

Using Investigational Tobacco Products

NIH-funded investigators who are designing a protocol involving administration of a tobacco product to humans should review the information below regarding the need for submitting their protocol to Food and Drug Administration (FDA) Center for Tobacco Products (CTP) for review.

Investigators are encouraged to work with tobacco product manufacturers to ensure availability of products to complete planned studies. FDA evaluates the specific uses of investigational tobacco products (ITPs) on a case-by-case basis according to potential human subject protection concerns or other impacts on public health. Generally, submission of protocols by industry and academic researchers for FDA review is a voluntary process; however, FDA will review all protocols submitted. FDA recommends submission of proposed use of ITPs to FDA for review only if the study design is more likely to raise concerns about human subject protection, public health, or both. As discussed by FDA in its February 2019 guidance, [Use of Investigational Tobacco Products](#), factors to consider would be studies that plan to enroll vulnerable populations, particularly those < 21 years old, studies that involve significant increases over the participants' usual exposure to nicotine, studies that modify the tobacco product in a manner different from that described by the manufacturer or study of a novel product for which there is limited experience and knowledge.

For all clinical studies involving use of ITPs, we recommend that you notify FDA, all participating clinical investigators, and any committee or group formally designated to oversee the study of any serious or unexpected adverse experience associated with the tobacco product you are investigating within a few weeks after initial notification, and that you supply FDA with a completed case report form for the adverse experience. We encourage the reporting of adverse experiences associated with a clinical investigation of an investigational tobacco product to FDA through the FDACTP [Safety Reporting Portal](#) for Researchers.

FDA is committed to furthering scientific research on tobacco products and has a major investment in regulatory science. If you plan to study tobacco products that do not have marketing authorization or that do not comply with an applicable tobacco product standard, you may submit your proposed protocol to FDA for review based on the criteria described above. FDA will review any protocols submitted and intends to evaluate specific uses of investigational tobacco products on a case-by-case basis according to potential human subject protection concerns or other impacts on public health. Generally, FDA does not recommend that investigators correspond with us about the use of investigational tobacco products in nonclinical studies as these are not ordinarily reviewed. You may refer to the draft guidance, *Use of Investigational Tobacco Products*, for more information regarding how to submit your proposed use of an investigational tobacco product and how FDA intends to make enforcement decisions regarding the use of investigational tobacco products.

FDA understands that investigators may choose to obtain tobacco products directly from a tobacco product manufacturer with the sole intent to use the products for research investigations without commercializing the products. In such cases, FDA recommends that investigators add language to all

product labels to indicate that these products are limited to investigational use, that study participants be instructed that the products may not be further distributed, and that study protocols include a plan to collect and account for all investigational tobacco products after the study has concluded.

If there are additional questions, investigators should reach out to the FDA CTP at: CTP-OS-ITP@fda.hhs.gov.

The email should:

- Clearly and uniquely identify the product(s) you wish to study by brand and sub-brand— including the type or category of tobacco product (e.g., cigarette, smokeless tobacco, cigar, electronic nicotine delivery systems [ENDS], waterpipe tobacco) and subcategory (e.g., closed or open e-cigarette, closed or open e-liquid).
- Provide additional available information such as packaging type, package quantity, and/or characterizing flavor that may help answer the specific question(s)

Once the FDA CTP receives the email, they will make every effort to respond via email within 2 weeks.

Note that the FDA CTP intends to respond to investigators within 60 days of receipt of protocols for review. Investigators should receive acknowledgement of the submission with the name and contact information for the assigned Regulatory Health Project Manager (RHPM). If investigators do not receive a response within 60 days, they should contact the RHPM. Investigators may also contact their NIH Program Officer to discuss additional steps/actions.

If the marketed products will be used with investigator-manipulated modification(s), then the investigator should submit an ITP request. In addition to the protocol and other information described in the FDA Draft Guidance, the ITP request should also include:

- A description of the planned modification(s).
- A rationale for how these modification(s) support the study design and do not increase risk to human participants.