

RESEARCH ANALYSIS REPORT

ESTIMATION OF PREVALENCE OF *IQOS* USE

Secondary Analysis of Relevant Data from the ALCS Adult Tobacco Consumer
Tracking Study

(Short Title: Secondary Analysis of ATCT)

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1. INTRODUCTION

1.1. Background

Philip Morris Products S.A. (PMP S.A.) developed the *IQOS* Tobacco Heating System and Marlboro HeatSticks (hereinafter referred to as *IQOS*) as novel tobacco and nicotine-containing products with the potential to reduce harm or the risk of tobacco-related disease associated with smoking cigarettes. PMP S.A. submitted Modified Risk Tobacco Product Applications for *IQOS* to the U.S. Food and Drug Administration (FDA) seeking authorization to market the products as modified risk tobacco products. On July 7, 2020, FDA issued “Modified Risk Granted Orders – Exposure Modification” authorizing *IQOS* to be marketed with a reduced exposure claim. The Orders are conditioned upon agreement to conduct postmarket surveillance and studies (PMSS) in accordance with protocols approved by FDA. This document is prepared as part of the PMSS program for *IQOS* pursuant to the Orders.

1.2. Rationale

The Federal Food, Drug and Cosmetic Act (FDCA) directs the Food and Drug Administration (FDA) to condition an exposure modification order received under FDCA § 911(g)(2) on the MRTP applicants’ agreement to conduct PMSS (FDCA §§ 911(g)(2)(C)(ii)). “The outcomes evaluated in postmarket surveillance and studies should focus on the effect of the MRTP on consumer perception, behavior and health under real world conditions of use” (Food and Drug Administration, 2012). For this reason, ALCS¹ on behalf of the applicant, PMP S.A., plans to conduct certain components of PMSS to assess the effect of the MRTP among U.S. consumers. The program will consist of a collection of data over time that supports an assessment of *IQOS* in the postmarket setting. This Estimation of Prevalence of *IQOS* Use Research Analysis is one component of the postmarket surveillance program. Specifically, it describes the analyses we conducted using data relevant to *IQOS* from ALCS’s ongoing Adult Tobacco Consumer Tracking Study (ATCT).

2. PURPOSE AND OBJECTIVES

2.1. Purpose

The purpose of this secondary analysis is to estimate *IQOS* prevalence among adults 21 years of age or older based on relevant data from a population-based consumer survey (i.e. ATCT).

¹ Altria Client Services (ALCS) and the parent of PMP S.A., Philip Morris International Management S.A., have entered into a distribution agreement by which ALCS and its affiliates have exclusive rights to distribute and sell *IQOS* in the U.S. after FDA authorization. ALCS affiliate PM USA markets *IQOS* in the U.S. Therefore, PMSS that involves the study of consumers and consumption in the U.S. will be conducted by ALCS to be submitted as part of PMSS reporting by PMP S.A.

2.2. Objectives

The objectives of the original analysis plan are to:

- 1) Estimate prevalence of *IQOS* use, in total and by demographic characteristics
- 2) Estimate prevalence of exclusive, dual and poly tobacco use with *IQOS*
- 3) Estimate the number of days and amount of tobacco product usage among current *IQOS* users
- 4) Describe initiation, quitting and complete switching behaviors relative to *IQOS* use

However, as stated in the original analysis plan, we are implementing a stepwise reporting process (described in Section 4). Before the number of current *IQOS* users reaches 20, only the raw count of current *IQOS* users will be reported. Based on the number of current *IQOS* users observed in ATCT from March 2023 to February 2024, we will only report the raw count of number of current *IQOS* users.

3. OVERVIEW OF THE ADULT TOBACCO CONSUMER TRACKING STUDY

We analyzed data from the ALCS Adult Tobacco Consumer Tracking Study, an on-going cross-sectional computer assisted random-digit dialing telephone interview administered to a nationally representative sample drawn from the U.S. adult civilian non-institutionalized population.

The ATCT annual sample includes approximately 28,800 U.S. adults 21 years or older. The sample is based on a sampling approach that utilizes Random Digit Dial (RDD) landline and cell phone interviewing frames following an equal probability selection method (EPSEM) design. The composition of the sample is 80% cell phone and 20% landline.

For any research that will have results projected to the overall population, and prevalence research in particular, probability samples (e.g., RDD telephone) are preferable to non-probability (e.g., internet-based). In probability samples, persons in the population have a known chance of being selected in the sample, margin of error is universally recognized and accepted, and results can be projected to the population at large with a known level of precision. In non-probability samples, some people in the population have no chance (or an unknown chance) of being selected in the sample (coverage bias). The amount of coverage bias and the exact nature of the bias will vary depending on the source (e.g., various online panels).

Quota controls for geography, sex, and other demographic characteristics are used to reduce the reliance on data weighting. It is important to have a demographically/geographically representative sample for the ATCT study, as tobacco usage behavior can vary greatly across different types of adult respondents. Accordingly, the weighting design for ATCT calls for the nesting of certain weighting variables (for example, race/ethnicity within region); however, these data “nests” can potentially include small sample sizes within a subgroup. In order to weight the data successfully, an adequate number of adult respondents are needed in all weighting subgroups, including those that are hardest to reach. This will ensure that the weighting will bring the data into better alignment with reality, rather than distort it from reality.

While data weighting is a common practice, excessive data weighting is not ideal (for example, heavy lifting of underrepresented subgroups and/or extreme reductions to overrepresented subgroups). Additionally, (as mentioned above), adequate numbers of adult respondents are needed within all weighting sub-groups. Therefore, the ATCT study includes quota controls to both reduce the reliance on weighting, as well as to ensure the success of the weighting.

The quota controls are as follows:

- Hard quota controls for region, sex, and mode (landline/cell)
- Soft quota “guardrails” for age, education, and race/ethnicity. These guardrails are not strict quotas for each sub-group, but rather loose guidelines of ± 13 percentage points (pp).

These controls are in place to prevent extreme oversampling of the easiest to reach adult respondents. These quota controls also assure that adequate numbers of adult respondents are available within the nested weighting subgroups, thereby assuring the overall success of the data weighting. In an effort to minimize reliance on these controls, those households reached on landline are asked first for the youngest aged adult male (the hardest population to reach) followed by the youngest aged adult female. However, the need for these controls introduces the possibility of selection bias. While it is impossible to measure selection bias, demographic metrics that are *not* controlled for (such as income) are frequently compared with other statistics reported by federal agencies to ensure consistency and that selection bias is in fact minimal.

3.1. ATCT Tobacco Categories

ATCT is a study designed to measure tobacco prevalence. Eligible adult respondents are asked if they have used any of the following products:

- Cigarettes
- Cigars
- Pipe tobacco
- E-Vapor
- Snus
- Chewing tobacco
- Moist smokeless tobacco or dip
- Oral nicotine products
- Hookah
- Heated tobacco products
- Any Other Tobacco Products not already mentioned.

“Heated tobacco products”, the category to which *IQOS* belongs, was added as a new category to ATCT in October 2019. For each of the above products that the adult respondent has used, additional questions are asked to measure amount of usage and consumption. The usual brand within categories used by consumers is also assessed in ATCT. The categories mentioned above will be combined into the following categories for data analysis:

- Cigarettes
- Cigars

- Pipe tobacco
- E-Vapor
- Smokeless tobacco (snus, chewing tobacco, moist smokeless tobacco or dip)
- Oral nicotine products
- Hookah
- Heated tobacco products

Note: Any other tobacco products not already mentioned will not be considered in the analysis.

3.2. ATCT Study Duration

ATCT is fielded on a continuous basis. Data will be analyzed across the most recent 12-month period for the purpose of reporting.

3.3. ATCT Recruitment

A nationally representative sample is drawn from the U.S. adult population through a computer-assisted, random-digit dialing telephone interview. The sample is based on a probability sampling approach that utilizes landline and cell phone interviewing frames following an equal probability selection method design. The composition of the sample is 50% cell phone and 50% landline. Quota controls for geography, sex, and other demographic characteristics are used to reduce the reliance on data weighting.

3.4. ATCT Inclusion and Exclusion Criteria

Participants must satisfy the following criteria at the time of screening to be enrolled into the ATCT study: civilian, non-institutionalized population of the U.S., 21 years or older, including residents of non-institutional group quarters such as college dormitories, group homes, shelters, rooming houses, and civilians dwelling on military installations.

Respondents who meet any of the following exclusion criteria are excluded from participation in the ATCT study:

1. Unable to read, speak or understand English
2. Under the age of 21
3. Potential participant is identified as being a non-civilian or member of an institutionalized population
4. Adults on active duty in any branch of the US armed forces

4. SECONDARY ANALYSIS PROCEDURES

Our analysis and reporting of *IQOS*-relevant information from ATCT for postmarket surveillance purposes will follow a step-wise process based on the number of current *IQOS* users (used *IQOS* brand of heated tobacco product in the past 30 days) identified within the ATCT dataset².

The process will unfold as follows:

- **Step 1 Reporting.** The number of current *IQOS* users in the ATCT dataset is reported when the MTRPA was granted for *IQOS*. The count will be based on data from the most recent 12 months. We will only report counts if the number of current *IQOS* users in the ATCT dataset is less than 20.
- **Step 2 Reporting.** When the number of current *IQOS* users in the ATCT dataset reaches 20, we will start to report prevalence at the national level. The reported results include the count and percentage of total current *IQOS* users with 95% confidence interval. The results will be based on either the most recent 12 months if we have reported *IQOS* use in all 12 months, or the months when ATCT starts to capture current *IQOS* users if it is less than 12 months.
- **Step 3 Reporting.** When the number of current *IQOS* users in the ATCT dataset reaches 100, we will start to report all other outcome measures as stated in this analysis plan. Based on sample size calculations, we need at least 100 current *IQOS* users in the ATCT data set to start reporting outcome measures for the four objectives.

5. OUTCOME MEASURES AND DATA ANALYSIS

As described in Section 4, when the number of current *IQOS* users in the ATCT dataset is less than 20, we will only report the number of current *IQOS* users in the ATCT dataset (i.e., Step 1 Reporting).

Objective 1: Report the number of current *IQOS* users in ATCT

Definitions of current use of *IQOS*:

- Selected 'Yes' to 'During the past 30 days, have you used: any form of heated tobacco product, that heats tobacco instead of burning it, such as *IQOS* or glo'

And

- Selected '*IQOS*' to 'What is your regular brand of HEATED TOBACCO DEVICE; specifically, the brand of the heated tobacco DEVICE you use most often?'

Note: For PMTA Quarterly Reports, the participants also need to select 'Marlboro' to the question "what is your regular brand of tobacco stick refills that you use with that (INSERT BRAND FROM Q.1305) device? These are sometimes referred to as 'HeatSticks' or 'neo sticks'".

² ALCS currently has a process in place to report *IQOS*-relevant information from ATCT for the purpose of the *IQOS* PMTA authorization. When fully executed, this analysis plan will extend beyond the reporting plan devised for the PMTA.

6. RESULTS

As stated in Sections 4 and 5, before the number of current *IQOS* users reaches 20, only the raw count of current *IQOS* users will be reported. Table 1 displays ATCT sample sizes with the raw count of current *IQOS* users in ATCT for each reporting month and in total (from March 2022 to February 2023). During this 12-month time period, a total of four respondents reported current use of *IQOS* and 1 respondent reported using Marlboro as the regular HeatStick brand.

Table 1: Raw Count of Current *IQOS* Users in ATCT by Survey Month

Survey Month	Monthly Sample Size	Raw Count of Current <i>IQOS</i> Users	Raw Count of Current <i>IQOS</i> Users who reported Marlboro as regular HeatStick brand ¹
March 2023	2,404	1	0
April 2023	2,406	0	0
May 2023	2,404	0	0
June 2023	2,406	1	0
July 2023	2,403	0	0
August 2023	2,401	0	0
September 2023	2,402	0	0
October 2023	2,404	1	1
November 2023	2,401	0	0
December 2023	2,400	0	0
January 2024	2,401	1	0
February 2024	2,403	0	0
Total	28,835	4	1

¹Reported in *IQOS* PMTA 2024 Annual Report Annex 5: Data on Product Purchasers.

7. APPENDIX 1 – SELECTED ATCT QUESTIONS RELATED TO IQOS AND RELEVANT TO THIS ANALYSIS PLAN

This appendix provides a list of ATCT March 2023 survey questions relevant to the current analysis. The appendix has two main parts: (1) past 30-day tobacco product usage and (2) questions from module designed for current heated tobacco product (HTP) users.

PAST 30-DAY TOBACCO PRODUCT USAGE

1. [SHOW ON SCREEN/READ FOR FIRST PRODUCT ONLY]
Now we would like to ask you a few questions about some products you may or may not have used in the past 30 days – that is, from **[DATEFILL]** up to and including today. During the past 30 days, have you used [first product]?

[SHOW ON SCREEN/READ FOR SECOND PRODUCT ONLY]
During the past 30 days, have you used [second product]?

[SHOW ON SCREEN/READ FOR THIRD – TENTH PRODUCTS]
REPEAT AS NECESSARY – “During the past 30 days, have you used [product]?”

(ROTATE AND ASK FIRST: CIGARETTES, CIGARS, PIPE TOBACCO, EVAPOR, SNUS, CHEWING TOBACCO, MST, OR DIP. CIGARETTES AND EVAPOR SHOULD ALWAYS BE ROTATED TOGETHER, WITH CIGARETTES FOLLOWING EVAPOR. CHEWING TOBACCO AND MST/DIP SHOULD ALWAYS BE ROTATED TOGETHER, WITH MST/DIP FOLLOWING CHEWING TOBACCO.)

(ROTATE AND ASK SECOND: ANY FORM OF HEATED TOBACCO PRODUCTS, ORAL NICOTINE PRODUCTS, AND HOOKAH)

(ASK LAST: ANY OTHER TOBACCO OR NICOTINE PRODUCTS NOT ALREADY MENTIONED.)

(NOTE: IF RESPONDENT INTERRUPTS AT ANY POINT DURING THIS QUESTION, AND SAYS THEY DON’T USE TOBACCO PRODUCTS, CLARIFY WITH: “Just to check, you **do not** use any tobacco products, including electronic cigarettes or eVapor?”)

[LIST OF PRODUCTS CHANGED IN 08/2019]

	Yes	No	Don't Know	Abbreviated Name (for Q.1B1)
Cigarettes [1b]	- 1	- 2	- 999	Cigarettes
Cigars [1c]	- 1	- 2	- 999	Cigars
Pipe tobacco [1d]	- 1	- 2	- 999	Pipe Tobacco
eVapor or vaping products, such as Juul, e-cigarettes, vape pens, or box mods [1a] [CHANGED 08/2019]	- 1	- 2	- 999	eVapor or vaping products
Snus, which is spelled S.N.U.S. and is a spit free tobacco product in pouches or packets [1e]	- 1	- 2	- 999	Snus
Chewing tobacco in leaf or plug form, sold in a resealable bag or pouch [1f]	- 1	- 2	- 999	Chewing tobacco
Moist smokeless tobacco or dip in loose or pouch form, sold in a round can [1g]	- 1	- 2	- 999	Moist smokeless tobacco or dip
[OTHER SMOKELESS DELETED 08/2019]				

Any form of heated tobacco product, that heats tobacco instead of burning it[1m] [ADDED 10/2019; REVISED 03/2023]	- 1	- 2	- 999	A heated tobacco product
Oral nicotine products that are free of tobacco leaf (These come in a variety of flavors, nicotine strengths, and forms such as nicotine pouch, lozenge, or chewable. Example: <i>on!</i> ®, Zyn®, Velo®) [1k] [CHANGED FROM TDN 08/2019; WORDING CHANGE 1/4/2023]	- 1	- 2	- 999	An oral nicotine product
Hookah tobacco products, which is flavored loose tobacco typically smoked using a long-stemmed water pipe [1l] [ADDED 08/2019]	- 1	- 2	- 999	Hookah
[OTHER SMOKEABLE DELETED 08/2019]				
[ANY OTHER TOBACCO DELETED 08/2019]				
Any other tobacco or nicotine products not already mentioned. Please do not include any products intended for nicotine replacement therapy. [1n] [ADDED 08/2019]	- 1	- 2	- 999	A tobacco or nicotine product

CURRENT HTP USER

[SECTION ADDED 10/2019]

ONLY READ T13 IF MENTION “HEATED TOBACCO PRODUCT” AT Q.1,
OTHERWISE SKIP TO DIRECTIONAL BEFORE T11

T13. Please only think now about the HEATED TOBACCO PRODUCTS that you use when answering these questions.

1305. What is your regular brand of HEATED TOBACCO DEVICE; specifically, the brand of the heated tobacco DEVICE you use most often? (DO NOT READ LIST)

IQOS	-1
Glo	-2
3T	-3
iSmoke OneHitter	-4
Ploom Tech	-5
Other (<i>Specify</i> _____)	-137
Don't Know	-999
No Regular Brand	-130

1305A. And what is your regular brand of tobacco stick refills that you use with that (INSERT BRAND FROM Q.1305) device? These are sometimes referred to as “heat sticks” or “neo sticks”.

Marlboro	-1
Kent	-2
Mevius	-3
Other (<i>Specify</i> _____)	-137
Don't Know	-999
No Regular Brand	-130

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Principal Scientist

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Signature Adoption: Drawn on Device

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In Person Signer Events	Signature	Timestamp
Editor Delivery Events	Status	Timestamp
Agent Delivery Events	Status	Timestamp
Intermediary Delivery Events	Status	Timestamp
Certified Delivery Events	Status	Timestamp
Carbon Copy Events	Status	Timestamp
Witness Events	Signature	Timestamp
Notary Events	Signature	Timestamp
Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	3/27/2024 2:54:40 PM
Certified Delivered	Security Checked	3/27/2024 2:55:02 PM

Envelope Summary Events	Status	Timestamps
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Completed	Security Checked	3/28/2024 4:39:51 AM
Payment Events	Status	Timestamps