The attached document represents CTP's then-current thinking on certain aspects of tobacco regulatory science. The information contained herein is subject to change based on advances in policy, the regulatory framework, and regulatory science, and, is not binding on FDA or the public. Moreover, this document is not a comprehensive manual for the purposes of preparing or reviewing tobacco product applications. FDA's review of tobacco product applications is based on the specific facts presented in each application, and is documented in a comprehensive body of reviews particular to each application.

Given the above, all interested persons should refer to the Federal Food, Drug, and Cosmetic Act, and its implementing regulations, as well as guidance documents and webinars prepared by FDA, for information on FDA's tobacco authorities and regulatory framework. This document does not bind FDA in its review of any tobacco product application and thus, you should not use this document as a tool, guide, or manual for the preparation of applications or submissions to FDA.

MEMORANDUM

Date: February 12, 2014

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Date: 2014.02.12 07:09:25 -05'00'

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Subject: Distribution of Menthol in Cigarettes and Smoke Transfer

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Background

The Federal Food, Drug, and Cosmetic Act (FD&C Act) provides a pathway for tobacco product manufacturers to introduce new tobacco products into interstate commerce by establishing that they are substantially equivalent (SE) to appropriate predicate products under section 905(j) of the FD&C Act. Menthol is considered a characterizing flavor in menthol cigarettes.[1] All characterizing flavors in cigarettes with the exception of menthol have been banned under section 907(a)(1)(A) of the FD&C Act. During the scientific review of SE Reports for menthol cigarettes by the CTP's Office of Science, several questions have been raised about the differences in the new and predicate products related to menthol:

- What are the effects of different menthol application methods on the menthol delivery of the products?
- How does menthol added to different parts of the cigarette equilibrate among the components of the product?
- What is the impact of product aging on the delivery of menthol in the mainstream smoke?
- Should the menthol smoke data be required for the SE determination of menthol cigarettes?

This memo attempts to address the above questions by providing an overview of the current scientific information of menthol distribution and smoke transfer in menthol cigarettes and an assessment of relevant scientific evidence on the topic. Recommendations are also made with regard to approaches for the scientific review of SE Reports involving menthol cigarettes.

Intrinsic Properties of Menthol

Menthol is a monocyclic terpene alcohol, either derived from natural sources or synthesized. It can exist as one of eight stereoisomers, each of which has distinct pharmacologic characteristics.[1,2,3] Menthol occurs generally as *l*-menthol, which displays the typical taste and sensory characteristics of menthol. Different types of natural menthol from various sources have distinctly different taste properties due to the different levels of minute quantities of impurities in each type.[3] The d isomer, *d*-menthol, lacks the minty character which U.S. menthol smokers highly desire. Synthetic menthol (*dl*-menthol) is a racemic mixture and exhibits about half of the cooling properties of *l*-menthol.[2] Both *l*-menthol and *dl*-menthol are used in tobacco products while *d*-menthol is only used for scientific purposes.

The enantiomeric isomers of menthol are considered to have similar physicochemical and toxicological properties.[4,5] Menthol has a melting point of 41-43°C, a boiling point of 212°C, and a vapor pressure of 0.0637 mm Hg (25°C), indicating that menthol is highly volatile. Menthol is soluble in ethyl alcohol and organic solvents, but only slightly soluble in water. Menthol has an estimated Henry's law constant of $1.5x10^{-5}$ atm-m^3/mole and is expected to be volatile from aqueous solution.[4] A furnace pyrolysis study of pure *dl*-menthol showed that menthol can undergo pyrolytic conversion at the burning temperatures of cigarettes (800 - 900°C).[6] At 860°C, only 16% of the menthol was recovered intact with pyrolysis products including PAHs, phenol, benzene, toluene, and vinyl methylcyclohexanone. While at a lower temperature of 600°C, 78% of the menthol was recovered intact, with no PAHs detected. It has been speculated that "extrapolation of this trend downward to the range of the boiling point of menthol (212°C) indicates that essentially all menthol applied to cigarette tobacco might be expected to volatilize intact in the temperature gradient of the heated zone ahead of the cigarette's advancing burning cone."[2]

Application of Menthol to Cigarettes

Menthol is present at varying levels in 90% of all tobacco products currently on the market, including cigarettes that are not marketed as menthol cigarettes.[1] According to a public submission from Lorillard to the FDA's Tobacco Products Scientific Advisory Committee (TPSAC),[7] menthol at levels around 0.1% (1000-ppm) of cigarette tobacco or higher provides a characterizing flavor. A study conducted by Brown & Williamson showed that 10 to 20% of U.S. menthol smokers can detect a relative difference of ±10% in a cigarette's menthol levels.[3]

Menthol concentrations in non-menthol cigarettes average about 0.01 to 0.03%.[8] Based on a Philip Morris USA menthol market study of 64 U.S. menthol cigarette brands marketed in 2008 and 2009,[9] the average menthol content in menthol cigarettes was found to be 0.7%, expressed as percent of tobacco weight, with a range from 0.3% - 1.6%. A recent CTP-funded CDC study of menthol cigarettes for 23 brands currently available in the U.S. market revealed that the menthol content in most of the examined menthol cigarettes ranges from 2.9 to 7.2 mg/cig with an average menthol content of 4.8 mg/cig,[10] which is comparable with the Philip Morris USA data.[9] In addition, the CDC study found that the measured menthol contents appear to be higher than the reported quantities submitted by manufacturers under section § 904(a)(1) of the FD&C Act for ingredient submissions for five of the cigarette products tested. This is not unexpected as it is well known that manufacturers frequently apply menthol at higher levels than the targeted menthol levels in the finished cigarettes to compensate for menthol lost due to evaporation during processing, manufacturing, packaging, and storage.[7]

According to public submissions to the FDA's TPSAC from tobacco companies,[7,8,11] typical methods of application of menthol to produce menthol cigarettes involve an alcohol-based menthol solution sprayed on tobacco cut filler and/or inner pack foil, or the application of mentholated triacetin to cellulose acetate filter tow during filter manufacturing, or a combination of both. The spray solution also usually contains the ingredient glycol to stabilize or retard the evaporation of the menthol after the cigarette package has been opened.[12]

Some new application methods may also be used such as insertion of a crushable capsule in the filter and placement of a menthol thread in the filter. Currently, Camel Crush is such a product on the market. In this case, menthol is not available for migration or loss to evaporation during the storage. Lorillard stated that it has researched the newer application methods for menthol, but determined that these methods resulted in less consistency and affected the menthol taste of the cigarette.[7]

Distribution of Menthol in Cigarettes

It is common knowledge in the tobacco industry that menthol is distributed among the components of a cigarette and the packaging during storage, irrespective of where it was applied.[12] The migration of menthol takes place through the vapor phase as a result of menthol's high vapor pressure. After the tobacco rod is combined with a filter to make a cigarette and put in a pack, the menthol immediately begins to distribute itself among the components of the cigarette and the packaging materials. It migrates steadily from the point of application within the cigarette until equilibrium is achieved between the menthol in the filter and the menthol in the tobacco rod. It is reported that some menthol will reside on the paper or packaging material, but the amount is small (< 5%) and does not change with time.[13] In addition, menthol can diffuse out of the packs through the packaging material and seams during storage. A study by Eastman Chemical Company showed that only small amounts of menthol were lost from cigarette packs stored over 300 days.[14]

A number of studies on menthol migration and smoke transfer in cigarettes were published in the 1970s and 1980s[15,16,17,18,19,20] and have been the subject of an R.J. Reynolds' internal training course[21] and review articles.[13,14] Based on these studies, there are a number of cigarette design parameters that can influence menthol's migration in a cigarette. The final distribution of menthol is determined by the relative affinities for menthol of the cigarette components. Solubility of menthol is thought to be the determining factor in the rate and the level of mass transfer of menthol in a cigarette component. The primary driving force for menthol to migrate to the filter is the plasticizer used in the filter tow, which increases the solubility of menthol in the filter for menthol and/or the rate of menthol diffusion into the fibers. It was found that the solubility of menthol in cellulose acetate based filter tow is appreciably greater than that in tobacco. Figure 1 shows that the presence of 7% triacetin significantly increased the amount of menthol on the filter compared to no plasticizer.

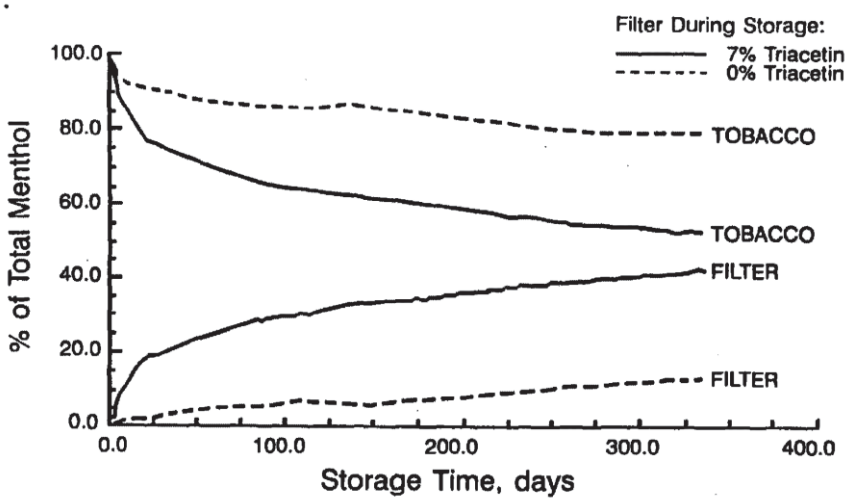


Figure 1. Menthol Distribution Between Tobacco Filler and Filter in Mentholated Cigarettes as a Function of Time (Source: Wilson 1993)

The amount and rate of menthol migrate to the filter are dependent mainly on the weight of the filter, the amount of plasticizer used, and the type of plasticizer used. In addition, it was found that the filter's affinity for menthol increased with denier per filament and total denier. The use of the humectant, 1,2-propanediol, in the filter has been shown to increase the rate of migration of menthol from the tobacco filler to the filter.[18]

The type of tobacco blend used can also affect menthol distribution.[3,14] It has been found in an R.J. Reynolds' study that different tobacco types have different affinities for menthol (oriental > flue-cured > burley > expanded burley/flue-cured blend > reconstituted sheet) that result in different rates of menthol migration to the filters or cigarettes made from a single tobacco type.[14] Unlike most non-menthol cigarettes, menthol cigarettes usually contain more flue-cured and less burley tobacco, along with reconstituted tobacco made without added ammonia. The effect of moisture is not clear at this time, although it does not appear to be important feature in driving the transfer of menthol probably due to the low solubility of menthol in water.

According to data published by industry in the 1970s and 1980s, the time at which menthol distribution between the tobacco filler and the cigarette filter reached equilibrium appears to be in the range of approximately 9 to 11 months. The projected menthol content in the filter at the distribution equilibrium in these earlier studies ranged from 30% to 50% of the total menthol in a cigarette. Based on the data from a more recent Philip Morris USA study,[9] the average amount of menthol in the filter was found to be ~ 35% of the total menthol in the cigarettes. On the other hand, a study of six (6) menthol cigarette brands marketed in China found that the menthol content in the tobacco filter accounts for 63 - 88% of the total menthol.[22] Therefore, the distribution of menthol among the cigarette components is product-specific (*i.e.*, depending on specific product design) and likely dependent on the time and conditions of storage. Since menthol's vapor pressure is affected by its environment and/or surroundings, any change in a component of a cigarette which would affect the vapor pressure of menthol will influence the migration rate and equilibrium level of menthol in menthol cigarettes.

Smoke Transfer of Menthol in Cigarettes

A tobacco cigarette column is degraded by combustion and pyrolysis during smoking.[12,13] Figure 2 illustrates the processes in a burning cigarette during puffing. Combustion (Zone A) occurs at the end and sides of the fire cone due to the availability of oxygen. Pyrolysis and distillation (Zone B) occur between the fire cone and the tobacco column throughout cigarette puffing because of the higher temperature (800 - 900°C) of the gases and the lack of oxygen. During puffing of the lit cigarette, menthol is vaporized into the mainstream smoke by the heat of the coal of the lit cigarette. Between puffs, menthol is vaporized into the sidestream smoke. In addition, there is filtration and condensation onto the tobacco column, as well as filtration and condensation by the filter tip.

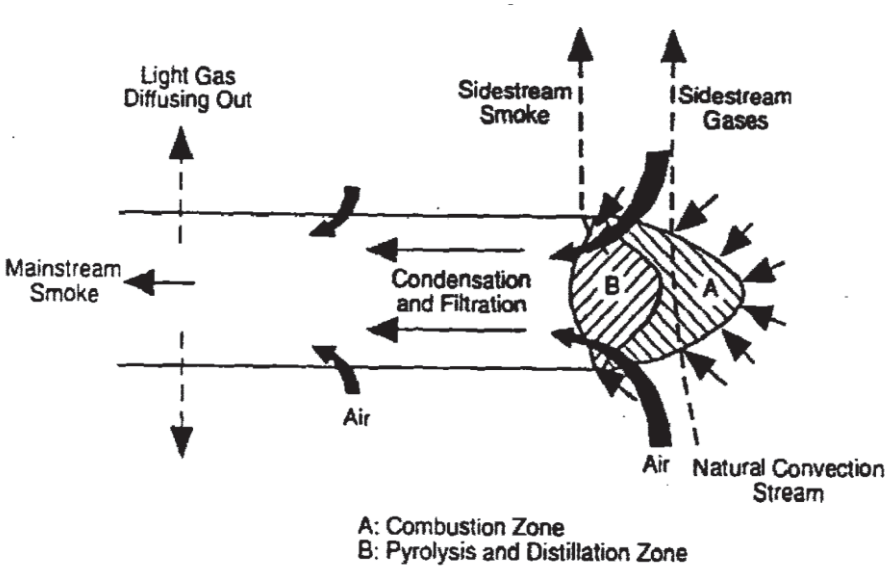


Figure 2. Processes in a Burning Cigarette During Puffing (Source: Wilson 1993)

A Philip Morris USA ^{14}C-menthol study conducted on unfiltered 70-mm cigarettes has been frequently cited by tobacco industry researchers as evidence for the fate of menthol

in cigarettes during smoking.[23] The study claimed that the mainstream smoke contains 29% of total radioactivity from menthol with 44% in the sidestream smoke and 27% in the unburnt cigarette butt (20 mm). The major ^{14}C-menthol smoke product in the mainstream smoke is unchanged menthol (98.9%) with little pyrolysis or decomposition (< 0.5%). The vast majority of menthol in mainstream smoke was found in the particulate phase, with only approximately 1% found in the vapor phase. It was hypothesized that an efficient vaporization of intact menthol, *i.e.,* distillation, had occurred in the heated zone just proximal to the pyrolysis zone. In this study, ^{14}C-menthol was spiked into the tobacco column using a syringe. In addition, the exact composition of the tobacco blend is unknown. It is likely that menthol was deposited on the surface of the tobacco and readily vaporized upon heating. It is possible that menthol is deeply absorbed into the tobacco and can still undergo pyrolysis in Zone B as shown in Figure 2, where high temperatures that can lead to menthol thermal decomposition exist.[6] Nevertheless, there does not appear to be evidence that menthol undergoes significant degradation under cigarette burning conditions. Additional studies with filtered cigarettes may be warranted to verify the Philip Morris USA finding by determining the effects of menthol absorption in tobacco on the extent of menthol pyrolysis during smoking of menthol cigarettes.

Menthol is a low-melting solid with high vapor pressure in the pure state and is believed to distribute itself between the particulate and the vapor/gas phase of the mainstream smoke.[12,13] Menthol has a high affinity for the substrates of the filter and can be removed from the mainstream smoke at a rate greater than that predicted from the tar removal efficiency, and this is known as "selective" filtration. Menthol can also dissolve in acetate filter fibers and diffuse away from the surface of the filter tow resulting in it no longer being available for elution or direct transfer to smoke.

Cigarette aging studies conducted by the tobacco industry have showed that total smoke menthol delivery from filtered cigarettes depends on the age of the products.[13,14,21] When menthol was first applied to the tobacco column, its smoke delivery increased initially with age until approximately 30 days and then leveled out and began to slightly decrease through 5-6 months of aging as a result of menthol migrations, both between the various components in the cigarette pack and out of the pack. A three-phase model was proposed to describe the smoke transfer efficiency of menthol in filtered cigarettes (defined as the ratio of menthol in the mainstream smoke to menthol in the cigarettes), as a function of cigarette aging time (see Figure 3.)[21] The model represented by a solid curve in Figure 3 depicts the profile of transfer efficiency for cigarettes when menthol is applied to the tobacco filler first. This model proposed by Perfetti illustrates that menthol delivery would shift to the left (dotted curve), if some menthol is added initially to the filter instead of the tobacco filler. During Phase I, little or no menthol is present in the filter and high filter efficiency for menthol results in low menthol delivery to the mainstream smoke. Menthol is removed as part of the particulate phase as well as through selective-filtration by the filter plasticizer. As menthol migrates to the filter and effectively decreases the cigarette filtering efficiency (selective removal) for menthol which results in greater transfers to mainstream smoke and eventually reaches a steady state in Phase II. In Phase III, menthol delivery decreases as some of menthol ultimately becomes absorbed into the filter tow or tobacco, such that the absorbed menthol is no longer available to be

transferred to the mainstream smoke. It is believed that preloading filters with menthol would eliminate or greatly reduce the effects of Phase I by shifting the transfer profile to the left as shown by the dotted curve in Figure 3. However, Phase III would occur at a much earlier life span of the cigarette. Therefore, proper aging or shelf-life is a critical factor in cigarette design of menthol cigarettes.

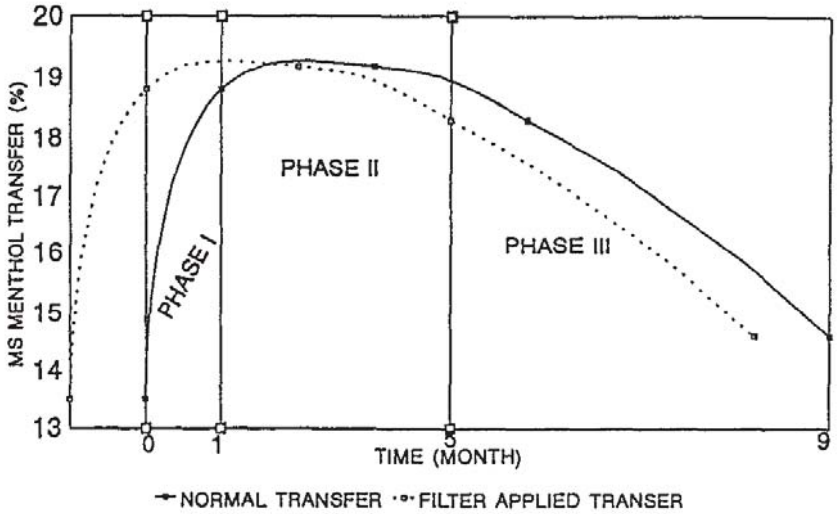


Figure 3. Proposed Model of Menthol Smoke Transfer for Filtered Cigarettes (Source: Perfetti 1985)
[solid curve: menthol applied to tobacco only; dotted curve: portion of menthol applied to filter]

Because of the low utilization and decreasing delivery of menthol with time, the studies reported include a possible means to improve efficiency of its use and stability of delivery. One method proposed is to apply some portion of the menthol to the filter as a solution in the plasticizer. One of these published studies showed that a menthol cigarette that had menthol applied to the filter, delivered menthol more efficiently than one that had menthol applied to the tobacco (see Figure 4).[17]

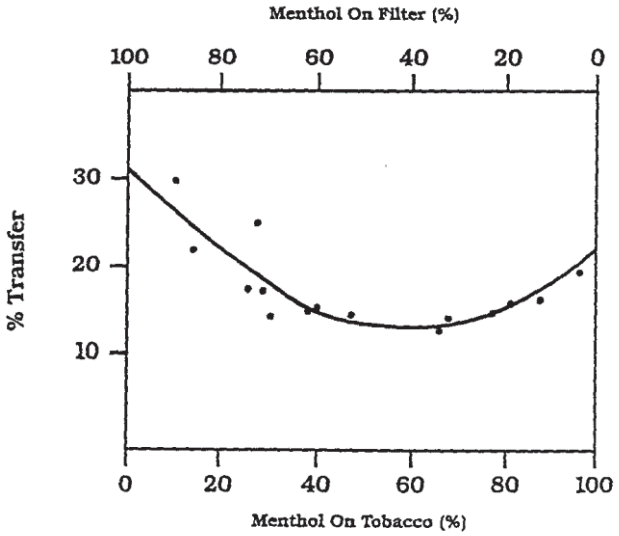
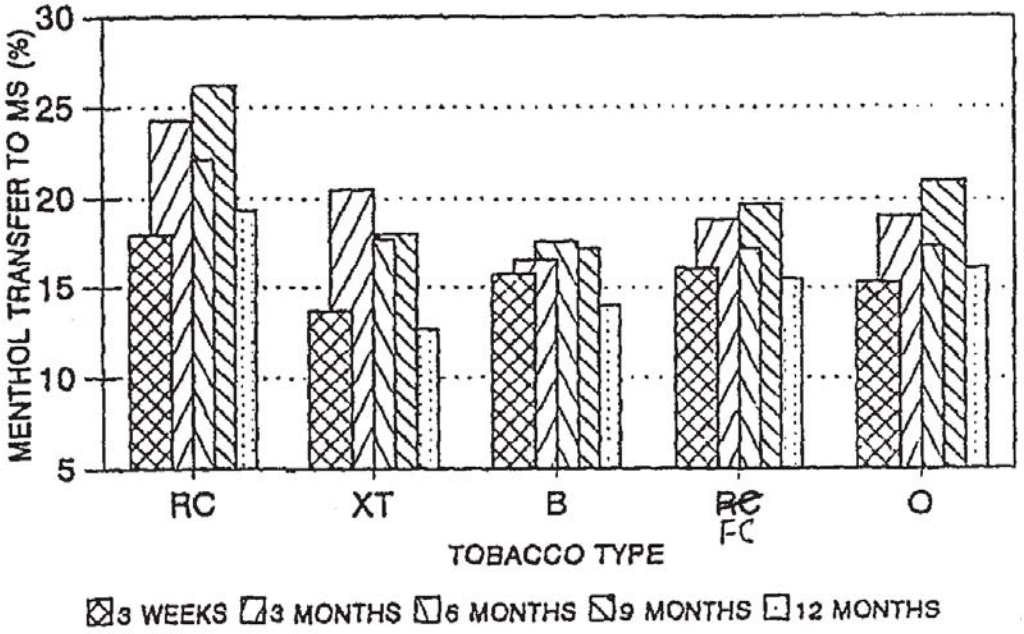


Figure 4. Menthol Transfer to Smoke from Different Menthol Distributions (Source: Riehl 1973)

With regards to the menthol delivery, in addition to product aging, product design features including cigarette draw resistance, menthol level, cigarette paper permeability, ventilation, and filter efficiency can all affect the transfer of menthol into the mainstream smoke.[9] For example, higher filter ventilation and/or cigarette paper permeability results in less tobacco being burned during puffing, reducing the menthol transfer efficiency to mainstream smoke. Menthol transfer efficiency tends to decrease with increased filtration and ventilation of lower tar delivery products. Consequently, additional menthol is added to lower tar yield menthol cigarettes to maintain a consistent menthol smoke delivery to account for the decrease in menthol transfer efficiency associated with the cigarettes ventilation.[9] The menthol application level is generally higher for lower tar yield (''light'') cigarette brands, compared with regular-yield brands.

The effect of tobacco types on menthol delivery was also investigated in the R.J. Reynolds' menthol migration study.[14] The results are shown in Figure 5 below. It appears that reconstituted sheet tobacco exhibited most efficient mainstream menthol transfer, which is approximately 20-30% higher than that of other tobacco types. It is also reported that the addition of propylene glycol or glycerol to filters resulted in decreased menthol transfer into cigarette smoke.[18]



XT = Expanded tobacco, RC = Reconstituted sheet,
B = Burley, FC = Flue-cured, O = Oriental

Figure 5. Menthol Transfer to Mainstream Smoke for Different Tobacco Types over Time (Source: Best 1993)

The Phillip Morris USA study of menthol cigarettes marketed in 2008-2009 showed an average mainstream smoke menthol transfer efficiency of 14%, with a range of 5% - 21%.[9] The study of menthol cigarette brands marketed in China found menthol transfer efficiency of 9 – 23% and an accompanying sensory perception study showed that the sensory characteristics of menthol cigarettes could be more accurately reflected by the mainstream

smoke menthol yields than the pack menthol contents.[22] Therefore, a definitive answer to the impact of design parameters on mainstream smoke transfer efficiency and sensory perception of menthol cigarettes would be only possible through the measurement of menthol in mainstream smoke.

Conclusions

Most of the published tobacco industry studies on the distribution and smoke transfer of menthol in menthol cigarettes were conducted prior to 1990. Many of these studies are internal research reports and some are conference presentations or proceedings. These generally did not undergo a process of peer review and editorial evaluation prior to publication or internal circulation. It is also noted that these documents lack details about the experimental methodologies (e.g., machine smoking regimens), testing methods and validation, data collection, and statistical analysis. Consequently, it is difficult to assess the completeness of the data and quality of the science presented. More studies would be needed to verify or substantiate some of the current menthol findings. Nevertheless, the information, albeit imperfect, provides a general overview of the current understanding of the subject, from which the following conclusions can be drawn about menthol cigarettes:

- Both *l*-menthol and *dl*-menthol are used in menthol cigarettes. Each menthol stereoisomer has distinct pharmacologic characteristics. Different types (sources) of natural menthol impart different taste and sensory perception.
- Menthol is volatile and migrates to various components of a cigarette pack during storage irrespective of where it is applied initially. Tobacco blend, tobacco additives, and filter plasticizers can affect the migration rates of menthol and the distribution of menthol in the product, which may take 9-11 months to reach equilibrium. There is no consistent and compelling evidence that menthol evenly distributes itself between tobacco rod and filter tip or exhibits similar distribution profiles in the cigarettes among different products.
- Menthol readily vaporizes during cigarette smoking and transfers intact to the mainstream smoke without significant pyrolysis. Menthol delivery is determined by the distribution of menthol between the various cigarette components, which is time (shelf-life) and storage condition dependent. Cigarette design parameters including ventilation, cigarette paper permeability, and draw resistance can impact the smoke transfer efficiency of menthol. Menthol appears to be transferred to mainstream smoke more efficiently from a mentholated filter than from mentholated tobacco filler.
- Menthol smoke yield measurement is more biologically relevant than the measurement of menthol quantities in the cigarette.

Recommendations for SE Reviews

Based on the above discussion, the following recommendations for scientific review of SE Reports in which the new product(s) is(are) marketed as menthol cigarette may be made with regard to the determination of substantial equivalence in terms of menthol delivery.

Product Modifications that Can Potentially Impact Menthol Delivery and Necessitate the Submission of Smoke Menthol Data:

- Any significant increase (≥ 10%) in the pack menthol content (*i.e.*, the total menthol level in the product including tobacco rod, cigarette paper, filter, and pack foil).
- Any change in the menthol application method that results in a significant change in the quantity of menthol applied to any cigarette component (≥ 10%).
- Any product design modification that can alter the cigarette mainstream smoke delivery, (*e.g.*, significant decrease in ventilation (<10%) or decrease in cigarette paper porosity).
- Any significant change in tobacco types (*e.g.*, addition of reconstituted tobacco that constitutes more than 30% of the total tobacco weight).
- Any significant decrease in humectants (*e.g.*, propylene glycol or glycerol) that can impact the menthol vapor pressure.

Required Menthol Information and Smoke Menthol Data:

- Information that fully characterizes the type of menthol used in the new and predicate products including CAS# and the sources of natural menthol material.
- Specification of menthol quantity added to each cigarette component during manufacture.
- Menthol levels in mainstream smoke under both ISO and Canadian Intense smoking regimens measured at the completion of production and over the shelf-life such as 3, 6, and 12 months after the completion of production.

Boilerplate Languages

DIFFERENCES in MENTHOL ADDED (INCREASE)

Your SE Reports list menthol is added in the [insert location of menthol, i.e., filter rod, tobacco rod] as xx [insert unit, e.g., g/filter rod] in the new products and xx [insert unit, e.g., g/filter rod] in the predicate products. This is an increase of xx percent in menthol quantity in the new products. Changes in menthol quantities applied to a cigarette could result in changes in menthol amounts in mainstream smoke that could cause the new products to raise different questions of public health. Provide menthol levels in mainstream smoke under both ISO and Canadian Intense smoking regimens. If there is a difference in mainstream smoke quantities of menthol between the new and corresponding predicate products, provide evidence and a scientific rationale why this difference in menthol content does not cause the new products to raise different questions of public health.

DESIGN/COMPOSITION DIFFERENCES THAT IMPACT MENTHOL DELIVERY

Your SE Reports identify significant design and/or composition differences between the new and corresponding predicate products. For example, [insert the changes]. These product modifications could result in increases in menthol amounts in mainstream smoke that could cause the new products to raise different questions of public health. Provide menthol levels in mainstream smoke under both ISO and Canadian Intense smoking regimens. If there is a difference in mainstream smoke quantities of menthol between the new and corresponding predicate products, provide evidence and a scientific rationale why this increase in menthol content does not cause the new products to raise different questions of public health.

References

1 TPSAC, Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations, 2011. Accessed at: [http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/tobaccoproductsscientificadvisorycommittee/ucm269697.pdf.]

2 Heck JD. A review and assessment of menthol employed as a cigarette flavoring ingredient. *Food and Chemical Toxicology* 2010; 48(Supplement 1): S1–S38.

3 Cantrell DV. Various aspects of menthol product development. 1990. Brown & Williamson Product Development Report. Accessed at: [http://tobaccodocuments.org/product_design/967595.html.]

4 Hazardous Substances Data Bank (HSDB). 2003. L-menthol. Accessed at: [http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~dbtqco:1].

5 Organisation for Economic Co-operation and Development (OECD). 2003 Screening Information Data Set (SIDS) Initial Assessment Report. Menthols. Accessed at: [http://www.inchem.org/documents/sids/sids/MENTHOLS.pdf].

[6] Schmeltz I, Schlotzhauer WS. *Nature*, 1968; 219: 370-371.

[7] Lorillard Tobacco Company. Response to the FDA requests for information on menthol cigarettes. *TPSAC submission* July 15-16, 2010. Accessed at: [http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM218780.pdf].

[8] Wayne GF, Connolly GN. Application, function, and effects of menthol in cigarettes: a survey of tobacco industry documents. *Nicotine & Tobacco Research* 2004; Volume 6, Supplement 1:S43–S54.

[9] Altria Client Services. Background information to Tobacco Products Scientific Advisory Committee menthol discussion. *TPSAC submission* June 30, 2010. Accessed at: [http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM218779.pdf].

[10] (b) (5) [redacted]

[11] RJ Reynolds. Topics on menthol cigarettes. *TPSAC submission* June 30, 2010. Accessed at: [http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM218782.pdf].

[12] Browne, CL, *The Design of Cigarettes*. the 3rd edition, 1990.

[13] Wilson SA. Theoretical aspect of menthol migration and transfer. *Recent Advances in Tobacco Science.* 1993; Volume 19, 129-153.

[14] Best, FW. Effects of some cigarette construction parameters on menthol migration and transfer. *Recent Advances in Tobacco Science.* 1993; Volume 19, 155–201.

[15] Perfetti, TA. "Effects of Long-Term Storage of Mentholated Products on Menthol Migration and Smoke Menthol Delivery" RDM 1983, No. 15, 4/12/83.

[16] Curran, JG. "Delivery of Menthol from Cigarettes Containing Either a Mentholated Filter or Mentholated Tobacco" Tobacco Sci. 16; 40-42, 1972.

[17] Reihl, TF, et al. "Menthol Distribution and Transfer" Tobacco Sci. 17; 10-11, 1973.

[18] Curran, JG. "Effect of Certain Liquid Filter Additives on Menthol Delivery" Tobacco Sci. 19; 69-70, 1975.

[19] Brozinski M. Studies of the distribution of menthol in tobacco, filter and smoke of menthol cigarettes. *Beitr. Tabakforsch.* 1972 Vol. 6: 124-130.

[20] Mathis DE. Migration and Delivery of Filter Flavors. *Beitr. Tabakforsch*. 1983; Volume 12: 1-8.

[21] Perfetti TA. Menthol and the Design of Mentholated Cigarettes; A Short Course by R.J. Reynolds Tobacco Company," R.J. Reynolds Tobacco Company, Winston Salem, NC, 1985.

[22] Huang L. Determination of menthol in cigarette and its smoke by capillary gas chromatography *Tobacco Science & Technology* 2007; 237: 32-39.

[23] Jenkins, RW, Newman, RH, Chavis, MK. Cigarette smoke formation studies II. Smoke distribution and mainstream pyrolytic composition of added 14Cmenthol. *Beiträge zur Tabakforschung* International/Contributions to Tobacco Research 1970, 5, 299–302.