Tobacco and Nicotine Products Regulatory Science Symposium

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ABSTRACTS

Best Practices for Maximizing Statistical Precision and Accuracy: Observational Studies of Exposure to Tobacco and Nicotine Products

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Non-randomized observational studies can track risk-induction and -reduction associated with real-world use of non-combusted nicotine and tobacco products. The objective of this session is to evaluate recent studies and to identify opportunities for further optimizing future study designs and discuss a framework for minimizing statistical bias and interpretation of findings. The session will begin with presentation by Gal Cohen and Steve Cook reviewing of recent epidemiology studies pointing out common errors in study designs and measurement leading to potential errors in study conclusions and a framework for minimizing these errors. Saul Shiffman and Jim Sargent will discuss efforts to develop reliable and valid measurement tools to assess changes in respiratory symptoms associated with product use and switching. Maciej Goniewicz will discuss the evidence on biomarkers of exposure and disease risk that can be built into epidemiologic study to evaluate risks associated with different tobacco products. framework for minimizing statistical bias was translated to specific considerations, which spanned the selection and quantification of cohorts, exposure and outcomes.

Utilizing a Consumer Purchasing Database to Determine the Magnitude of Impact for Vuse Alto Menthol and Market Comparators

TBD, RAI Services Company (RAISC) (Reynolds American Inc.)

In determining the weight of evidence for the benefit to a new product provides to adult consumers, the ability of a product to transition consumers away from higher risk products is of paramount importance. The mechanisms for determining this transition have varying degrees of success and generalizability to the actual consumer population. Utilizing a consumer purchasing database, a retrospective longitudinal cohort study was designed to determine the magnitude of impact of Vuse Alto Menthol and market comparators on a population of cigarette consumers who switch to ENDS.

The Role of Flavored Alternatives in Tobacco Harm Reduction: Results from Two Six-Month Randomized Experimental Studies Supporting Premarket Tobacco Product Applications

Jessica Zdinak, Chief Research Officer and CEO, Applied Research and Analysis Company LLC

PMTA applicants seeking marketing authorization for flavored products must provide FDA with reliable and robust scientific evidence demonstrating that the use of flavors causes a greater reduction in combustible cigarette use compared with the use of comparable tobacco-tasting products. This paper presents data from two Longitudinal Randomized Switching Studies (LRESS) examining how flavored disposable e-cigarettes and e-liquids influence switching behavior among adults who smoke. In one study, a total of 320 participants were randomly assigned to one of two conditions, receiving either tobacco tasting (n = 160) or flavored (n = 160) disposable e-cigarettes over six months. Separately, a total of 599 participants were randomly assigned to receive either a 'flavored' tobacco-derived e-liquid (n = 150) product, a 'flavored' synthetic derived product (n = 149), a tobacco-tasting (n = 150) tobacco derived e-liquid, or a tobacco-tasting (n = 150) synthetic derived e-liquid product, including a 'menthol' tobacco-tasting product. The results from the disposable e-cigarette study demonstrate that complete substitutions from combustible cigarettes to the candidate product were more common among the flavored group compared to the tobacco tasting group. Initial results from the e-liquid study suggested that the participants from either group were equally likely to switch. However, further analyses revealed that much of the cessation benefit within the tobacco-tasting e-liquid group came from a menthol-flavored tobacco-tasting product, without which the participants who received tobacco-flavored e-liquid products were statistically significantly less likely to completely switch than those randomized to the flavor group. In combination, these results contribute to a growing body of literature highlighting the key role of flavored alternatives in facilitating smoking cessation. A range of flavored alternatives, including tobacco, would protect public health by facilitating switching among adult smokers more effectively than tobacco-tasting products alone.

An Actual Use Study of a Rechargeable Pod-Based ENDS and Changes in Cigarette Smoking Behavior Among Adult Smokers in the United Kingdom

Layla Malt, Behavioural Sciences & Surveillance Senior Manager, Imperial Brands PLC

As a responsible manufacturer, Imperial Brands is committed to making a meaningful contribution to tobacco harm reduction (THR). To substantiate the THR potential of our Next Generation Products, we use a multi-stage and multi-disciplinary approach known as the Scientific Assessment Framework, which includes behavioral studies. To assess the real-world impact of the blu 2.0 electronic nicotine delivery system (ENDS), an Actual Use Study (AUS) was commissioned to assess changes in smoking behavior among 429 UK adult smokers after familiarization with a diverse portfolio of blu 2.0 products. Participants had the freedom to choose, without direction, if they used blu 2.0, or alternative nicotine and tobacco products over a 6 week observational period. A follow-up assessment at 24 weeks post-enrolment was also included. To be more reflective of the real world situation, the study used an innovative methodology. We assessed ad libitum purchasing of blu 2.0 rather than supplying test products to the participants. Smokers were provided with a prepaid debit card during the 6 week observational period which could be used to purchase any variety of blu 2.0 directly from retailers of their choice. This more closely reflects real-world conditions around product acquisition and retail availability whilst also

minimizing participant contact and burden of frequent travel to a study site. The study found that 36.3% participants substantially altered their smoking behavior at week 6; 5.8% quit smoking and completely switched to blu 2.0, 30.5% substantially reduced their daily cigarette consumption (≥50%) while continuing to use blu, and 0.7% quit using cigarettes and blu 2.0. The proportion of smokers who altered their smoking behavior was sustained at the 24 week follow up when the free provision of blu 2.0 ended. However, there were substantial increases in the number of participants who reportedly quit smoking and completely switched to blu 2.0 (14.5%), and who quit using cigarettes and blu 2.0 (8.6%). Overall, this study used novel methodology more reflective of real-word settings to demonstrate that blu 2.0 ENDS may support adult smokers to transition away from smoking to exclusive use of a potentially reduced risk product, substantially reduce cigarette consumption or quit using nicotine and tobacco products. Ongoing Post-Market Surveillance will verify these findings in time, particularly in other populations outside of the UK. Our research indicates blu 2.0 has an important role to play in helping Imperial Brands make a meaningful contribution to tobacco harm reduction.

Harm Reduction Opportunity for Adults Who Use Moist Smokeless Tobacco Products

Mohamadi Sarkar, Fellow, Regulatory Science, Altria Client Services LLC

This presentation will discuss the scientific evidence in support of our PMTA for on! PLUS™ nicotine pouches. These products are intended for adults who use moist smokeless tobacco products (MST), including those who exclusively use MST (adult dippers, AD), as well as those who dual-use MST and combustible cigarettes (adult duals users, ADU). We will discuss our product stewardship and chemical characterization of these products compared to MST products. We will present findings regarding absolute and relative risk perceptions as well as intentions to try and use the products among users and non-users of tobacco products. We will show data from national surveys to infer likelihood of use among youth which is expected to be low. Additionally, evidence from our actual use study will show that AD and ADU switch completely or reduce the consumption of MST/cigarettes. Results from a randomized controlled clinical study characterizing nicotine pharmacokinetics (PK) and subjective responses along with findings from physiologically based PK modelling will be included. Based on a synthesis of this information, we will illustrate that the abuse liability of these products can be expected to be lower or comparable to MST and cigarettes. Finally, we will integrate different lines of evidence to demonstrate that these products are appropriate for the protection of public health.