FOOD AND DRUG ADMINISTRATION  
Center for Tobacco Products (CTP)  
Tobacco Products Scientific Advisory Committee (TPSAC)  

Questions to the Committee  

April 16, 2014:  

1) What are your views on the differences, if any, between dependence and addiction? Have these changed over time? If so, what are the factors that influenced this change?  

2) How can current assessments of dependence/addiction be used for non-traditional products and/or nondaily users? How can current assessments be applied to individuals who use multiple products? Are new assessments necessary?  

3) On the topic of dependence/addiction, what review factors should be included in the evaluation of product submissions?  

April 17, 2014:  

1) Considering the examples of modeling approaches presented for assessing the effects of tobacco product on population health:  
   • What are merits and limitations to these approaches for assessing these effects prior to allowing a product to market?  
   • Are there other modeling approaches that may be appropriate for assessing these effects prior to allowing a product to market?  

2) Discuss the quality of data sources for parameter inputs for modeling.  
   • Specifically, do you have recommendations for the process of assessing the best sources of data used for inputs?  
   • Do you have recommendations for addressing gaps in the information used to needed as model input parameters?  
   • Are there particular inputs that you deem critical for modeling the effects of tobacco products on population health?  
   • Discuss the need for common terminology in defining key parameters, for example, initiation, cessation, smoking status (former or current smoker).  

3) Do you have recommendations regarding metrics that may be used to assess the effects of tobacco products on the population as a whole? For example:  
   • Morbidity and mortality (all-cause, cause-specific mortality).  
   • Quality-adjusted Life Years (QALYs), Disability-adjusted Life-years (DALYs).  

April 18, 2014:  

1) For MRTPAs seeking to market a product under Section 911(g)(1) of the FD&C Act, i.e., risk modification order:
• What concerns, if any, do you have about the use of certain types of studies, or data, to draw inferences about the potential impact of product use on health outcomes in individuals?

• What recommendations do you have for placing greater weight on certain types of data or studies, as they relate to the assessment of health outcomes in individuals?

Examples to consider:
• Epidemiological data in the tobacco product, but on populations outside of the US
• Epidemiological data for a class of tobacco products, but not on the individual tobacco product
• Clinical trials in adult smokers only, in the absence of long-term epidemiological data

2) For MRTPAs seeking to market a product under Section 911(g)(1) of the FD&C Act, i.e., exposure modification order:
• What concerns, if any, do you have about the use of certain types of studies, or data, to draw inferences about the potential impact of product use on exposures in individuals?
• What concerns, if any, do you have about the use of certain types of studies, or data, on exposures to individuals to infer potential health outcomes?
• What recommendations do you have for placing greater weight on certain types of data or studies, as they relate to the assessment of exposures to individuals?

Examples to consider:
• Epidemiological data on the impact from exposure(s) to certain constituents, but not on the use of a tobacco product
• Chemical analyses that demonstrate a substantial reduction in all harmful and potentially harmful constituents identified by FDA, in the absence of toxicological data on the product itself
• Toxicological analyses that indicate that a substance that has been removed from the product is harmful, in the absence of a well-characterized dose-response relationship for the substance

3) For all MRTPAs:
• What concerns, if any, do you have about the use of certain types of studies, or data, to draw inferences about the potential impact of the marketing of an MRTP on tobacco use behavior, such as product adoption, initiation, poly-tobacco use, or likelihood of cessation?
• What recommendations do you have for placing greater weight on certain types of data or studies, as they relate to the assessment of tobacco use behaviors?

Examples to consider:
• Perception studies on adult users that indicate that users have a high level of interest in trying the product, in the absence of information on non-users
• Actual use studies that demonstrate that the majority of established smokers use the product as directed and are likely to switch completely from smoking to the product after a certain period of use, in the absence of strong evidence that demonstrates comprehension of modified risk information
4) When making a determination to allow an MRTP to market, FDA will need to assess the impact on the population as a whole:
   - What recommendations do you have for placing greater weight on certain types of data or studies, as they relate to the either the assessment of health outcomes or tobacco use behaviors, when considering the impact on the population as a whole?
   - Examples to consider:
     - Conclusive data that risks of using the product are significantly lower than risk of smoking, but only suggestive data that young adults are not likely to initiate tobacco use with the product
     - Conclusive data that risks that marketing of the product as an MRTP will not have deleterious impacts on the likelihoods of initiation or cessation, but suggestive data that the reduction in exposures to smokers that switch to the product may reduce the risks of tobacco-related disease

5) An evaluation of an MRTPA will require reliance on indirect evidence on various impacts on exposure, health, and tobacco use behavior. In addition, the data in an MRTPA may not provide direct evidence of the long-term impacts of an MRTP.
   - What recommendations do you have for strategies that industry or FDA could undertake to address any areas of concern after an MRTP has been allowed to market to the US population?