Comment on

Use of Investigational Tobacco Products: Guidance for Industry and Investigators
Docket No. FDA-2014-D-1939

UCSF TCORS[1]

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FDA's draft guidance exempting tobacco products intended for investigational use from premarket submission requirements supports public health research, protects the health of human subjects, and ensures that investigational tobacco products are not commercialized

We support FDA's understanding that academic and public health researchers, in their efforts to protect the public health, need to conduct studies involving new tobacco products (some of which may not have marketing authorization or do not comply with an applicable tobacco product standard) and investigational tobacco products (ITPs).

Academic and public health researchers who demonstrate: (1) appropriate controls on how and to whom the ITPs are distributed; (2) appropriate procedures for protecting human subjects; (3) appropriate study designs that ensure the quality and integrity of the study data; and (4) appropriate procedures that ensure ITPs are not commercialized should be exempted from premarket submission requirements and permitted to use ITPs in their public health research. It is important to note that research conducted by academic and public health researchers for the purpose of testing tobacco products for their safety and efficacy (in the case of products regulated by CDER) or their risks and public health impact (in the case of products regulated by CTP) is not intended to commercialize new products.

In contrast, research conducted by commercial and industry researchers (and their contractors) may be intended to commercialize new tobacco products, so FDA should carefully scrutinize ITPs used in this research as outlined in the proposed guidance.

The proposed guidance correctly distinguishes between new tobacco products that are legally marketed (those that have obtained premarket authorization, substantial equivalence order, provisional status, or are grandfathered), and those that are not legally marketed or do not comply with a tobacco product standard and are "investigational tobacco products."

Academic and public health researchers should not be hampered in conducting research on products that are currently available in the marketplace and legally marketed.

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FDA should provide an easily accessible (online and in print) list of all legally marketed tobacco products and their marketing order numbers (e.g., STN-SE/EX/PM######), provisional status numbers (STN-SE######), or grandfathered status numbers (GF######) so that academic and public health researchers can comply with FDA's Proposed Use of an ITP application procedures.

Additionally, academic and public health researchers should be unhampered in conducting research on components, ingredients, and additives that are available in the marketplace and legally marketed, even if they are sold separately from other ITPs. For example, a water pipe consists of a device (the pipe), a heater (charcoal or electric), and some water pipe tobacco (dried fruit with or without tobacco). Electronic cigarettes (in particular, electronic cigarettes that are not prepackaged and marketed like cigarettes, commonly known as "cigalikes") consist of a complex device with several components including heating devices, coils, batteries, and a liquid composed of several chemicals of variable composition and strength. The liquid and the device can be sold separately, permitting a great number of permutations of electronic cigarettes currently used. Academic and public health researchers need to study water pipe and electronic cigarette use as they are currently used by the public, which often requires interchanging various components (all of which are marketed to the public, either together with or separately from the primary product being investigated). FDA's guidance should explicitly permit researchers to conduct research using interchangeable components of ITPs, so long as all the components that are being studied are legally marketed.

If academic and public health researchers wish to conduct research on ITPs that (by definition) are not *legally* marketed, but are available in the marketplace to consumers and researchers alike, these researchers would not have access to the detailed and possibly proprietary information (including descriptions of design features, performance specifications, product chemistry, methods of manufacture, and other product information requested on pages 8-9 of the proposed guidance) required by FDA. In such cases, the researchers should be permitted to use these products for investigational purposes, and FDA should waive the requirement to submit information to which these researchers could not possibly have or legally gain access. FDA apparently recognizes this problem, and appropriately states on page 8 of its proposed guidance that researchers may, where applicable, submit "an explanation of why such information is unavailable".

The Draft Guidance document states on page 6, lines 189-191, that "nonclinical laboratory studies should be conducted in laboratories accredited by a nationally or internationally recognized external accreditation organization." It would be helpful to clarify the requirements for individual research laboratories within universities, because the laboratories themselves are not accredited, but the universities presumably are. We suggest rewording the quoted sentence above with: "nonclinical laboratory studies should be conducted in laboratories accredited by a nationally or internationally recognized external accreditation organization, or in academic laboratories within institutions that are similarly accredited."

On page 6, lines 194-197, the document states that "FDA encourages sponsors to meet with CTP early in the development process to discuss what, if any, animal testing is appropriate and the suitability and acceptability of non-animal tests for their particular tobacco product." We suggest that the standard sections of NIH grant applications should fulfill this condition, and that this be stated in the guidance.

On page 12, under Additional Recommendations Regarding Human Subject Protection, it would increase ease and clarity to simply require that copies of approved IRB applications, modification forms, adverse event forms and termination of study forms be submitted to the FDA.

FDA recommends on page 16 that "persons who intend to study investigational tobacco products meet with FDA to discuss research plans." We hope that a phone call will be sufficient and suggest that this be clarified here.

In summary, we believe the draft guidance on the use of investigational tobacco products appropriately allows researchers to use tobacco products and components of tobacco products that are legally marketed and widely available to consumers and researchers alike, and appropriately provides exemptions from premarket submission requirements for ITPs that are not legally marketed. FDA should be vigilant when considering the use of ITPs by commercial and industry researchers, since this research (in contrast to academic and public health research) may be aimed at commercializing new tobacco products. In either case, ensuring the protection of human subjects and that appropriate procedures and protocols are followed must be FDA's paramount concern.