



PRINCIPLES TO GUIDE FDA PREMARKET REVIEW OF E-CIGARETTES AND OTHER DEEMED PRODUCTS

American Academy of Pediatrics,
American Cancer Society Cancer Action Network,
American Heart Association, American Lung Association,
Campaign for Tobacco-Free Kids and Truth Initiative

Enforcement

Consistent with the Remedial Order of the U.S. District Court for the District of Maryland in *AAP v. FDA*, FDA should aggressively bring enforcement actions against: (1) products on the market as of the effective date of the Deeming Rule, which remain on the market after the court-ordered deadline for premarket applications (September 9, 2020) without having submitted complete applications for marketing orders; (2) products that entered the market after the effective date of the Deeming Rule without marketing orders; and (3) products for which marketing orders are denied but remain on the market.

FDA should provide sufficient education, training and resources to manufacturers, distributors, and retailers to promptly stop the sale of products that are illegally on the market after the September 9, 2020 deadline.

Transparency

1. FDA should act promptly, after the application deadline set by the U.S. District Court of the District of Maryland (September 9, 2020) to make public sufficient information about the premarket review process to allow the public to assess industry compliance with, and FDA enforcement of, that deadline, including a list of all products (and their manufacturers):
 - a. for which complete Premarket Tobacco Product applications (PMTAs), Substantial Equivalence (SE) reports and requests for SE exemption were filed on or before September 9, 2020;
 - b. for which premarket orders (including SE orders and SE exemption requests) were denied and “no marketing” orders issued, updated on a monthly basis;
 - c. for which FDA issued “refused to accept” determinations (monthly);
 - d. for which FDA issued “refused to file” determinations (monthly);
 - e. for which applications have been withdrawn (monthly);
 - f. for which FDA has taken any negative action (monthly);
 - g. that FDA exempts from the premarket application requirement for “good cause,” as provided for in the Remedial Order of the U.S. District Court for the District of

Maryland, updated on a monthly basis, with a statement of the basis for FDA’s finding of “good cause”;

- h. a list of all deemed products on the market as of the September 9, 2020 deadline, which are new tobacco products requiring premarket authorization and, if such a list does not exist, an explanation of why such a list has not been compiled by FDA.
2. FDA should disclose to the public each premarket application (allowing trade secrets and confidential commercial information to be redacted), including all studies and data relied on by the applicant company in support of the application, to allow the public to assess the sufficiency of the evidence to meet the relevant statutory standards and, without delaying the process of FDA review, to enable the public to provide input to the agency on the sufficiency of the evidence. Disclosure of such information to the public should be comparable to that made by FDA for Modified Risk Tobacco Product applications, particularly since the products for which applications will be filed are already on the market.
3. For PMTA orders that are issued, FDA should disclose all information about the product sufficient to fully inform the public of the basis for FDA’s finding that the product meets the statutory standard of being “appropriate for the protection of the public health,” including information about the impact of the product on users and non-users of tobacco products and all studies and data relied on by FDA in making its determination.
4. For SE orders that are issued, FDA should disclose all information sufficient to fully inform the public of the basis for FDA’s finding that the product is substantially equivalent to a product on the market as of the grandfather date of February 15, 2007, including any agency determination that the product does not raise different questions of public health and all studies and data relied on by FDA in making its determination.
5. For Exemption from SE orders that are issued, FDA should disclose all information sufficient to fully inform the public of the basis for FDA’s finding that an SE report is not necessary to ensure that permitting the product to be marketed would be appropriate for protection of the public health, including any agency determination that the additive modification is a minor modification to a legally marketed tobacco product as well as all studies and data relied on by FDA in making its determination.

Process

1. The Remedial Order entered by the U.S. District Court for the District of Maryland provides that deemed products for which applications have been filed by September 9, 2020 may remain on the market without being subject to FDA enforcement actions for a period not to exceed one year from the date of application while FDA considers the application. However, even prior to expiration of the one-year review period, FDA should refuse to file, or should rapidly and summarily deny, any application which, upon FDA’s initial review, does not include competent scientific studies necessary to determine whether the product appeals to, or has been used by, youth and that examines

the use of the product by tobacco users in order to determine whether the product meets the applicable statutory standard for a marketing order.

2. If FDA permits an amendment to a PMTA, or a SE report, or Exemption from SE request, the filing of the amendment should not restart the one-year review period.
3. FDA should refer PMTA applications to the Tobacco Products Scientific Advisory Committee (TPSAC) if they raise scientific issues distinct from those previously addressed. The committee should also be consulted on issues common to multiple applications. TPSAC's expertise is likely to be of assistance to FDA in determining whether applicants have met the relevant statutory standard. However, referral of an application to TPSAC should not function to extend the one-year period for FDA review.
4. No product shall remain on the market for an application filed after the court-ordered application deadline, absent a showing of good cause on a case-by-case basis, as provided for in the Remedial Order.
5. Under no circumstances should any product without a marketing order be permitted to remain on the market after the expiration of the one-year FDA review period (September 8, 2021), absent a showing of good cause on a case-by-case basis, as provided for in the Remedial Order.

Application of the Public Health Standard

Given that the vast majority of tobacco products that will undergo premarket review beginning on September 9, 2020 have already been on the market with observable consequences for public health, based on the scientific evidence currently available:

1. No flavored tobacco product, including e-cigarettes or e-liquids, should be authorized for sale, including mint and menthol flavors, (other than tobacco-flavored products) because no flavored product can be shown to be "appropriate for the protection of the public health." This conclusion is supported by:
 - a. The current epidemic of e-cigarette use among youth and young adults and the clear evidence that this epidemic is driven largely by the appeal to youth of flavored products;
 - b. The data show that young people who use flavored electronic cigarettes are more at risk for smoking cigarette progression;
 - c. The growing scientific evidence that certain substances in e-cigarettes and e-liquids producing characterizing flavors are hazardous when inhaled;
 - d. The finding of the Surgeon General's Report on Smoking Cessation that there is presently inadequate evidence to conclude that e-cigarettes, in general, enable smoking cessation; and
 - e. The absence of evidence that flavors in e-cigarettes enable smoking cessation.
2. FDA's premarket review of these new tobacco products should require, as prerequisites for authorization, all of the following:

- a. The submission by applicant companies of direct evidence of how American youth (up to age 21) and nicotine-naïve American adults perceive the specific product with its specific components, including its labeling, marketing and advertising, as well as data on use of the specific product by American youth and nicotine-naïve American adults, sufficient to establish that availability of the product will not lead youth and nicotine-naïve adults to initiate, or continue, use of the product or other tobacco products. Among youth, patterns of use of tobacco products and responses to tobacco marketing are substantially different than that of adults. Therefore, it would be inappropriate to extrapolate adult data to youth. Data on youth must be derived from studies that include youth as subjects rather than relying on extrapolation of data from one population to another (from young adults to youth). This evidence must be developed from studies performed with sufficient safeguards imposed by FDA to minimize the risk that the study itself, or the resulting data, will be misused by the company to promote the product being studied or other tobacco products.
- b. The submission by applicant companies of evidence sufficient to establish that the product, as actually used by consumers, poses less risk to the population and to existing tobacco users than other tobacco products and would confer a substantial public health benefit. At a minimum, applicant companies must submit evidence sufficient to establish that (1) the product will predominantly be used by smokers who otherwise would continue to smoke; (2) that it does not deter or lead to a significant decrease in the number of users who would otherwise have quit using tobacco products altogether from doing so; (3) a significant majority of those who use the product switch completely to the applicant’s product and have stopped the use of other tobacco products altogether; and (4) the product is significantly less harmful than using other tobacco products.
- c. Given the wide variability in nicotine delivery and other characteristics of e-cigarettes, data from products other than from the applicant company’s product are not sufficient to establish that a significant number of smokers who otherwise would continue to smoke have switched completely to the applicant’s e-cigarette product or have stopped the use of tobacco products altogether.
- d. FDA’s premarket review should require the submission of data by applicant companies that the rate and magnitude of nicotine delivery to the user of an e-cigarette product is “appropriate for the protection of the public health” and would not increase the risk of abuse among youth. This evaluation must take into account not only nicotine concentration, but also chemical and other product characteristics—such as electrical properties and the use of nicotine salts—that can increase nicotine delivery. As nicotine absorption increases, evidence suggests products become more highly addictive and pose increased abuse liability, especially for youth. Indeed, products with high levels of nicotine are largely responsible for generating an epidemic of use of e-cigarettes among children. Companies should bear the burden to show that the nicotine delivery of a product will not pose abuse liability for youth and nicotine naïve individuals,

and this evidentiary burden should increase commensurate with the nicotine absorption in the product.

- e. Given the disproportionate burden of tobacco use on certain populations, and the history of the industry's role in targeting such populations, FDA's premarket review should require the submission of data sufficient to allow an assessment of the public health impact of the applicant company's product on those populations, including lower-income and less educated populations, certain racial and ethnic groups, the LGBTQ community and persons with mental health conditions and/or substance use disorders. No new product should be authorized without consideration of the impact of authorization on health disparities and health equity and without restrictions that will address the impact of the product on the health of vulnerable populations and on health disparities.
3. It is necessary for FDA to set out the criteria specified in Section 2 above because, to date, the agency's application of the statutory standards for premarket review have authorized the introduction of products (1) without sufficient evidence of the perception of, or use by, the product by youth and nicotine naïve adults in the United States, facts critical to determining the impact of authorizing the marketing of the product on non-users; (2) without adequate evidence of the impact of the product as it will actually be used even though there may be substantial uncertainty about the degree to which use of the product is less hazardous than smoking or the likelihood that users will continue to use cigarettes while also using the product; and (3) without sufficient evidence that introduction of the product would lead substantial numbers of smokers, who otherwise would continue to smoke, to switch completely to the applicant's product or stop the use of tobacco products altogether and would not deter smokers who might otherwise have quit from doing so. The result has been to authorize the marketing of new tobacco products without first requiring the manufacturer to meet its burden of demonstrating that the marketing of the product is "appropriate for the protection of the public health" taking into account the criteria set forth in the statute.