SUMMARY: TPSAC REPORT ON DISSOLVABLE TOBACCO PRODUCTS

Introduction and Statement of Charge
This document provides a summary of the report of the Tobacco Products Scientific Advisory Committee (TPSAC) on dissolvable tobacco products (DTP). Under Section 907(f) of the Family Smoking Prevention and Tobacco Control Act, the TPSAC was charged with developing a report on “...the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children.” (see Table 1) As detailed below, the TPSAC reviewed and discussed a wide array of materials, submissions, and presentations relevant to its charge. Those materials, along with the transcripts of the open portions of the TPSAC meetings, constitute the evidence evaluated by TPSAC in responding to its charge. This summary, together with the materials considered by TPSAC and the transcripts of its meetings, constitute its report.

<table>
<thead>
<tr>
<th>Table 1. Charges to the Tobacco Products Scientific Advisory Committee (TPSAC) under the Family Smoking Prevention and Tobacco Control Act</th>
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<tr>
<td><strong>Section 907(a)(3)(B) Tobacco Product Standards</strong></td>
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<td>TPSAC is to consider:</td>
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<td>“(I) the risks and benefits to the population as a whole, including users and nonusers of tobacco products, of the proposed standard;”</td>
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<td>“(II) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and”</td>
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<td>“(III) the increased or decreased likelihood that those who do not use tobacco products will start using such products.”</td>
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<tr>
<td><strong>Section 907(f) Dissolvable Tobacco Products</strong></td>
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<tr>
<td>TPSAC is required to review and provide recommendations to the FDA regarding the “the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children.”</td>
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Committee Approach
The committee completed the task of developing this report over the course of three meetings, July 21-22, 2011, January 18-20, 2012, and March 1-2, 2012. The initial meeting was largely for the purpose of information-gathering, as were the initial two days of the second. The TPSAC spent most of January 20, 2012 in open discussion of the full set of materials that it had received. In this discussion, the committee members: 1) evaluated the relevant papers from the peer-reviewed literature for key findings; 2) considered the findings of the scan of the industry documents and the main points of the tobacco industry presentations; 3) reviewed themes from the open public hearing and submissions to FDA; and 4) considered the presentations on the experience and perceptions of youth with regard to DTPs. Following this meeting a summary was prepared and reviewed by the TPSAC on March 1 and revised based on these discussions before approval on March 2, 2012.
Committee Framework
To guide its integration of the evidence, the TPSAC developed a conceptual framework describing the potential roles of DTPs in smoking experimentation and initiation, addiction and regular tobacco use, and risks to health (Figure 1). The TPSAC acknowledges that the framework necessarily oversimplifies the potential complexities of tobacco use, particularly if the array of nicotine-containing products continues to expand. The framework represents three potential patterns of tobacco-product use: cigarettes alone, DTPs alone, and mixed patterns involving multiple products, including DTPs. The numbers on the figure indicate those points at which the availability of DTPs could have impact. In this framework, the availability of DTPs might affect the likelihood of experimentation and initiation of tobacco product use (#1 in the figure) and also affect progression to addiction (#2); the model also reflects the possibility that DTPs would influence the maintenance of nicotine addiction and the likelihood of cessation (#3). Further, the framework acknowledges that risk for morbidity and premature mortality caused by use of tobacco products could be affected by use of DTPs (#4). In addressing its charge, TPSAC searched for evidence relevant to determining if the availability of DTPs might have any consequences at these points in the framework and to estimating the potential magnitude of any effects.

Figure 1. Conceptual Framework: From Experimentation to Disease

Hypothesized mechanisms by which dissolvable tobacco products could have impact on public health. The pathways include 1) increased experimentation and initiation of cigarette smoking as a consequence of access to an oral, nicotine-containing product; 2) experimental use leading to an established pattern of mixed use of tobacco products (e.g., dissolvable products, other smokeless products, and/or cigarettes); 3) decreased likelihood of smoking cessation, given a nicotine-delivering product that can be used where smoking is not permitted; and 4) differing risk profile for tobacco-caused diseases and premature mortality.
Key Findings from the Evidence Review

As described, the TPSAC reviewed a variety of sources of evidence on DTPs. The transcripts of the TPSAC discussions document the synthesis and summarization of the evidence by the TPSAC. A brief, tabular summary of the main findings of TPSAC’s review of the evidence follows, organized by the type of evidence:

**Peer-Reviewed Literature**

- Constituent yields: There is variation across products in yields of nicotine and tobacco-specific nitrosamines (TSNAs). Heavy metals are present, also in variable amounts. The yields of nicotine and TSNAs are lower than those of cigarettes.
- Abuse liability: Abuse liability should be lower for DTPs than for conventional cigarettes and for other SMTs now available in the United States.
- Health risk: Based on information on TSNAs, nicotine, and studies of cancer risk of SMTs, exclusive use of DPTs should be less hazardous than either cigarettes or SMTs now marketed in the United States.
- Consumer perception: One study showed that Ariva was perceived as being a non-tobacco product. This perception may extend to other DTPs.
- Consumer response: Consumers have not responded positively to current products.
- Childhood poisoning: Studies in the literature indicate that there have been few accidental ingestions with serious consequences to date.

**Industry Presentations and Documents**

- Product range: There are a variety of products with different nicotine and TSNA yields.
- Cigarette use: Users of DTPs smoke fewer cigarettes than nonusers.
- Marketing: DTPs are presently marketed as accessory products for smokers or other tobacco users to deal with craving in circumstances where social perceptions or bans make smoking difficult or impossible.
- Cessation: Presently, DTPs are not being positioned by the industry as useful for cessation.
- Youth: Presentations by industry indicate that DTPs are not directed at youth.

**Open Public Hearing and Public Submissions**

- Product perception: Based on the reports of individuals, TPSAC found evidence that DTPs were neither well liked nor being used by themselves for smoking cessation. Some commenters suggested that people may have a perception of the risks of DTPs that is exaggerated.
- Government actions: Concern was expressed by some that DTPs might be banned. Additionally, some recommended that government agencies should more pro-actively educate the public on the risks associated with various products without combining all tobacco products.
Review of Swedish Experience with Snus

- Context: The context of the Swedish experience with snus has unique characteristics (historic use of snus, marketing, voluntary product standard and exclusive use pattern) that limits generalizability for DTPs in the United States.
- Health benefits: For health benefits to be obtained, complete substitution of snus for cigarettes was needed.
- New users: At present, 50% of snus users are new tobacco users.
- Use by sex: Males tend to be exclusive snus users while females are more likely to use snus and continue to smoke.

Indiana Experience and Youth Presentations

- Youth use of DTPs: To date, there is little use of DTPs by youth, even though several products have been on the market for about 10 years. The Indiana experience during test marketing of DTPs suggested that some youth would try DTPs, particularly those already smoking cigarettes.
- Packaging: Appeal to youth is likely to depend on packaging. Newer packaging may have greater youth appeal.

Responses to Charge Issues

This element of the charge addresses the risks and benefits of DTPs. As noted, the TPSAC considerations of this question are based in counterfactual comparisons of a scenario of the United States, absent DTPs, to scenarios with DTPs available. In constructing comparison scenarios, the TPSAC was constrained by the limited “real world” experience to date—10 years with products from Star Scientific Inc. (Ariva and Stonewall) and test marketing of new products in several locations in the United States by several companies. Consequently, the TPSAC posed scenarios that would be most useful to addressing its charge. In particular, TPSAC gave weight to a scenario of widespread availability and marketing of DTPs, as representing a bounding case useful for addressing the charge. The current situation was judged as one in which DTPs are having no impact on the elements of the framework.

The risks and benefits to the population as a whole, including users and non-users of tobacco products;

TPSAC considered the burden of tobacco-related morbidity and premature mortality to be the appropriate indicator in addressing this element of its charge. That burden reflects the number of users of tobacco products, their patterns of use, and the risks of the products that they use, as set out in Figure 1. The TPSAC framework indicates several ways that DTPs could reduce the disease burden caused by tobacco use: decreasing the number of smokers, if availability of DTPs increases successful cessation, and decreasing the risk of tobacco caused disease, if availability of DTPs sufficiently reduces cigarette smoking or use of other types of SMT. The TPSAC members concurred that available evidence supports a conclusion that DTPs are likely to be associated with far lower disease risks than cigarettes.
The framework also shows how availability of DTPs could increase the disease burden, by either increasing the number of tobacco users or reducing cessation.

The TPSAC noted the great uncertainty concerning how availability of DTPs would impact the burden of tobacco-caused morbidity and premature mortality in the population. To date, experience is limited and observational evidence on how DTPs might affect use of tobacco products is lacking. After 10 years of availability, the products made by Star Scientific, Inc. have had extremely limited market penetration and no overall impact on disease burden. Furthermore, TPSAC concluded that the context set by industry marketing will be critical in determining the impact of DTPs. The committee was concerned that availability of DTPs with lower risks to health than cigarettes might affect the public perception of all tobacco products, leading to increased use because of reduced concern about health risks of tobacco products generally.

Given the substantial uncertainties and the potential for either risks or benefits, TPSAC could not reach a conclusion as to the potential point of balance between potential risks and benefits of DTPs.

_The increased or decreased likelihood that existing users of tobacco products will stop using such products;_

TPSAC concluded that DTPs are presently being positioned as a tobacco product that provides nicotine in circumstances where smoked products and specifically cigarettes cannot be used. Smokefree regulations and changing social norms have narrowed the range of venues where smoking is allowed and acceptable. Marketing strategies examined by TPSAC gave emphasis to use of DTPs in circumstances under which nicotine intake by smoking is not possible. Additionally, findings of several peer-reviewed papers, industry studies, and anecdotal reports from the public hearing speakers suggest that cigarette smokers do not find the current DTPs to be sufficient by themselves, as an alternative to cigarette smoking. Beyond some anecdotal reports, TPSAC found no information on whether DTPs would increase the likelihood of cessation of cigarette use or of SMTs.

In considering scenarios for addressing this element of its charge, TPSAC offers the reminder that context will be critical in determining use patterns for DTPs. Will current marketing approaches be continued, giving emphasis to use of DTPs when smoking is not possible or perceived unfavorably? Will DTPs be marketed as facilitating cessation? Will the nicotine yield be different from that of current products?

TPSAC concluded that the availability of DTPs could either increase the likelihood of cessation of use of tobacco products, if they proved to facilitate cessation, or decrease the likelihood of stopping if they served to maintain use of tobacco products and nicotine addiction by offering a product that can be used in circumstances where smoking is generally not possible. As noted, TPSAC could not reach any overall judgment as to whether the net consequence of DTPs would be an increase or decrease in the number of people who successfully quit smoking. This uncertainty provides a strong rationale for close surveillance of cessation and any impact of DTPs.
The increased or decreased likelihood that those who do not use tobacco products will start using such products.

For this component of the charge, the TPSAC concluded that the available evidence, while limited, leads to a qualitative judgment that availability of DTPs could increase the number of users of tobacco products. This judgment was based on experience with other SMTs, data presented from the State of Indiana showing that some adolescents were already using DTPs, the survey data on youth perceptions of the products from the State of Virginia, and the potential for youth to be drawn to a novel product. The TPSAC could find no basis for the contrary finding—that availability of DTPs would decrease tobacco use. With the very limited information available, however, the TPSAC could not estimate the magnitude of any potential increment in numbers of tobacco-product users because of sales of DTPs. Based on its finding, the TPSAC offers strong recommendations as to the need for informative surveillance related to DTPs and youth.

Recommendations for Further Information Gathering, Surveillance, and Research

Additional Product Testing
- Further characterization of within-product variation in yields of nicotine, TSNAs, and other health-relevant components.
- Characterization of variation in product composition at point-of-sale across the country.
- Characterization of change in product composition with time since manufacture, and heat and moisture exposure.
- For each product, doses of key components delivered to users should be assessed with an appropriate suite of biomarkers.
- For each product, detailed information is needed on topography in actual use.
- To facilitate accumulation of data on various DTPs, a standard product description is needed.

Surveillance
- Existing surveillance systems should be reviewed for their sensitivity to track patterns of DTP use and the various mixed use patterns, particularly among key sentinel populations, e.g., youth.
- Surveillance instruments will need to be developed for tracking DTP use.
- The impact of availability of DTPs on use of other tobacco products, particularly cigarettes, needs to be monitored closely.
- Research/surveillance will be needed to assess perceptions of DTPs and how availability of DTPs affects perception of other tobacco products.

Research
- Short-term bioassay systems are needed that may prove useful for assessing potential risks to health. Studies with biomarkers of response/injury might prove useful for this purpose.
- Developing useful population models for assessing consequences of DTP availability.