TOBACCO INDUSTRY SAID ABOUT NICOTINE AND WHEN

- “In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized, and stylized segment of the pharmaceutical industry. Tobacco products uniquely contain and deliver nicotine, a potent drug with a variety of physiological effects.” (R. J. Reynolds, 1972)

WHAT THE TOBACCO INDUSTRY SAID ABOUT NICOTINE AND WHEN

- The “confirmed smoker”

  “His choice of product and pattern of usage are primarily determined by his individual nicotine dosage requirements and secondarily by a variety of other considerations…Our industry is then based upon design, manufacture and sale of attractive dosage forms of nicotine.” (R.J. Reynolds, 1972)

WHAT THE TOBACCO INDUSTRY SAID ABOUT NICOTINE AND WHEN

- The "pre-smoker" or "non-smoker"

  "…the things which keep a confirmed smoker habituated and 'satisfied'…are unknown and/or largely unexplained to the non-smoker…only after experiencing smoking for some period of time do the physiological 'satisfactions' and habituation become apparent and needed…we must somehow convince him with wholly irrational reasons that he should try smoking, in the hope that he will for himself then discover the real 'satisfactions' obtainable." (R. J. Reynolds, 1972)

WHAT THE TOBACCO INDUSTRY SAID ABOUT NICOTINE AND WHEN

- “BAT should learn to look at itself as a drug company rather than as a tobacco company.” (British American Tobacco, 1980)

WHAT THE TOBACCO INDUSTRY KNEW ABOUT NICOTINE AND CIGARETTE DESIGN IN 1959

- “Cigarette smoke is comprised largely of particles approximately 1.0 micron in diameter, a size that is near the optimum for retention in the lungs.”
- “The particle size of about 1.0 micron is undesirable in that the retention of tar particles is high, but desirable in that there is maximum retention of physiologically active components.”
- “Moreover, one must preserve the physiological response. If the size of the smoke particles were to be changed, alternative means might be required to increase the alkaloid content in the smoke.” (Philip Morris, 1959)

KEY PROVISIONS OF THE TOBACCO CONTROL ACT RELATED TO PRODUCT STANDARDS

SECTION 907(a)(3) OF THE TOBACCO CONTROL ACT

"**A. In General.** The Secretary may adopt tobacco product standards…if the Secretary finds that a tobacco product standard is appropriate for the protection of the public health.

B. Determinations

i. Considerations. In making a finding described in subparagraph (A), the Secretary shall consider scientific evidence concerning

I. the risks and benefits to the population as a whole, including users and nonusers of tobacco products, of the proposed standard;

II. the increased or decreased likelihood that existing users of tobacco products will stop using such products; and

III. the increased or decreased likelihood that those who do not use tobacco products will start using such products."

SECTION 907(a)(4)

"**Content of Tobacco Product Standards.** A tobacco product standard established under this section for a tobacco product

A. shall include provisions that are appropriate for the protection of the public health, including provisions, where appropriate

i. for nicotine yields of the product"

SECTION 907(d)(3)

“Limitation on Power Granted to the Food and Drug Administration.

Because of the importance of a decision of the Secretary to issue a regulation…(B) requiring the reduction of nicotine yields of a tobacco product to zero, the Secretary is prohibited from taking such actions under this Act.”

“NOTICE AND COMMENT” RULEMAKING

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- Any product standard proposed by FDA can only go into effect following completion of “notice and comment” rulemaking; governed by the requirements of the Administrative Procedure Act
- Phases of a rulemaking:
  - Drafting and clearing a proposed rule
  - Publication of a proposed rule
  - Public comment period (typically 60 to 90 days)
  - Agency review of the comments; go/no go decision to move forward with a final rule
  - Drafting and clearing a final rule
  - Publication of a final rule with an “effective date”

“NOTICE AND COMMENT” RULEMAKING

- FDA bears the legal burden in putting any product standard forward
- It makes its evidentiary case in the “preamble” of any proposed or final rule
- The “preamble” is where the scientific evidence (e.g. nicotine addiction, modeling results, nicotine reduction studies) is laid out in support of the product standard
- At the final rule stage, the “preamble” is also where the Agency responds to substantive comments and explains what, if any, changes have been made to the proposed rule in light of the submitted comments

“FINAL AGENCY ACTION” AND POTENTIAL LITIGATION

“FINAL AGENCY ACTION” AND POTENTIAL LITIGATION

- Litigation challenging a rulemaking can only be brought after an agency has taken “final agency action”
  - A proposed rule is not final action, and litigation generally cannot be brought at this stage in the rulemaking process
- Publication of a final rule is considered “final agency action”
- Lawsuits against a final nicotine product standard would commence in federal district court
  - Would likely include a request for a “stay” of the effective date pending the outcome of the lawsuit
  - The losing party in district court could appeal to a circuit court
  - The Supreme Court could also, in its discretion, hear an appeal from a circuit court ruling
- Depending on how many rounds of litigation, add 1 to 3 years following publication of a final rule before it could go into effect, assuming a “stay” had been issued

THANK YOU!