Can a system like the U.S. OTC monographs work for ENDS?

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Disclosures

My employer, PinneyAssociates, provides consulting services on tobacco harm minimization (including nicotine replacement therapy and digital vapor products) to Niconovum USA, RJ Reynolds Vapor Company, and RAI Services Company, all subsidiaries of Reynolds American Inc. In the past three years, PinneyAssociates has consulted to GlaxoSmithKline Consumer Healthcare on smoking cessation and NJOY on electronic cigarettes. I also own an interest in intellectual property for a novel nicotine medication an option for which has been sold to Niconovum USA.

Through PA, I also provide consulting services on the regulation of a broad range of CNS acting drugs, particularly with respect to the dependence potential and regulatory control, as well as OTC drugs.

The US OTC Monograph System: A Brief History

- 1960s: Thousands of drugs available without prescription regulation, many with wild claims, few with significant scientific support, and many posing safety concerns
- There was substantial uncertainty and mistrust among the general public and health care professionals about many of these products
- Challenge: How to bring oversight without the potentially disruptive process of banning products and costly burden on manufacturers of then being required to submit pre-market applications for approval of all of these products

Purpose of the OTC Monograph System: Commissioner Charles C. Edwards, 1972

". . . to build a permanent system offering all American consumers the best possible assurance that every over-the-counter drug...

not only is safe and adequately labeled, but that it will do what the manufacturer claims it will do…"

OTC Monograph Process

For diverse uses (e.g., antacid/antiflatulents, cough, dandruff, dental/oral care, eye-redness, foot fungus, headache & minor pain, premature ejaculation, sleep aids), regulatory standards (an allowable "recipe book") were developed based on expert opinion of FDA staff and consultants as to allowable ingredients, dosages, indications, claims and labeling

Already marketed OTC and newly marketed products that which conformed to the monograph could be manufactured and sold without an individual product license

When is the process complete? FDA regulatory lawyer Peter Barton Hutt response to question by US Senator: "*Never*"

[it is an ongoing evolutionary process] (source: John Pinney)

OTC Monographs Today

- Monographs cover over 300,000 OTC products in more than 80 therapeutic classes involving more than 800 active ingredients
- New monographs are in development and existing monographs periodically revised. Sponsors can petition for revisions to address potential new ingredients and labeling
- New and revised monographs are published in the Federal Register, comments taken, and monographs finalized
- Once a monograph is implemented, companies can make and market conforming products without FDA pre-approval
- Products intended for OTC use, which do not conform to existing monographs must be reviewed by the New Drug Application process

Characteristics of OTC Products

Because OTC products are widely available and used without a learned intermediary, they must allow:

- Safe use of the product without a prescription
- Consumers to appropriately self-select and properly use following the label
- Low abuse potential (however, flexibility allows antihistamines, dextromethorphan, nicotine and other products that meet criteria as controlled substances)
- Benefits of use outweigh the risks – consistent with public health standard

OTC Drug Requirements

- The OTC Monograph Process successfully provides safety and efficacy standards and information on:
  - Ingredients
  - Doses
  - Formulations
  - Labeling
  - Testing
- Packaging requirements
  - Poison Prevention Packaging Act (PPPA) requires child-resistant packaging for certain OTCs
  - Tamper resistant packaging
- Advertising and promotion regulated by Federal Trade Commission (FTC)

Can the OTC Monograph process work for ENDS?

- ENDS are diverse in form and ingredients but many include nicotine and are used for smoking reduction and substitution and the category could be defined
- A monograph system would likely result in limitations that would ban some ingredients, and place limitations on others
- Some sponsors might submit ENDS (conforming or nonconforming to a monograph) through the NDA process to allow ingredients, doses, and/or claims beyond those covered by the monograph

The Monograph Process Could Provide Standards for Safety

- The review process can help standardize labeling that is reflective of the actual content of the e-liquid
  - Limits on hazardous chemicals at room temperature and upon heating
  - Standards for the metallic components
  - Safety and durability standards for batteries.
- Required testing for chemicals that could come from heating of the metals and liquids in ENDS
- Child-resistant packaging (Poison Prevention Packaging Act)
- Tamper resistant designs e.g., to reduce ease of using for delivery of substances of abuse

Plausible Conditions in an ENDS Monograph or Guidance

- Label will include nicotine dosing potential and instructions for use. Precedents include asthma inhalers, antacids, and nicotine gum
- Different labeling and possibly different warnings for closed vs. open systems
- Upper limits standards on nicotine and toxicants
- Flavor regulation
  - Flavor variations, flavor names
  - Standard limits on likely highly toxic flavors, e.g., benzaldehyde, cinnamaldehyde, vanillin
- Standards for all ENDS components, e.g. batteries, e-liquids, and packaging

Condensed Proposed Review of ENDS by an OTC Monograph Based Process

Phase 1: Review Efficacy and Safety Data

Advisory Panel reviews safety data and recommends labelling and safety standards for ENDS & related products	Review comments submitted to docket on deeming regulation

Phase II: Publish a Tentative Monograph

Proposed dosing, labeling, toxicity limits, flavor regulation, etc.	Review additional product data

Publish a Final Monograph or Guidance

Define dose, labeling, open vs. closed system, etc. for ENDS	All other products will be removed from the market