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Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2012-N-0212

Ladies and Gentlemen:

The Campaign for Tobacco-Free Kids presents the following comments in the above-designated docket.

The issues addressed in this docket have important regulatory ramifications. Section 904(a) of the Food, Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act ("the Act") requires all tobacco manufacturers and importers of tobacco products to provide FDA with "a list of all constituents, including smoke constituents, as applicable, identified by the Secretary as harmful or potentially harmful to health in each tobacco product. . .by brand and quantity." Such information is to be reported from testing done pursuant to requirements established by FDA under Section 915 of the Act. Pursuant to section 904(d), FDA has established a list of 93 harmful and potentially harmful constituents in tobacco products and tobacco smoke. Section 904(e) of the Act requires FDA to establish a list of such constituents by brand and quantity and Section 904(d) of the Act requires the Secretary to publish the list "in a format that is understandable and not misleading to a lay person." The establishment of a set of procedures required for the testing of such constituents is a basic foundation for the development of any such list.

The development of a required methodology for testing tobacco products to determine the quantity of harmful constituents is also important for the development of product standards pursuant to section 907 of the Act. That section permits FDA to issue product standards for tobacco products that may include provisions "for nicotine yields of the product; for the reduction or elimination of other constituents, including smoke constituents, or harmful

components of the product,. . .[and] provisions for the testing. . .of the tobacco product." 21 USC § 907(a)(4). A product standard that established a ceiling for one or more constituents would imply the existence of a testing methodology sufficiently accurate to determine if the standard had been met. Thus, the establishment of appropriate procedures for the testing of tobacco products is an important part of FDA's regulatory responsibilities.

I. Testing of TSNAs

A significant portion of the workshop was devoted to testing procedures for the measurement of tobacco-specific nitrosamines. Several TSNAs occur in tobacco and are carcinogens listed as harmful or potentially harmful constituents by FDA. The most important of these TSNAs are NNN and NNK. TSNAs develop in unburnt tobacco subsequent to harvest. The curing process used affects the level of TSNAs in such tobacco. The large majority of TSNAs in tobacco smoke is derived directly from the existence of those substances in the unburnt tobacco and is not a product of combustion. Reliance on testing for TSNAs in unburnt tobacco rather than in smoke eliminates any potential inconsistencies due to differences in the smoking regime used for the measurement of smoke constituents.

Professor Stephen S. Hecht of the University of Minnesota presented a detailed history tracing the evolution of analytical methods for TSNAs. Furthermore, Professor Hecht has summarized his conclusions in a written submission to FDA in this docket. Among those conclusions are the following: "validated, standardized, state-of-the-art methods for the analysis of tobacco-specific nitrosamines in tobacco products now exist and these methods can be applied in a regulatory environment. There is no need for further development or testing of such methods." A large number of distinguished scientists with backgrounds in the measurement of analytes have endorsed Professor Hecht's conclusions in a submission in this docket. The Campaign for Tobacco-Free Kids also endorses Professor's Hecht's conclusions.

Test results among different laboratories are sufficiently consistent to provide assurance of accurate measurement for regulatory purposes. Any product standard for TSNAs would likely require reductions by orders of magnitude, a level far in excess of any difference in measurement that might be experienced as a result of inter-laboratory differences.

II. Testing other harmful constituents in unburnt tobacco.

Reliable and repeatable measurement of analytes in unburned tobacco smoke is both feasible and desirable for analytes other than TSNAs. Such testing would eliminate any variables inherent in testing smoke constituents. As no machine testing method accurately approximates the way consumers actually smoke cigarettes, a method that measures analytes in unburned tobacco has much to recommend it. Although there might be differences in the yield of such analytes to smokers based on individual smoking topography or product design, establishment of a baseline level of such analytes in unburnt tobacco would provide highly

relevant information for the regulatory process. For most such analytes it should be possible to establish the maximum percentage of such analytes in unburnt tobacco that are passed through to the smoke. Using such percentages, it would be possible to use test results for analytes in unburnt tobacco as a basis for product analysis and regulation, including the establishment of product standards for such analytes. Analytes for which such a procedure would be appropriate include not only TSNAs, but also nicotine, heavy metals, and pesticides.

III. Measurement of Representative Analytes as an Alternative to Measuring All Analytes.

There was discussion at the workshop about whether separate measurement of each of the 93 HPHCs was necessary or whether analysis of a selected group of analytes could provide sufficient assurance about the content of other analytes to preclude the need for separate measurement of each. Most of the discussion centered on the sixteen polycyclic aromatic hydrocarbons ("PAHs") on the list of HPHCs. Several participants in the discussion suggested that analysis of Benzo[a]pyrene could serve as a surrogate for measurement of other PAHs. We believe that it would be inappropriate to adopt such a policy in the absence of a clear demonstration that measurement of one or more representative compounds in fact, on a consistent and reliable basis, produces sufficient information about the levels of other compounds to preclude the need for separate testing. Such a demonstration would require persuasive experimental evidence that variances in the level of a measured analyte reliably and consistently reflected similar variances in the levels of other analytes.

IV. Evaluation of the Significance of Variance in Measurement.

The Tobacco Control Act gave FDA authority to establish product standards for the protection of the public health. Measurement of analytes is a relevant consideration in evaluating the appropriateness of such standards. Tobacco product manufacturers have suggested that the existence of variances in measurement results may provide an argument against the establishment of such standards. For example, if the analytical method for a given constituent had a relative standard deviation of 40% and measurement showed a median level of 1 mg per gram of tobacco, the variation in measurement could range from 0.6 mg per gram to 1.4 mg per gram. If the agency were considering a product standard that reduced the allowable maximum level of the constituent to a point within the range of variation, such variations might have some significance. However, if the proposed product standard reduced the maximum permissible level for such constituent by a far greater amount, for example, from 1 mg per gram to 0.1 mg per gram, then the proposed standard would still result in a sharp reduction in the level of such constituent, regardless of such variation. The fact that some variation in measurement is inevitable is not an argument against the promulgation of a product standard. Regulatory action need not await the development of methodologies that can sharply reduce current levels of variation. The methods developed to date provide a sufficient foundation for effective regulation.

V. Cost as a Consideration in Testing.

Several participants in the workshop mentioned the cost of testing as an important element in determining the level of testing FDA should require. We believe it would be inappropriate for FDA to permit cost concerns to determine the level of testing required by tobacco product manufacturers. Tobacco product manufacturers have argued that existing methods of measurement are insufficiently reliable to constitute a basis for regulatory policy. At the same time they have refused to devote sufficient resources to improving such measurement. In fact, the level of HPHCs in tobacco products has never been the primary concern of the major tobacco companies and the development of sophisticated testing methodologies for such constituents has never been a priority. The major tobacco companies in the United States had combined net operating income of $ 11.4 billion in 2012. Therefore, there is little doubt that the industry has sufficient, readily available resources for doing accurate testing. However, so long as it remains in the interest of tobacco product manufacturers to claim that measurement techniques are insufficiently sensitive to provide a basis for regulation, they will not devote the necessary resources to improvement of such techniques.

The extensive discussion at the workshop demonstrated that methodologies for reliable and repeatable measurement of the most important analytes do exist and are sufficiently sensitive to provide a basis for product regulation. If such methods can be refined by the allocation of greater resources to testing and measurement, tobacco product manufacturers have ample resources at their disposal to accomplish this objective. They should not be permitted, however, to devote insufficient resources to testing and measurement of HPHCs and argue at the same time that the testing methods that have emerged as a result are insufficiently sensitive to provide a foundation for regulation of their products.