PMP S.A. MODIFIED RISK TOBACCO PRODUCT APPLICATIONS

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OUTLINE

- Statutory framework for modified risk tobacco products and review process
- Summary of PMP S.A. applications under review
- Questions for the committee

MRTP STATUTORY FRAMEWORK AND REVIEW PROCESS

MODIFIED RISK TOBACCO PRODUCTS (MRTPS) DEFINED

- Tobacco products sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products; this includes tobacco products whose
  - Label, labeling or advertising represents, implicitly or explicitly, that:
    - The product is less harmful or presents a lower risk of tobacco-related disease than one or more commercially marketed tobacco products
    - The product or its smoke contains a reduced level of, presents a reduced exposure to, or does not contain/is free of a substance

MRTP CONTEXT

- Before an MRTP can be marketed in the United States, an order from FDA under section 911(g) of the FD&C Act must be in effect with respect to the tobacco product.

- To legally sell an MRTP that is also a new tobacco product, a company must have authorization from FDA under both section 911 (i.e., an MRTP order) and section 910 (SE order, PMTA order, and/or exemption from substantial equivalence).

  – PMP S.A. has stated it has submitted a premarket tobacco product application for the *IQOS* system and *HeatSticks*.

THE STANDARD FOR RISK MODIFICATION ORDER - 911(G)(1)

The FD&C Act requires FDA to determine if a proposed MRTP, as it is actually used by consumers, will:

(1) significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and

(2) benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products

THE STANDARD FOR EXPOSURE MODIFICATION ORDER - 911(G)(2)

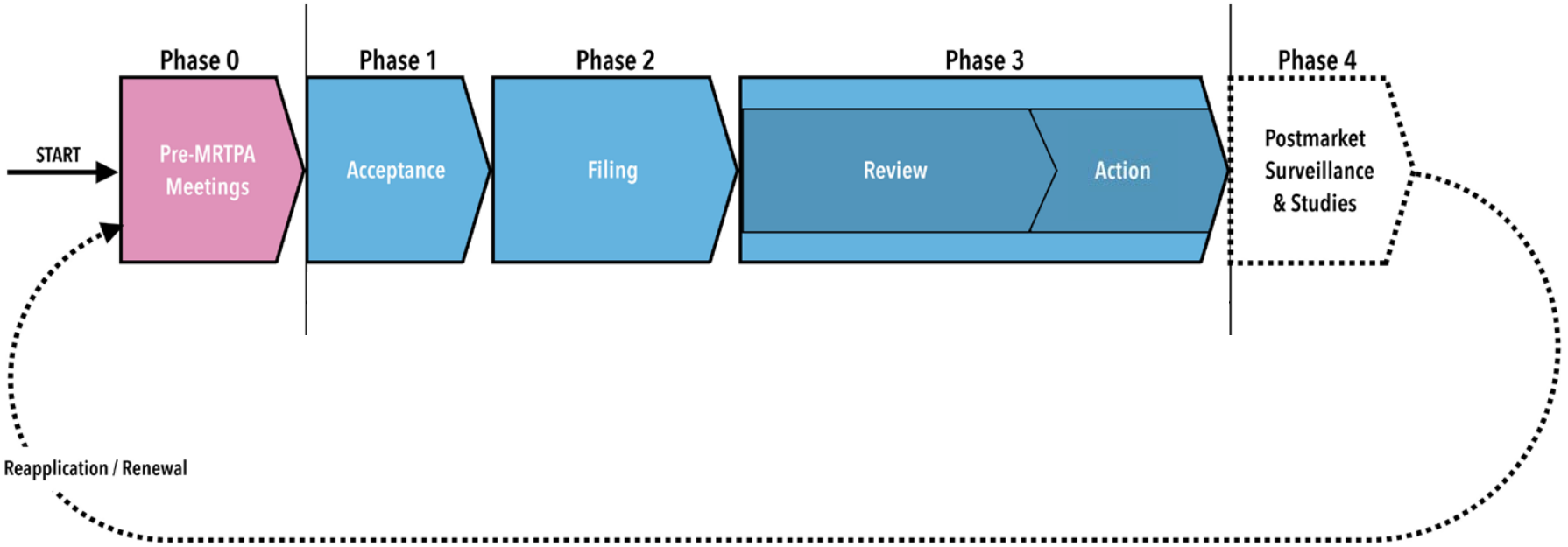
- Alternatively, for products that cannot receive an order under 911(g)(1), FDA may issue an order under 911(g)(2) if it determines that the applicant has demonstrated that, among other things:
  - it is appropriate to promote the public health;
  - the label, labeling, and advertising is limited to a claim that the product does not contain or is free of a substance or contains a reduced level or presents a reduced exposure;
  - scientific evidence is not available, and cannot be made available without conducting long-term epidemiological studies, for an application to meet the standard for a 911(g)(1) order;
  - scientific evidence that is available demonstrates that a reduction in morbidity or mortality is reasonably likely; and
  - testing shows that consumers will not be misled into believing that the product has been demonstrated to be less harmful or present less risk.

QUESTIONS RELEVANT TO THE MRTP EVALUATION

These questions are relevant to the evaluation of whether the applicant has met the applicable 911 standard:

1. Is there adequate scientific substantiation of the proposed modified risk information?
2. What are the relevant health risks of the MRTP to individual tobacco users?
3. How do consumers perceive, understand, and comprehend the modified risk information? How does consumer perception, understanding, and comprehension affect or impact potential benefits and harms?
4. What are the potential benefits and harms to the health of the population as a whole?

MRTPA REVIEW PROCESS



PMP S.A. MRTP APPLICATIONS

IQOS SYSTEM DESCRIPTION

The applicant describes the *IQOS* Tobacco Heating System as a "heat-not-burn tobacco product," consisting of :

- ***IQOS HeatStick*:** A filtered non-combusted cigarette containing a tobacco plug. It is designed to function with the *iQOS* holder to produce an aerosol when the plug is heated.
- ***IQOS* Holder:** The *HeatStick* is inserted into the Holder which heats the tobacco material by means of an electronically controlled heating blade.
- ***IQOS* Charger:** The Charger is used to recharge the Holder after each use.

Figure 1: Components of *IQOS* Tobacco Heating System (Source: Application Section 2.7)

MODIFIED RISK CLAIMS

PMP S.A. requests modified risk orders to market these products as follows:

Modified Risk Claim #1:

- The *IQOS* system heats tobacco but does not burn it.
- This significantly reduces the production of harmful and potentially harmful chemicals.
- Scientific studies have shown that switching completely from cigarettes to the *IQOS* system can reduce the risks of tobacco-related diseases.

MODIFIED RISK CLAIMS

Modified Risk Claim #2:

- Switching completely to *IQOS* presents less risk of harm than continuing to smoke cigarettes.

Modified Risk Claim #3:

- The *IQOS* system heats tobacco but does not burn it.
- This significantly reduces the production of harmful and potentially harmful chemicals.
- Scientific studies have shown that switching completely from cigarettes to the *IQOS* system significantly reduces your body's exposure to harmful or potentially harmful chemicals.

HEALTH WARNINGS

- The applicant acknowledges that the statutorily mandated cigarette warnings are applicable to the products that are the subject of these applications, given their regulatory classification as cigarettes.

- However, the applicant has developed and tested alternative statements intended to improve comprehension and understanding, described in the applications as “PMI Important Warnings”.
  - For example:

IMPORTANT WARNING:
- Reduced risk does not mean no risk. The best way to reduce your risk of tobacco-related diseases is to completely quit tobacco use.
- HeatSticks™ contain nicotine, which is addictive.
- Using the iQOS system can harm your health.

PMP S.A. APPLICATIONS

The PMP S.A. MRTPAs utilized evidence from various types of scientific studies:

- Product analyses (chemistry, engineering, microbiology)
- Toxicological assessments
- Pharmacokinetic studies
- Clinical trials
- Epidemiological studies
- Consumer perception and comprehension
- Statistical modeling
- Plans for postmarket surveillance and studies

QUESTIONS FOR THE COMMITTEE

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1. Discuss evidence related to the health risks of the *IQOS* system and the appropriateness of the proposed modified risk information.

   a. Has the applicant demonstrated that the following statement in their proposed modified risk labeling and advertising is true: “Scientific studies have shown that switching completely from cigarettes to the *IQOS* system can reduce the risks of tobacco-related diseases.”? **(Vote)**

   b. Has the applicant demonstrated that the following statement in their proposed modified risk labeling and advertising is true: “Switching completely to *IQOS* presents less risk of harm than continuing to smoke cigarettes.”? **(Vote)**

QUESTIONS FOR THE COMMITTEE

2. Discuss evidence related to human exposure to harmful or potentially harmful chemicals when combusted cigarette smokers completely switch to the *IQOS* system, including the implications of changes in exposure for long-term disease risk and the appropriateness of the proposed modified risk information.

   a. Has the applicant demonstrated that the following statement in their proposed modified risk labeling and advertising is true: "Scientific studies have shown that switching completely from cigarettes to the *IQOS* system significantly reduces your body's exposure to harmful or potentially harmful chemicals."? **(Vote)**

   b. If the answer to question 2a is "yes", has the applicant demonstrated that the reductions in exposure are reasonably likely to translate to a measurable and substantial reduction in morbidity and/or mortality? **(Vote)** *[To be answered by Committee members who voted "yes" to 2a.]*

QUESTIONS FOR THE COMMITTEE

3. Discuss evidence regarding the likelihood that existing combusted cigarette smokers will initiate use of the *IQOS* system, completely switch to *IQOS*, and/or become long-term dual users of *IQOS* and combusted cigarettes.

   a. What is the likelihood that that U.S. smokers would completely switch to use of the *IQOS* system? **(High/Medium/Low)**

   b. What is the likelihood that U.S. smokers would become long-term dual users of *IQOS* and combusted cigarettes? **(High/Medium/Low)**

QUESTIONS FOR THE COMMITTEE

4. Discuss evidence regarding the likelihood that persons who do not use tobacco products will start using the *IQOS* system.

   a. What is the likelihood that U.S. never smokers, particularly youth, will become established users of the *IQOS* system? **(High/Medium/Low)**

   b. What is the likelihood that former smokers will re-initiate tobacco use with the *IQOS* system? **(High/Medium/Low)**

QUESTIONS FOR THE COMMITTEE

5. Discuss evidence regarding consumer comprehension and perceptions of the proposed modified risk labeling and advertising.

   a. Has the applicant demonstrated that, after viewing the proposed modified risk labeling and advertising, consumers accurately understand the risks of *IQOS* use as conveyed in the modified risk information? **(Vote)**

   b. What additional information, if any, needs to be communicated, other than what has been proposed by the applicant, for consumers to understand the health risks of the *IQOS* system?

CLARIFYING QUESTIONS?