June 4, 2012

COMMENTS ON GUIDANCE REGARDING TESTING FOR HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS Docket ID: FDA-2012-D-0049

The undersigned organizations submit these comments in the above-designated docket regarding the Guidance for Industry on Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act.

Section 904(a)(3) of the Family Smoking Prevention and Tobacco Control Act of 2009 ("Tobacco Control Act" or "the Act") requires all tobacco product manufacturers and importers to submit to the Secretary, within three years after the date of enactment (i.e., by June 22, 2012), " a listing of all constituents, including smoke constituents as applicable, identified by the Secretary as harmful or potentially harmful to health in each tobacco product, and as applicable in the smoke of each tobacco product, by brand and by quantity in each brand and sub-brand. Section 904(e) of the Act requires FDA to establish and periodically revise as appropriate "a list of harmful and potentially harmful constituents, including smoke constituents, to health in each tobacco product by brand and by quantity in each brand and sub-brand." The reports made by tobacco product manufacturers and importers under Section 904(a)(3) were intended to provide the data for the listing under Section 904(e).

After receiving advice from the Tobacco Products Scientific Advisory Committee ("TPSAC") (which had itself convened a subcommittee of scientific experts), FDA began the process by publishing for comment a list of 96 harmful and potentially harmful constituents. The guidance made clear that the term included not only constituents that are toxicants, carcinogens, or addictive substances, but also constituents that "[1] potentially facilitate initiation of the use of tobacco products; [2] potentially impeded…cessation of the use of tobacco products; or [3] potentially increase…the intensity of tobacco product use [e.g., frequency of use, amount consumed, depth of inhalation]." The definition also states that it includes "a constituent that may enhance the harmful effects of a tobacco product constituent."

The FDA's notice made it clear that the list of constituents contained in the notice is not exhaustive and specifies three additional categories of constituents that may be added in the future. Subsequently, on April 3, 2012, FDA published a revised list of 93 harmful and potentially harmful constituents. The broad definition in the Guidance as to the constituents that fall within the definition of "harmful and potentially harmful" is consistent with the statute and should be reaffirmed even though the specific list of 93 constituents focuses much more narrowly.

The notice in this docket provides that, for purposes of their submission under Section 904(a)(3) manufacturers need to submit, by June 22, 2012, test data on only 20 of the 93 substances on the most recent list. The notice defers the requirement for submission of data on the remaining 73 constituents (and any constituents added to the list in the future) until an unspecified future date. This will be the first time that tobacco product manufacturers or importers are required to report quantities of HPHCs, therefore, contract laboratories may not be prepared for the large volume of requests. In addition, some

contract laboratories may not yet be able to test for each of the constituents on the established list of HPHCs.

The undersigned organizations note that, at least with regard to the major tobacco U.S. cigarette manufacturers whose brands account for 85 percent of all cigarette sales, resources would not appear to be limited and we recommend that full information on all 93 substances from these companies should be required and a schedule be established for others to do so as well, so that they can prepare to comply.

We understand from the notice that FDA expects to require submission of all such data and that the only question is the schedule. We recommend that this process be completed with a minimum of delay.

Establishing that this guidance has no bearing on what information must be submitted in substantial equivalence, new tobacco product, or modified risk tobacco product applications.

The most serious short-term potential consequence of FDA's decision to require submission of testing information on only 20 HPHCs pursuant to Section 904 is the possible impact of such a decision on regulatory decisions of great importance, including action on 4,000 pending substantial equivalence applications, as well as New Product applications under Section 910 and Modified Risk Tobacco Product applications under Section 911. FDA's decision to defer the requirement for submission of testing information on HPHCs applies to Section 904(a)(3) and 904(e) only and FDA should state explicitly that it has no bearing whatsoever on what information must be submitted in applications pursuant to section 905(j), 910, or 911.

Substantial equivalence

A new product that is the subject of a report under Section 905(j) is "substantially equivalent" to a predicate product only if

It has the same characteristics as the predicate tobacco product or;

If it has different characteristics and the information submitted contains information (including clinical data if deemed necessary by the Secretary) that demonstrates that it is not appropriate to regulate the product [as a new product] because the new product does not raise different questions of public health.

Sec. 910(a)(3)(A)

The term "characteristics" is defined by the statute as "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."

Sec. 910(a)(3)(B)

In comments previously submitted to the FDA, the undersigned groups endorsed a framework for evaluating substantial equivalence applications. That framework incorporated, inter alia, the following principles:

1. In determining whether a new product has "the same characteristics as the predicate product," the "same characteristics" has a quantitative as well as a qualitative meaning."

2. Any physical aspect of the tobacco product that is intended to be consumed and any physical aspect of its combustion product is a "characteristic" and thus must be "the same" as in the predicate product.

3. Products containing greater quantities of substances of harmful or potentially harmful or potentially addictive substances than the predicate product "raise different questions of public health."

Under these principles, no product containing a higher level of *any* harmful or potentially harmful constituent than the predicate product could be designated as substantially equivalent to such predicate product. A manufacturer or importer seeking a substantial equivalence designation can only meet this standard if it has submitted the testing data required by Section 904(a)(3) with regard to *all* harmful or potentially harmful constituents and shown that the product for which the designation is sought contains no such constituents in any quantity higher than that contained in the predicate product. Accordingly, the submission of testing data on only the 20 substances designated in the guidance of the docket in question cannot possibly meet this standard.

The notice in this docket recognizes the distinction between the information required by this guidance and the information necessary to satisfy the requirements of sections 905, 910 or 911. It states,

> Depending on the nature of a new tobacco product or modified risk product, testing and reporting HPHCs on the list in Table 1 *may not be adequate* to meet the statutory standards for marketing authorization; quantities for additional HPHCs may be necessary. (emphasis added)

This statement is both inaccurate and misleading. Submission of information regarding the HPHCs on the list in Table 1 *cannot possibly* be adequate to meet the statutory standards for marketing authorization; quantities for additional HPHCs will *always* be necessary. It is inconceivable that FDA could designate a product as substantially equivalent to a predicate product without a demonstration that the product at issue contains *no* HPHC in a quantity greater than that in the predicate product. We strongly urge that the draft guidance be amended to make this point clear. Any suggestion that this standard could be compromised could only encourage misunderstanding of the statutory criteria.

New Product applications under Section 910

The Secretary is directed to deny any such application if, upon the basis of the information submitted, the Secretary finds that there is a lack of a showing that permitting such tobacco product to be marketed would be appropriate for the protection of the public health. An application that does not provide accurate test data on all 93 harmful and potentially harmful constituents that meet the statutory definition cannot possibly meet the New Product standard. Deferral of reporting of test data under Section 904 has no bearing on what data must be submitted to support a New Product application under Section 910. We strongly urge that the draft guidance be amended to make this point clear.

Modified Risk Tobacco Product applications under Section 911

Under Section 911, no person may introduce into commerce a modified risk tobacco product unless the Secretary "determines that the applicant has demonstrated that such product, as it is actually used by consumers, will (A) significantly reduce harm and the risk of tobacco related disease to individual tobacco users; and (B) benefit the health of the population as a whole taking into account both

users of tobacco products and persons who did not currently use tobacco products." Section 911(g)(1) states that no such showing could possibly be made without the submission of complete testing information with regard to every harmful and potentially harmful constituent that meets the statutory definition, including those not on the list contained in the guidance. We strongly urge that the draft guidance be amended to make this point clear.

Selection of constituents

Given FDA's decision to require submission of testing information on fewer than all constituents, the choice of particular constituents as a representative sample is not unreasonable. As noted above, however, we believe that at least the three major domestic manufacturers should be required to submit information on all 93 constituents by June 22, 2012.

Expansion of the List of Harmful and Potentially Harmful Constituents

When FDA circulated its proposed list of harmful and potentially harmful constituents, it explicitly noted that the list was incomplete and would be expanded in the future. In particular, the notice identified three categories of constituents that may be added in the future: those that may not have been adequately studied or systematically reviewed by relevant agencies, those that may contribute to disease outcomes other than the five specified in the notice, and those that may meet "additional criteria." In addition, in our October 11, 2011 comments on the prior notice, the undersigned organizations suggested the addition to the list of constituents that while not toxic, carcinogenic, or addictive themselves, may nevertheless contribute to the toxicity, carcinogenicity, or addictiveness of one or more tobacco products, such as pH modifiers and buffering substances.

We urge FDA to establish a schedule to include all these categories to the list and require submission of testing information concerning them at the earliest possible date. To the extent that FDA has concerns about the availability of testing facilities for smaller tobacco companies, we suggest that these concerns should not result in deferring the effectiveness of testing requirements for the major domestic cigarette manufacturers.

Deferral of the Reporting Date for Manufacturers that are not Small Manufacturers

As noted above, even if a deferral of the reporting requirements for some manufacturers was permitted, we oppose such a deferral for the three major domestic tobacco product manufacturers whose sales account for 85% of the cigarettes sold nationally.

Deferral for Small Manufacturers

Provisions granting a deferral of the statutory reporting date for small manufacturers should establish a schedule for all such manufacturers to eventually provide the required information for all harmful and potentially harmful constituents – any deferrals should be as limited in scope and duration as possible.

Inclusion of Additional Constituents on the List

The undersigned organizations have previously submitted comments on FDA's proposed list.[1] Those comments, inter alia, listed eight constituents that had been included in the list compiled by the TPSAC but were not on the FDA list and recommended their inclusion on FDA's list. Not only did FDA did not include those constituents on its list published on April 3, but FDA provided no reason why those constituents were not included. We once again urge inclusion of these constituents for the reasons provided in our previous comment. If FDA has concluded that inclusion of such constituents on the list is not warranted, we request an explanation.

Publication of Information

Section 904(d) requires the Secretary to publish the list compiled pursuant to Section 904(e) that will contain an enumeration and quantification of the harmful and potentially harmful constituents in each tobacco product, by brand and sub-brand. Section 904(d)(2) requires the Secretary to conduct "periodic consumer research to ensure that the list published under paragraph (1) is not misleading." In our previously submitted comments we urged FDA to begin to undertake this research before the list was published for the first time. Because the effects of publication of such information are potentially misleading, we believe it is very important for FDA to base any decisions regarding the method of publication on actual data regarding consumer understanding of such data.

The limitation of the scope of the initially reported information to 20 constituents increases the likelihood that publication of such information would be misleading. Since the list would provide no information on nearly 80% of the harmful or potentially harmful constituents already identified by TPSAC, its potential to mislead consumers would increase. Unless and until FDA has concluded that different levels of one or more of these constituents will alter the relative health risk of the tobacco products containing them and unless and until FDA has determined that this information can be communicated without misleading consumers as to the actual health impact of this information, FDA should proceed with caution. This consideration makes it more important for FDA to base its decision on how to publish the information on the results of tests designed to ascertain what conclusions consumers would draw from such information.

We note that FDA has submitted a revised request to OMB for an "Experimental Study on the Public Display of Lists of Harmful and Potentially Harmful Tobacco Constituents" and solicited public comment. The undersigned will provide comments in that docket.

Sincerely,

Campaign for Tobacco Free Kids
American Cancer Society – Cancer Action Network
American Heart Association
American Lung Association
Legacy
Tobacco Control Legal Consortium

[1] For ease of reference, a copy of the prior comment, listing these constituents and providing reasons for their inclusion on the list, is attached.