Memorandum

To:	The Food and Drug Administration's Center for Tobacco Products
From:	Environmental Resources Management, Inc. on behalf of Phillip Morris Products S.A.
Date:	10 August 2016
Subject:	**Environmental Impact Assessment** Summary of Information for the Tobacco Heating System (THS) with Menthol Tobacco Stick – Public Document

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5.2.1 Executive Summary

An environmental assessment has been prepared for the Tobacco Heating System (THS) with Menthol Tobacco Stick variants (referred to herein as THS Menthol), containing the Dorado I Blend, Mint Vinny Low and Dorado I, Mint Vinny High Flavor system tobacco sticks, in accordance with 21 CFR §§ 25.20 and 25.40, the Food and Drug Administration's (FDA's or Agency's) regulations implementing the National Environmental Policy Act of 1969. Philip Morris Products S.A. (PMP S.A.) plans to submit to the Center for Tobacco Products, U.S. Food and Drug Administration a Modified Risk Tobacco Product (MRTP) Application for the THS under § 911(g) of the Federal Food, Drug and Cosmetic Act (FD&C Act). THS is composed of the Tobacco Heating Device (THD) and the Tobacco Stick.

Environmental Resources Management, Inc. (ERM) conducted the environmental assessment in accordance with 21 CFR §§ 25.20 and 25.40 and relevant aspects of the FDA technical guidance document(s) including the *Guidance for Industry: Environmental Assessment of Drug and Biologics Applications, Section III.A.2 (July, 1998)*. This assessment was specifically focused on the MRTP Application for THS with the Menthol Tobacco Stick variants (THS Menthol) containing the Blend Dorado I, Mint Vinny Low and Dorado I, Mint Vinny High Flavor systems, and is prepared following the direction of PMP S.A.. The potential atmospheric, aquatic, and terrestrial environmental impacts were considered using a conservative set of assumptions. The overall conclusion from this assessment is that there are no significant environmental risks identified, and a Finding of No Significant Impact for this environmental assessment of THS Menthol by FDA is warranted.

5.2.2 Analysis and Assumptions

The THS Menthol Tobacco Sticks are part of the THS that comprises a consumable tobacco stick and a reusable THD, which includes a holder and a charger. The potential shipping forecast for THS Menthol and associated Tobacco Sticks formed the basis for the environmental exposure estimates provided in the environmental assessment.

ERM made the following assumptions for this assessment. It was assumed that the entire production volume of tobacco sticks is introduced to commerce and enters the environment. ERM further assumed that there is no metabolism or significant environmental depletion. These two assumptions are conservative. Formulation data are presented as percent composition. For example, in accordance with FDA environmental assessments for drugs, Environmental Introduction Concentrations (EICs) are based on product weight and projected units sold and calculated as a "per day" value. Air exposure values are calculated as a function of the surface area of the United States and a vertical dilution volume.

The EICs for the aquatic, atmospheric and terrestrial introductions posed by the tobacco stick have been calculated using conservative, literature-supported assumptions; formulation and production forecasting information provided to ERM by PMP S.A.; and relevant and available FDA guidance documents, including the equation given in the

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Guidance for Industry: Environmental Assessment of Drug and Biologics Applications, Section III.A.2 (July, 1998).

Potential misuse has been included in the assessments. Thus, for the aquatic compartment, the entire production volume was considered to enter the aquatic environment even though only a small proportion of some ingredients would actually enter the aquatic environment through human excretion or environmental transport. For the terrestrial assessment, the tobacco stick constituents should all be consumed or disposed of to landfill. However, some improper disposal may occur. Therefore, the impact of tobacco stick constituents to land is assessed as if the entire production volume is dropped, unused, onto the ground and distributed across the United States land surface area.

THD is an electronic device. The concept behind "heat-not-burn" is that heating tobacco, rather than burning it, reduces or eliminates the formation of many of the compounds that are produced at the high temperatures associated with combustion. Research has demonstrated that most of the harmful and potentially harmful constituents (HPHCs) in conventional cigarette smoke are formed by thermal decomposition of tobacco when it is burned (Smith 2016). The research concluded that combustion does not occur in the tobacco stick used with the THD for a variety of reasons, including that the temperatures in the tobacco stick (< 350°C) are below the temperature required to initiate combustion. The "heat-not-burn" principle therefore offers the possibility of significantly reducing both the number and the levels of HPHCs in the tobacco aerosol generated by THS as compared to conventional cigarette smoke. Exposure to ash was not considered because combustion does not occur.

ERM assumed that THS produces negligible waste. This waste is expected to consist primarily of tobacco stick components and their residual products. The amount of solid waste remaining from cleaning would be comparable to the solid waste remaining after smoking a cigarette and is expected to be minimal. This waste is expected to be disposed of as household solid waste. The reusable THD, when eventually discarded, would be managed as solid waste.

5.2.2.1 Composition of THS

5.2.2.1.1 Tobacco Stick Formulation

The THS Menthol Tobacco Stick comprises a tobacco blend, a tobacco ingredient package, outer paper, outer paper adhesive, plug wrap papers, plug wrap adhesives, filter material and mouth end paper.

The formulation of the tobacco stick is presented in the confidential environmental assessment of the THS Menthol Tobacco Stick (see Appendix A5.2.1); however, this information is considered to be Confidential Business Information (CBI).

5.2.2.1.2 Tobacco

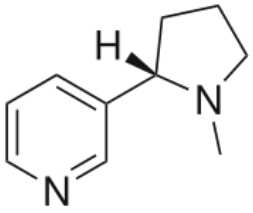
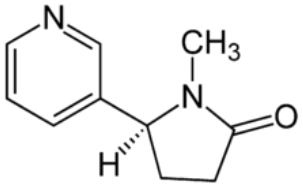
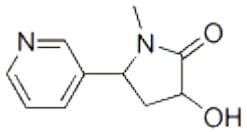
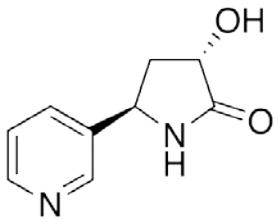
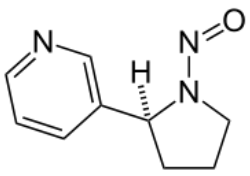
The total tobacco content and total nicotine content were reported for the THS Menthol Tobacco Sticks, and are also considered to be CBI. In general, tobacco comprises over 35% of a tobacco stick weight, and is itself composed of a complex assemblage of

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individual constituents (Roberts 2012). The vast majority of these constituents are typical phytochemical plant components (cellulosics, carbohydrates, phenolics) (Rosa 2010). Assessing the environmental impact of all of these constituents, most of which are non-specific to tobacco, would not be expected to change the overall conclusion of this assessment. Consensus reports indicate that the bioactive tobacco compounds in tobacco have been identified and are used to assess environmental health impact of tobacco *per se* (Lange 2010), (IARC 2007). These compounds are tobacco alkaloids including nicotine and related compounds and tobacco-specific nitrosamines. These substances are given in the following table.

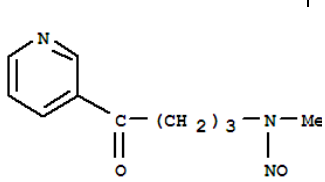
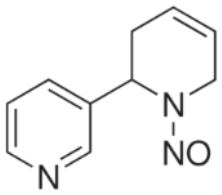
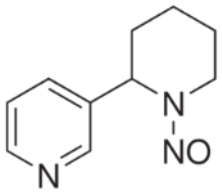
Table 1 Nicotine, Tobacco-Specific Nitrosamines, and Related Compounds

Substance	Chemical Descriptor	Structure
Nicotine	3-(1-Methyl-2-pyrrolidinyl)pyridine CAS 54-11-5	
Cotinine	(S)-1-Methyl-5-(3-pyridinyl)-2-pyrrolidinone CAS 486-56-6	
Trans-3'-hydroxycotinine	3-Hydroxy-1-methyl-5-(3-pyridinyl)-2-pyrrolidinone CAS 34834-67-8	
Norcotinine	2-Pyrrolidinone, 5-(3-pyridinyl)- CAS 17114-40-8	
N-nitrosonornicotine	3-(1-Nitroso-2-pyrrolidinyl)pyridine CAS 16543-55-8	

(table continues)

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Substance	Chemical Descriptor	Structure
4-methyl-N-nitrosamino-1-(3-pyridyl)-1-butanone	4-(Acetoxymethylnitrosamino)-1-(3-pyridyl)-1-butanone CAS 127686-49-1	
N-nitrosoanatabine	1,2,3,6-Tetrahydro-1-nitroso-2,3'-bipyridine CAS 119738-26-0	
N-nitrosoanabasine	(S)-3-(1-Nitroso-2-piperidinyl)pyridine CAS 1133-64-8	

The bioactivity of these compounds is illustrated by literature reports of some level of mutagenicity or carcinogenicity associated with each of them (IARC 2007); however, with the exception of nicotine, there are few data for their environmental impact.

5.2.2.1.3 Device

The THD comprises a holder and a pocket charger, and is sold with accessories such as an AC adaptor, a USB cable and a cleaner. In general, these components comprise plastic, metal, printed circuit board (PCB), tape, battery, wire, ink, ceramic, and glass materials.

5.2.2.1.4 Packaging

The packaging material in direct contact with the Tobacco Stick consists of an inner frame, an inner liner and, when the pack is opened, the hinge lid. These materials comprise paperboard, inks/varnishes, lacquer, adhesives, aluminum foil, and cardboard.

Further packaging material not in contact with the Tobacco Stick comprises plastic wrapping film and tear tape. Ten individual Tobacco Stick packs are packed in a cardboard box. Shipping cases are used during transport and display cartons might be used at the point of sales. Packaging material for the THD include plastic, cardboard, ink, film, glue and tape.

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5.2.2.2 Atmospheric Assessment

The smoking of cigarettes generates Environmental Tobacco Smoke (ETS). ETS is a combination of the sidestream smoke from the lit end of a cigarette and the smoke exhaled by smokers. Markers for ETS can be either non-specific [Respirable suspended Particles (RSP), carbon monoxide (CO), aldehydes] or specific [solanesol (Sol-PM), 3-ethenylpyridine (3-EP), nicotine].

By heating instead of burning, it is possible to substantially reduce or eliminate the formation of a large number of Harmful and Potentially Harmful Constituents (HPHCs). In addition, THS does not produce sidestream smoke, a major source of ETS. Consequently, the environmental aerosol from THS is significantly different than ETS in terms of impact on Indoor Air Quality.

Over the past years, multiple studies (Frost-Pineda 2008, Tricker 2009, Goujon-Ginglinger 2015) have compared indoor air quality for "heat-not-burn" products [electrically heated cigarette smoking systems (EHCSSs), THSs] versus cigarettes and have shown that levels of ETS constituents were substantially reduced and even absent in the environmental aerosols from "heat-not-burn" products. More specifically:

- Frost-Pineda 2008 compared the levels of certain compounds [RSP, CO, ammonia, Total Volatile Organic Compounds, Sol-PM, ultraviolet absorbing particulate matter (UVPM), fluorescent particulate matter (FPM), nicotine, 3-EP] in the air of a conference room under three circumstances: after test subjects smoked conventional cigarettes, after test subjects used a third-generation electrically heated cigarette smoking system (EHCSSs), and under no-smoking conditions. The use of EHCSS led to reduce concentrations of ammonia by 41% and concentrations of constituents of ETS by 87-99%. Concentrations of CO were in the same range as during non-smoking.
- Tricker 2009 compared the effects on indoor air of smoking conventional lit-end cigarette and an EHCSS in simulated "office" and "hospitality" environments. When the research team compared measurements of approximately 30 parameters made after smoking conventional cigarettes and after using EHCSS, the mean and standard deviation of the reduction of all analytes was 94 ± 4%.
- Goujon-Ginglinger 2015 compared the Indoor Air Quality before and after test subjects (adult smokers) smoked cigarette or used THS. Office, hospitality and residential was simulated as indoor environment using a dedicated facility under strictly controlled experimental conditions. Eighteen analytes were measured, respectively: ETS markers according to International Organization for Standardization (ISO): Respirable Suspended Particles (RSP-gravimetric), Ultra-Violet Particulate Matter (UVPM-THBP) ((2,2',4,4'-Tetrahydroxybenzophenone) equivalent), Fluorescent Particulate Matter (FPM-scopoletin equivalent), solanesol, 3-ethenylpyridine (3-EP), nicotine and constituents that are likely to be found in ETS and environmental Aerosols and/or are part of the FDA's abbreviated list of 18 HPHCs: carbonyls (acetaldehyde, acrolein, crotonaldehyde, formaldehyde), Volatile Organic Compounds (VOCs) (acrylonitrile, benzene, 1,3-butadiene, isoprene, toluene), gases (carbon monoxide, nitrogen oxide, nitrogen

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oxides). While levels of all eighteen analytes were drastically and significantly increasing when cigarette was smoked, the use of THS showed different results: only two compounds were measured systematically (irrespective of the condition) at levels above the ones measured before the use of THS. The two compounds were acetaldehyde and nicotine; however, their concentrations in environmental aerosols after use of THS were more than 1,000 times lower for acetaldehyde and 250 times lower for nicotine than air quality guidelines established by the United States Occupational Safety and Health Administration (OSHA) (Air Contaminants, 2016). In light of the above results, it can be concluded that THS does not produce ETS and has no negative impact on Indoor Air Quality.

One study did suggest that a larger number of VOCs were emitted at device activation and during device use, as compared to e-cigarettes (O'Connell 2015). However, this study did not quantify or qualify specific VOCs. The experimental set-up was based on a small chamber (approximately the size of a shoe box) connected to a Proton Transfer Reaction-Mass Spectrometer (PTR-MS). The PTR-MS technique is a soft ionization technique, without prior separation of compounds, potentially producing multiple peaks for single compounds by fragmentation. As a consequence, the reported results were neither quantitative nor did they provide an unambiguous identification of the detected peaks. Based on this limited information, no science based conclusions can be derived from this publication on the environmental impact of the THS.

The THD is a reusable and rechargeable device. The lifespan of the charger and holder is approximately one year, based on certain assumptions of daily consumption, tested and documented in the functional specifications. If and when the user does dispose of the device, it is expected to be disposed of as household solid waste. Packaging components will be disposed of by the user as household solid waste. Disposal of the device and packaging is not expected to result in significant atmospheric emissions.

That the THS does not produce sidestream smoke, combined with the expectation that there would be minimal exposure by animals in the natural environment to any emissions that did occur and lack of atmospheric emissions associated with disposal of the device and packaging, provides the basis for a Finding of No Significant Impact for this atmospheric environmental assessment of THS Menthol.

5.2.2.3 Terrestrial and Aquatic Assessments

This assessment focused on the components of the tobacco stick, based on the assumption that the THD and packaging will be responsibly managed as solid waste at the end of their useful life, and therefore will not pollute terrestrial or aquatic environments.

5.2.2.3.1 Nicotine as a Marker Compound

For evaluation of both the terrestrial compartment and the aquatic compartment, nicotine was used as a marker compound for tobacco that will enter these environments via excretion and leaching out of improperly disposed of new or used tobacco sticks.

Nicotine accounts for approximately 95% of the alkaloid content of tobacco (Lange 2010) with the remainder being made up of the nitrosamines and nicotine-related

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compounds from Table 1. In animals, these alkaloids have been reported to be pharmacologically active but less so than nicotine. Thus, we used nicotine as a marker compound to represent the toxicity of the alkaloid substances in tobacco in the terrestrial and aquatic environments. This is a conservative assumption because nicotine is more pharmacologically active than the remaining alkaloid substances.

With the exception of nicotine, there are few data on the toxicity of these alkaloids to terrestrial or aquatic organisms. Quantitative Structure Activity Relationships (QSARs) have been used to describe the physical-chemical properties of these materials and to provide predicted aquatic toxicity values to support the use of nicotine as a marker compound. Acceptable QSARs are not available to predict toxicity to terrestrial organisms. All QSAR predictions were determined using the Environmental Protection Agency's (EPA's) EpiWeb 4.1.[1] Note that the fate and toxicity predictions for nicotine were based on pure nicotine. Nicotine in tobacco is in a complex matrix from which nicotine and other alkaloids are extracted. The actual availability and exposure to nicotine will be reduced by the matrix (i.e., the tobacco leaf).

5.2.2.3.1.1 Physical-Chemical Properties

The physical-chemical properties of nicotine (CAS 54-11-5) and its metabolites are presented in Table 2. Nicotine's physical-chemical properties can be used to determine the fate of nicotine introduced into the environment.

Nicotine introduced into the water will stay mainly in water and will not readily partition to the air based on its low Henry's Law Constant ($3x10^{-9}$ atm-m^3/mole), and negative air/water partitioning coefficient (K_{aw} = -6.911). Nicotine in water should not bioaccumulate or bioconcentrate in aquatic organisms (measured Log K_{ow} = 1.17) (Hansch 1995). The predicted bioconcentration factor (log BCF) for nicotine of 0.44 supports this conclusion.

Nicotine introduced into the soil can volatilize to air based on a vapor pressure of 0.032 mm Hg (Boublik 1984). However, the extent to which it actually volatilizes will depend on its sorption. The log K_{oc} predicted at neutral pH is 2.72 and indicates that nicotine in soil has moderate mobility. The mobility of nicotine, a weak acid (pK_a 8.5), is pH dependent and will increase at alkaline pH. Because nicotine is highly soluble (predicted solubility $1.00x10^6$ mg/L) and has a negative K_{aw}, it will most likely partition to soil pore-water rather than air.

[1] The EPI (Estimation Programs Interface) Suite™ is a Windows®-based suite of physical/chemical property and environmental fate estimation programs developed by the EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). EPI Suite™ uses a single input to run the following estimation programs: KOWWIN™, AOPWIN™, HENRYWIN™, MPBPWIN™, BIOWIN™, BioHCwin, KOCWIN™, WSKOWWIN™, WATERNT™, BCFBAF™, HYDROWIN™, KOAWIN and AEROWIN™, and the fate models WVOLWIN™, STPWIN™ and LEV3EPI™. ECOSAR™, which estimates ecotoxicity, is also included in EPI Suite™.

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Table 2 Physical-Chemical Properties of Tobacco Specific Nitrosamines, Nicotine and Related Compounds

CAS	Name	Water Solubility	Vapour Pressure	Henry's Law Constant	Log K_{ow}	log K_{oc}	Log K_{oa}	Log K_{aw}	BCF	Photo-chemical half-life	Half-life in water	Half-life in soil
		mg/L	mm Hg	atm-m^3/mol						hrs	days	days
54-11-5	3-(1-Methyl-2-pyrrolidinyl)pyridine	1.00E+06	0.032	3.00E-09	1.00	2.72	8.08	-6.91	0.44	1.41	37.5	75
486-56-6	(S)-1-Methyl-5-(3-pyridinyl)-2-pyrrolidinone	9.99E+05	3.81E-04	3.33E-12	0.34	2.11	8.04	-8.04	0.50	4.90	37.5	75
34834-67-8	3-Hydroxy-1-methyl-5-(3-pyridinyl)-2-pyrrolidinone	1.00E+06	2.16E-07	5.20E-13	-1.20	1.01	9.19	-10.67	0.50	4.30	37.5	75
171140-40-8	2-Pyrrolidinone, 5-(3-pyridinyl)-	1.00E+06	1.66E-05	1.52E-12	-0.30	2.10	9.90	-10.27	0.50	7.99	60	120
16543-55-8	3-(1-Nitroso-2-pyrrolidinyl)pyridine	6.03E+05	5.12E-04	1.97E-10	0.32	3.20	8.48	-8.16	0.50	5.40	60	120
127686-49-1	4-(Acetoxymethylnitrosamino)-1-(3-pyridyl)-1-butanone	5.04E+03	5.13E-07	3.00E-14	0.69	2.19	12.60	-11.91	0.50	4.20	60	120
119738-26-0	1,2,3,6-Tetrahydro-1-nitroso-2,3'-bipyridine	3.06E+05	6.04E-05	1.97E-10	0.60	3.47	8.69	-8.09	0.50	1.43	60	120
1133-64-8	(S)-3-(1-Nitroso-2-piperidinyl)pyridine	1.96E+05	6.68E-05	8.58E-11	0.81	3.47	8.85	-8.03	0.50	3.38	60	120

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5.2.2.3.1.2 Degradation

Nicotine lacks hydrolyzable groups and therefore will not undergo abiotic hydrolysis. However, nicotine has the potential to undergo direct photolysis. Nicotine's electronic absorption spectrum shows an intense absorption band at 260-262 nanometers (nm) with some absorption above 290 nm (toward sunlight spectral region) (Sangster 1965). The predicted photochemical half-life for nicotine in air is 1.4 hours (hrs). Nicotine can also degrade in surface waters via indirect photolysis by naturally occurring photosensitizers such as dissolved organic matter and hydroxyl radicals. Thus, indirect photolysis can play an important role in the degradation of nicotine.

Biotransformation of nicotine in soils and water-sediment systems has been documented. In soils, nicotine is oxidized by the bacteria *Arthrobacter oxydans* (now known as *Arthrobacter nicotinovarans*) (Hochstein 1959). The relative amounts and conditions of biotransformation will vary with soil and bacterial populations. The nature of the transformation in soil is not as well defined as those in animals. It has been demonstrated *in vitro* that the first metabolite of nicotine is 6-hydroxynicotine which further breaks down to 6-hydroxypseudonicotine (oxynicotine) and other compounds (Hochstein 1959). Cotinine, which is a major oxidation product of nicotine in the liver, has not been reported to form in soils.

Nicotine and cotinine have been reported to biotransform in soils (Bradley 2007). Under oxidizing conditions nicotine and cotinine degrade completely to CO_2 within 72 days. Under anoxic conditions the biotransformation of nicotine and cotinine are slower. EpiWeb 4.1 predicts half-lives of 37.5 days for nicotine and cotinine in water and 75 days in soil.

Data on the transformation products or metabolites of nicotine are very limited. In order to have a common frame of reference, we compared the predicted values for nicotine to the predicted values for the metabolites. Predicted physical-chemical properties of nicotine metabolites and transformation products are similar to those of nicotine. Predicted log K_{ow} values range from -1.2 to 0.998. Predicted log K_{oc} ranges from 1.01 to 3.47. Predicted water solubilities range from 5.04 $x10^3$ to $1.00x10^6$ mg/L, with nicotine being among the more soluble substances. Predicted Henry's Law Constants range from $3.0x10^{-9}$ to $3.0x10^{-14}$ atm-m^3/mole for nicotine and related compounds. Predicted photochemical half-lives range from 1.41 to 7.99 days for nicotine and related compounds. Predicted half-lives in water are all less than 60 days and half-lives in soil are predicted to be less than 120 days. Thus, the fate and transport of these compounds is expected to be quite similar.

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5.2.2.3.1.3 Toxicity

Tobacco (*Nicotiana tabacum, Nicotiana rustica, Nicotiana* spp.)[2] is a member of the nightshade family (*Solanaceae*). This family also includes potatoes, tomatoes, eggplant and peppers. Members of the *Solanaceae* family contain alkaloids that can be desirable, toxic, or both. The predominant alkaloid in tobacco is nicotine. Other alkaloids and nicotine degradation products are present in lesser amounts. QSAR analysis and some limited data indicate that these compounds are of lesser toxicity than nicotine, supporting the use of nicotine as a conservative marker compound for tobacco.

QSAR predictions in Table 3 were used here as a basis of comparison among the compounds and should be taken as qualitative rather than quantitatively definitive. Equations for different classes of compounds used to develop the ECOSAR model within OECD Toolbox V2.38 (OECD 2012) are of differing reliabilities depending on the dataset used to develop the equation.

Table 3 Acute Aquatic Toxicity of Tobacco-Specific Nitrosamines, Nicotine and Related Compounds

CAS	Name	Algal 96-hr EC_{50}	Daphnia 48-hr - EC_{50}	Fish 96-hr LC_{50}
		mg/L	mg/L	mg/L
54-11-5	3-(1-Methyl-2-pyrrolidinyl)pyridine	44.70	0.20	4.86
486-56-6	(S)-1-Methyl-5-(3-pyridinyl)-2-pyrrolidinone	17.80	1920.00	811.00
34834-67-8	3-Hydroxy-1-methyl-5-(3-pyridinyl)-2-pyrrolidinone	176.00	53500.00	11100.00
171140-40-8	2-Pyrrolidinone, 5-(3-pyridinyl)-	22.20	2750.00	1060.00
16543-55-8	3-(1-Nitroso-2-pyrrolidinyl)pyridine	131.00	0.22	8.66
127686-49-1	4-(Acetoxymethylnitrosamino)-1-(3-pyridyl)-1-butanone	42.50	38.00	372.00
119738-26-0	1,2,3,6-Tetrahydro-1-nitroso-2,3'-bipyridine	93.30	0.23	7.57
1133-64-8	(S)-3-(1-Nitroso-2-piperidinyl)pyridine	69.00	0.24	6.55

Predicted algal 96-hr EC_{50} values range from 17.8 mg/L to 176 mg/L. The EC_{50} for nicotine (CAS 54-11-5) is 44.7 mg/L. While not predicted to be the most toxic compound, nicotine toxicity is within a factor of 2 of the most toxic compounds and likely not significantly different (i.e., within the confidence limits of the prediction). Measured 96-hr EC_{50} values for the toxicity of nicotine to the alga Selenastrum capricornutum were 72.9 mg/L for growth and 115 mg/L for biomass (Seckar 2008). The predicted EC_{50} values for nicotine were lower than the measured values but within a factor of 2.

The predicted 48-hr EC_{50} of nicotine to *Daphnia* is 0.2 mg/L. Predicted toxicity values for the nicotine metabolites range from 0.22 mg/L to 53,500 mg/L. The measured EC_{50} value for *Daphnia pulex* is 0.24 mg/L (Savine 1989).

[2] The focus of this EA is on the *tabacum* and *rustica* species.

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The predicted fish 96-hr LC_{50} for nicotine is 4.86 mg/L. The predicted LC_{50} values for metabolites of nicotine range from 6.55 to 11,100 mg/L. The measured 96-hr LC_{50} value for nicotine toxicity to *Oncorhynchus mykiss* larvae is 4 mg/L (Edsall 1991).

5.2.2.3.2 Terrestrial Assessment

5.2.2.3.2.1 Tobacco Stick

The tobacco sticks should be consumed prior to disposal in a landfill. However, some improper disposal of unused tobacco sticks could occur. Therefore, a terrestrial assessment has been calculated for the tobacco stick components which assumes that they, in their entirety, are improperly disposed of to the terrestrial environment.

In calculating the terrestrial EICs, ERM assumed that the entire production volume was introduced to commerce and entered the terrestrial environment. ERM further assumed that there was no metabolism or significant environmental depletion.

The terrestrial EICs presented as a production tonnage distributed across the surface area of the United States (nanograms per square meter per day, or ng/m^2) range from 0.005 ng/m^2 to 194.990 ng/m^2as determined using the following calculation:

EIC-terrestrial (ng/m^2) = A*B*C*D*E; where A = mg/yr produced, B = $1/9.158x10^6$ km^2 surface area of the United States, C = year/365, D = 10^{-6} km^2/m^2, E = 10^6 ng/mg

The single tobacco stick component mass values range from 0.005 mg to 217.285 mg. Actual exposure concentrations will be somewhere between the EIC calculated based on the surface area of the United States (ng/m^2) and the tobacco stick mass value (mg). The tobacco stick, when properly disposed of, will go to landfill and not directly to the terrestrial environment.

Assuming a vertical dilution depth of 1 foot in soil (0.305 meters) and a default soil bulk density of 1.1 megagrams per cubic meter (Mg/m^3), EICs in ng/m^2 can be converted to units of ng/kg according to the following equation:

$$\text{EIC } (ng/m^2) \times \frac{1}{\text{Soil Bulk Density } (Mg/m^3)} \times \frac{1}{\text{Soil Depth (m)}} \times \frac{\text{Mg soil}}{\text{1000 kg soil}} = \text{EIC (ng/kg soil)}$$

The maximum terrestrial EIC of 194.990 ng/m^2 represents a soil concentration less than 1 ng/kg (less than one part per trillion). One foot dilution depth may be a high estimate, but even assuming a smaller mixing zone would not produce estimates of concern. Therefore, all terrestrial EIC values represent very low environmental concentrations, below potential levels of concern in the terrestrial environment.

5.2.2.3.2.2 Tobacco

According to the analysis presented above, the environmental impact of tobacco was assessed as nicotine. The terrestrial EIC value for nicotine was calculated as production tonnage distributed across the surface area of the United States (ng/m^2).

The EIC for nicotine in the THS Menthol Tobacco Stick distributed across the surface area of the United States was < 5 ng/m^2. For a single tobacco stick, the mass of nicotine

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is < 5 mg. These values represent the direct disposal of the tobacco stick to the environment. In this case, the actual concentration of nicotine that is disposed of to the terrestrial environment would be somewhere between the concentration distributed across the United States and the single tobacco stick mass. It is unlikely that tobacco sticks would be routinely disposed of to the terrestrial environment.

When managed properly, the waste from the THS Menthol Tobacco Stick will be disposed of to landfill. Nicotine that is released directly to the terrestrial environment as leachate from tobacco sticks will provide a variable exposure concentration due to differences in the habits of individual consumers. Nicotine that ends up on the ground will not sorb strongly to the soil (log K_{oc} = 2.72) and will migrate to the soil pore-water. Nicotine has been shown to be biodegradable in both water and soil (Bradley 2007). Therefore, the exposure to nicotine from an intermittent release will decrease over time.

Toxicity data that present LD_{50} values for terrestrial invertebrates were of limited availability. Because nicotine has a history of use as a pesticide, it is expected that terrestrial invertebrates will be very sensitive to nicotine. A study by Rizvi 1990 reported that the 24-hr LD_{50} of nicotine dust was 7.2 µg/nymph for *Dysdercus koenigii (Fabr.)*. Additional toxicity data are included on dermal toxicity to the brown tree snake, oral toxicity to rats, and dermal toxicity to rabbits. Dermal toxicity to the brown tree snake (*Boiga irregularis*) is reported as 40 mg/kg, a dose that killed 100% of snakes (Brooks 1998). The oral LD_{50} dose for nicotine in rats is 50 mg/kg to 60 mg/kg (Klaasen 1995). The dermal LD_{50} in rabbits is reported as 140 mg/kg (Lewis 1996).

In summary, the EIC (ng/m^2) for nicotine disposed of to the terrestrial environment as calculated based on the surface area of the United States is at a sub-nanogram per meter squared level and is therefore not expected to pose an environmental risk.

The mass of nicotine disposed of to the terrestrial environment in a localized area by a single tobacco stick could cause some local adverse effects on terrestrial organisms. However, adverse effects are highly unlikely for the following reasons: 1) the nicotine released from a single tobacco stick disposed of outside of a landfill is expected to be localized, 2) the paper, tobacco and nicotine would be decomposed by microbes resulting in decreasing concentrations over time, 3) rainfall would release the nicotine from the tobacco stick but also dilute the nicotine and transfer it into the groundwater for further dilution, 4) the physical-chemical properties of the nicotine indicate that it would not sorb to the sediments or accumulate in organisms. All of these factors indicate that any potential for effects would be localized, limited and would improve over time without the likelihood of additional inputs of nicotine to the same location.

5.2.2.3.2.3 Device

The THD is a reusable and rechargeable device. The lifespan of the charger and holder is approximately one year, based on certain assumptions of daily consumption, tested and documented in the functional specifications. If and when the user does dispose of the device, it is expected to be disposed of as household solid waste.

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5.2.2.3.2.4 Packaging

Packaging components will be disposed of by the user as household solid waste.

ERM herewith provides the basis for a Finding of No Significant Impact for this terrestrial environmental assessment of THS Menthol.

5.2.2.3.3 Aquatic Assessment

5.2.2.3.3.1 Tobacco Stick

In calculating the EICs for the tobacco stick, ERM assumed that the entire production volume was introduced to commerce, entered the publicly owned treatment works (POTW) system, and that there was no metabolism or significant environmental depletion in the wastewater treatment process.

The annual aquatic EICs for non-tobacco constituents of the tobacco stick were presented both as an annual load (kg/yr) and as an aquatic EIC (µg/L) in the environmental assessment of the THS Menthol Tobacco Stick; however, this information is considered to be CBI and therefore is not provided in this supplemental summary. The calculations used were as follows:

(mass/tobacco stick)x(annual production forecast)x(relative amount in formulation)

EIC-aquatic (ppb or µg/L)=A*B*C*D; where A=kg/yr produced, B=1/1.214x1011 L/day entering POTW (Source: 1996 Needs Survey, Report to Congress), C=year/365, D=109 µg/kg

ERM noted that for all substances except five, the EICs for the THS Menthol Tobacco Stick ingredients are less than 1 µg/L at the point of entry into the aquatic environment. The substances with aquatic EICs greater than 1 µg/L have either no known toxicity or potential effect thresholds that are multiple orders of magnitude above the aquatic EIC. Therefore, all aquatic EIC values represent very low environmental concentrations, below potential levels of concern in the aquatic environment.

5.2.2.3.3.2 Tobacco

According to the analysis presented above, the environmental impact of tobacco was assessed as nicotine. The estimated aquatic EIC for nicotine in the THS Menthol Tobacco Sticks is < 0.4 µg/L. This is orders of magnitude less than any toxicity figure of note in Section 5.2.2.3.1.3.

5.2.2.3.3.3 Device

The THD is a reusable and rechargeable device. The lifespan of the charger and holder is approximately one year, based on certain assumptions of daily consumption, tested and documented in the functional specifications. If and when the user does dispose of the device, it is expected to be disposed of as household solid waste.

5.2.2.3.3.4 Packaging

Packaging components will be disposed of by the user as household solid waste.

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ERM herewith provides the basis for a Finding of No Significant Impact for this aquatic environmental assessment of THS Menthol.

5.2.3 Attachments

As a final measure of substantiation for the minimal environmental risk associated with the use of these substances, ERM has included in the CONFIDENTIAL ATTACHMENT (see Appendix A5.2.1) a brief summation of the available physico-chemical properties, toxicity and ecotoxicology for the substances contained in THS Menthol.

5.2.4 Conclusion

ERM herewith provides the basis for a Finding of No Significant Impact for this environmental assessment of THS with the THS Menthol Tobacco Sticks due to *de minimis* exposure and from a safety (i.e., ecotoxicity) perspective.

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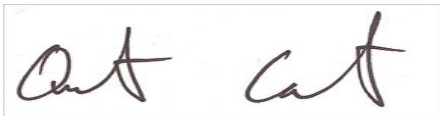
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5.2.6. CERTIFICATION

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