Exhibit 18

UNITED STATES INTERNATIONAL TRADE COMMISSION

WASHINGTON, DC

Before the Honorable Clark S. Cheney
Administrative Law Judge

In the Matter of **CERTAIN TOBACCO HEATING ARTICLES AND COMPONENTS THEREOF**	**Investigation No. 337-TA-1199**

REBUTTAL EXPERT REPORT OF DR. STACEY M. BENSON

RELATING TO THE PUBLIC INTEREST

Stacey M. Benson

October 23, 2020

ranged from 13.7 to 14.8 ng/mL with each having a comparable T_{max} value of just over 37 minutes. These products deliver consistent nicotine, but not as efficiently has combustible tobacco because the uptake of the tobacco for these products is much slower than that which is observed with combustible cigarettes.

There are a number of nicotine products available on the market with varied maximum plasma nicotine concentrations and time to maximum plasma nicotine concentrations. As shown above, PRRP oral nicotine products have lower maximum nicotine concentrations and it takes longer for that peak concentration to be experienced. This finding indicates that, in general, the nicotine delivery efficiency of these products is much lower than IQOS®. In my opinion, due to the differences experienced with the physical act of using these products (e.g. aesthetics of spitting or chewing gum), their lower nicotine delivery efficiency, and the increased risks of cancer some of them are associated with, it is inappropriate to consider them equivalent alternatives to IQOS®.

C. ENDS Products Are Not Substitutes for IQOS®

ENDS is a diverse category of non-combustible nicotine-containing inhalation product and is used for describing nicotine-containing e-liquid delivery systems. According to Dr. James Figlar, Executive Vice President of Research & Development and Scientific & Regulatory Affairs at RJ Reynolds Tobacco, "e-cigarettes don't work the same way as heat-not-burn product[s]," and "[e-cigarettes are] a different animal all together."[47] For several reasons, ENDS products are not IQOS® substitutes.

1. No ENDS Product Has Received the Same FDA Authorizations that IQOS® Has

As discussed elsewhere in this report and by other of Respondents' experts, IQOS® has been granted both PMTA and MRTP authorization by FDA. As of October 22, 2020, there are no other inhalable non-combustible tobacco/nicotine containing products with such authorizations or that have MRTPAs pending. This includes the category of ENDS products.

2. ENDS Products Have Highly Variable Characteristics

ENDS are highly variable, where the power settings, nicotine concentration, type of nicotine, puffing topography, and humectant can greatly affect the chemical composition of the aerosol and overall user aerosol exposure. It is my opinion that ENDS user exposure and corresponding experience is entirely dependent on the aerosol produced by the device, as well as other device characteristics such as the mouthpiece, size, and shape that make each device unique.

a) ENDS Product Components Affect Aerosol

The National Academies of Sciences, Engineering, and Medicine (NASEM) highlights in their report on the *Public Health Consequences of E-Cigarettes* how vastly different types of ENDS product characteristics can be. ENDS, some of which are modifiable, vary in their component parts. NASEM stated "the design and composition of e-cigarette devices (including e-liquid composition, device battery power, activation voltage, and coil resistance) vary considerably, and these variations influence the e-cigarette aerosol

[47] Figlar Dep. 113: 5-7

produced."[48] There is a large amount of variability amongst the three main components (battery, atomizer, and fluid reservoir) of ENDS. The design of ENDS have changed over time, with the first generation (e.g., cig-a-like), second generation (clearomizer), third generation (modifiable "mod"), and fourth generation ("pod" style). As suggested by Dr. Murrelle in his Table 1 list of ENDS products, there are 100s of device, component, and/or e-liquid brands, many of which are available to U.S. consumers.[49]

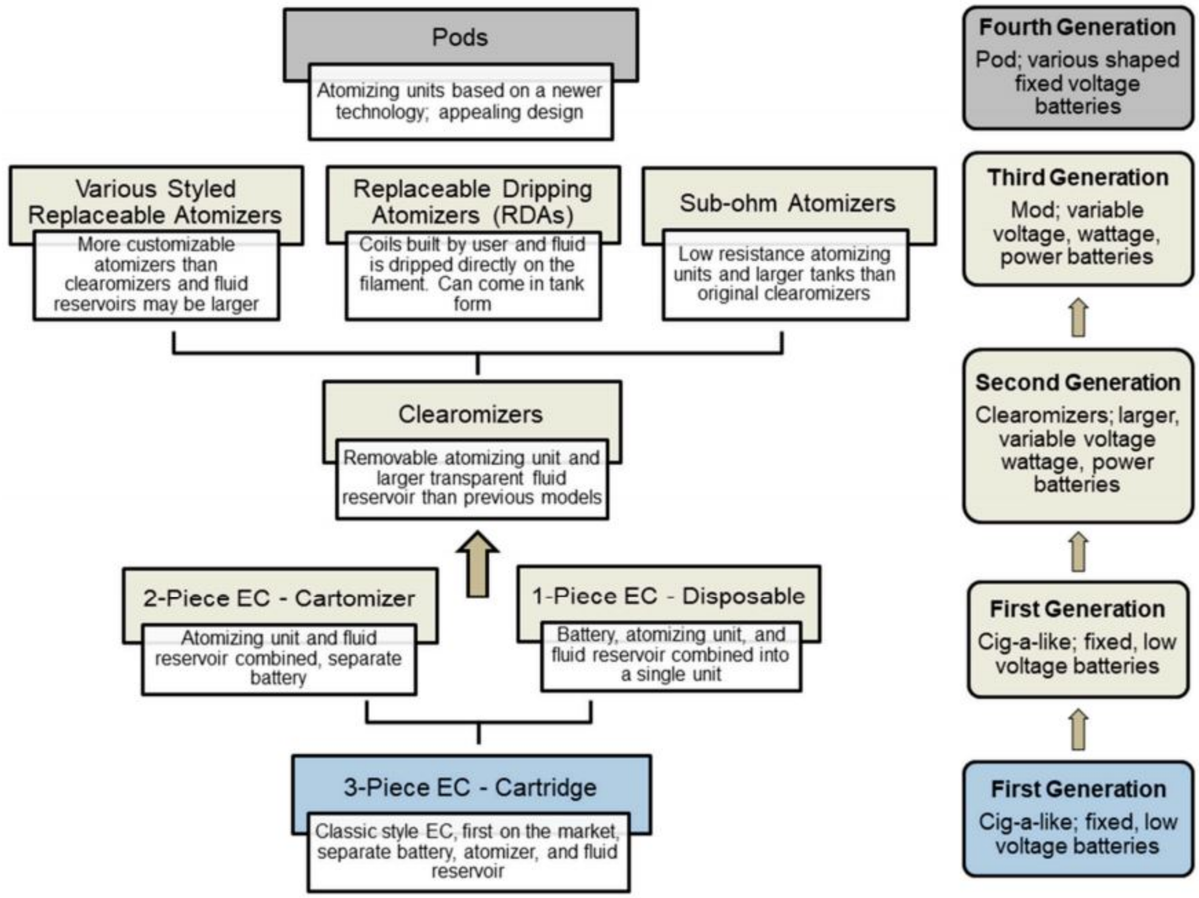

Figure 1. Characteristics of the four generations of ENDS. Reprinted from Williams and Talbot 2019.

b) Modifiable Physical Components of ENDS Products Affect Aerosol

Heating coils and atomizers in ENDS influence the aerosol properties, therefore affecting the taste and potential health effects of the product. If, for instance, the heating power is too high, the user experiences a negative sensation called a "dry hit" because of the thermal decomposition of components such as

[48] NASEM (2018). Public Health Consequences of E-Cigarettes. Washington (DC), National Academy of Sciences, Engineering and Medicine., p. 75

[49] Murrelle, E. L. (2020). Expert Report of Edward L. Murrelle. Dated October 5th, 2020., p. 15-16

propylene glycol and glycerol.[50,51] The amount of power applied to the atomizer is variable, and can affect the mass of aerosol produced: more power creates a denser aerosol per puff.[52] First- and second-generation devices are known to produce lower power, ranging from 3.0-12.6 W, whereas newer devices produce between 10.0 and 162.4 W.[53, 54, 55] Power, in combination with higher voltage, can also increase nicotine delivery. [56] Talih et al.[57] found that increasing the wattage of the device from 3.0 to 7.5 resulted in a 4- to 5-fold increase in nicotine yield. Similarly, Farsalianos et al.[58] conducted an experimental study to investigate the relationship between ENDS power settings and puff topography. Study investigators provided a third generation electronic cigarette battery and rebuildable tank atomizer, which subjects filled with their own choice of e-liquid. Participants vaped *ad libitum* in two blinded sessions, using a different power setting in each (6 W and 10 W). Generally, participants on the 6W power setting took statistically significantly more puffs of longer duration compared to the 10 W setting (57 vs. 46 puffs, p = 0.001; 4.6 s/puff vs. 3.8 s/puff, p = 0.001). NASEM also concluded based on aerosol exposure studies that e-cigarettes have the potential to contain and emit toxic substances, but that the quantity and characteristics of those substances were highly variable based on the device and liquid characteristics.

A review by Fearon et al.[59] summarized the differences in pharmacokinetics of ENDS devices reporting both *ad libitum* and regimented puffing scenarios. To minimize the variability in the pharmacokinetic response associated with *ad libitum* puffing, I only compared C_{max} for the regimented puffing conditions of 5 minutes to 7.5 minutes. For cig-a-like and first generation ENDS, the C_{max} ranged from 2 ng/mL for a V2 cig, to 9.1 ng/mL for a V2 cigs blu. For newer generation devices the range of C_{max} values under regimented conditions were broad with a minimum of 2.7 ng/mL after use of an eVIC (open tank) for five minutes and up to 20 ng/mL for subjects who used their own first or second generation devices.

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[50] Farsalinos, K. E., V. Voudris and K. Poulas (2015). "E-cigarettes generate high levels of aldehydes only in 'dry puff' conditions." Addiction **110**(8): 1352-1356.
[51] Geiss, O., I. Bianchi and J. Barrero-Moreno (2016). "Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours." Int J Hyg Environ Health **219**(3): 268-277.
[52] Gillman, I. G., K. A. Kistler, E. W. Stewart and A. R. Paolantonio (2016). "Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols." Regul Toxicol Pharmacol **75**: 58-65.
[53] Alexander (2015). "Electronic cigarettes: the new face of nicotine delivery and addiction." Journal of Thoracic Disease **7**(8): E248-E251.
[54] Voos, N., L. Kaiser, M. C. Mahoney, C. M. Bradizza, L. T. Kozlowski, N. L. Benowitz, R. J. O'Connor and M. L. Goniewicz (2019). "Randomized within-subject trial to evaluate smokers' initial perceptions, subjective effects and nicotine delivery across six vaporized nicotine products." Addiction **114**(7): 1236-1248.
[55] Wagener, T. L., E. L. Floyd, I. Stepanov, L. M. Driskill, S. G. Frank, E. Meier, E. L. Leavens, A. P. Tackett, N. Molina and L. Queimado (2017). "Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users." Tob Control **26**(e1): e23-e28.
[56] Alexander (2015). "Electronic cigarettes: the new face of nicotine delivery and addiction." Journal of Thoracic Disease **7**(8): E248-E251.
[57] Talih, S., Z. Balhas, T. Eissenberg, R. Salman, N. Karaoghlanian, A. El Hellani, R. Baalbaki, N. Saliba and A. Shihadeh (2015). "Effects of user puff topography, device voltage, and liquid nicotine concentration on electronic cigarette nicotine yield: measurements and model predictions." Nicotine Tob Res **17**(2): 150-157.
[58] Farsalinos, K., K. Poulas and V. Voudris (2018). "Changes in Puffing Topography and Nicotine Consumption Depending on the Power Setting of Electronic Cigarettes." Nicotine Tob Res **20**(8): 993-997.
[59] Fearon, I. M., A. C. Eldridge, N. Gale, M. McEwan, M. F. Stiles and E. K. Round (2018). "Nicotine pharmacokinetics of electronic cigarettes: A review of the literature." Regul Toxicol Pharmacol **100**: 25-34.

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