## **Evaluation Summary of Clary Oil for Use as a Cigarette Ingredient**

Clary oil is used in the food industry as a flavor ingredient. Clary oil is a pale yellow or pale olive colored liquid with a sweet herbaceous and tenacious odor and a soft and somewhat bittersweet undertone reminiscent of ambra. Perfumers have described the oil to have a tobacco-like, balsamic or tea-like odor that resembles cistus oil and Moroccan chamomile.<sup>1</sup> The oil is obtained fom clary sage, *Salvia sclarea* L. (Family Labiatae or Laminaceae), a perennial or biennial aromatic plant thriving in temperate regions.<sup>2,3</sup> The plant was used by the Greeks and Romans for medicinal purposes, and clary oil continues to be used in alternative medicines today.<sup>2,4-7</sup> In the 1500s it became popular for addition to food and beverages.<sup>5,8</sup> Because of its unique flavor, a combination of sage and mint with a coriander note, clary continues to be used in Europe for seasoning various foods and wines.<sup>1,9</sup> United States Food and Drug Administration (21 CFR §182.20, 582.20), the Flavor and Extract Manufacturers' Association (FEMA No. 2321)<sup>10,11</sup>, the International Organization of Flavor Industries<sup>12</sup> and the Council of Europe (CoE No. 415){CoE, 1981 241 /id} approve clary oil for food use.

Two unpublished studies reported the acute oral toxicity in rats as 5.0 - 6.2 g/kg, while the acute dermal toxicity in rabbits as > 2 g/kg, respectively.<sup>13-15</sup> Moderate amount of skin irritation was reported from the use of full strength clary sage oil applied to the intact or abraded rabbit skin and maintained under occlusion for 24 hours.<sup>14</sup> However, in 24- and 48-hour closed patch test studies with humans, there were no positive reactions identified from use of full strength clary oil or clary oil in 8% petrolatum. Further, there were no sensitization reactions observed in volunteers tested with 8% clary oil in petrolatum.<sup>13,16,17</sup>

Clary oil is applied directly to the tobacco as a flavoring material. Clary oil is currently used worldwide at levels below 5 ppm in selected cigarette brands manufactured and/or distributed by Philip Morris USA Inc. (PM USA) and/or Philip Morris Products SA (PMP SA). As such, clary oil may be subject to pyrolysis-type reactions when smoked. Clary oil may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures.

As suggested by the purge and trap studies conducted by PM USA<sup>18</sup> clary oil applied to tobacco would be expected to distill at 100°C. At the higher temperatures used in pyrolysis studies conducted by PM USA, results indicated that remaining clary oil would not be pyrolyzed and would be delivered to the smoke relatively intact.<sup>19</sup>

Clary oil was part of a PM USA testing program that was designed to evaluate the potential effects of 333 ingredients added to typical commercial blended test cigarettes on selected biological and chemical endpoints.<sup>20-23</sup> Three pairs of test cigarettes were produced, each containing different groups of ingredients. Clary oil was added to one pair at target levels of 3 and 9 ppm. No significant effects were noted in cytotoxicity, mutagenic studies or in respiratory tract endpoints in 90-day rat inhalation studies. In addition, smoke chemistry studies from cigarettes containing a mixture of flavors including clary oil did not significantly alter the smoke chemistry profile compared to control cigarettes. Based on the results of these

studies, the authors concluded that these ingredients (including clary oil) added to tobacco do not add significantly to the overall toxicity of cigarettes.

The results of this evaluation of clary oil involving a review of current published information and internal studies, suggests that addition of clary oil to cigarette tobacco at current use levels does not discernibly alter the biological effects normally associated with cigarette smoke.

## References

1. Arctander, S. (1960) *Perfume and Flavor Materials of Natural Origin*. Arctander, S., Elizabeth, N.J. p.567-570.

2. Leung, A.Y. and Foster, S. (1996) Clary Sage. In *Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics, Second Edition.* John Wiley & Sons, Inc., New York. p.173-174.

3. Small, E. (1997) Culinary Herbs. NRC Research Press, Ottawa, Canada. p.537-539.

4. Duke, J.A. (1985) *CRC Handbook of Phytochemical Constituents of GRAS Herbs*. CRC Press, Boca Raton, FL. p.-422.

5. Grieve, M. (1971) A Modern Herbal: The Medicinal, Culinary, Cosmetic and Economic Properties, Cultivation and Folk-Lore of Herbs, Grasses, Fungi, Shrubs & Trees with all their Modern Scientific uses. Vol. Vol. I. Dover Publications, Inc., New York. p.203-205.

6. Uhl, S.R. (2000) *Handbook of Spices, Seasonings, and Flavorings*. Technomic Publishing, Lancaster-Basel. p.157-158.

7. Bremness, L. (1994) Herbs. In *Eyewitness Handbooks*. 1st American Edition. Dorling Kindersley, New York. p.-126.

8. Sharma, A.; Kumar, A. and Virmani, O.P. (1985) A review on clary sage (Salvia sclarea L.). *Current Research on Medicinal and Aromatic Plants* 7:39-48.

9. Kiple, K.F. and Ornelas, K.C. (2000) *Cambridge World History of Food*. Vol. Vol. 2. Cambridge University Press, p.-1758.

10. Hall, R.L. and Oser, B.L. (1965) Recent progress in the consideration of flavoring ingredients under the food additives amendment III. GRAS substances. *Food Technology* 19:151-197.

11. NACGM (1977) The National Association of Chewing Gum Manufacturers. (Personal Communication)

12. Clydesdale, F. M. (1997) Food Additives: Toxicology, Regulation and Properties. CRC Press, Boca Raton, FL. CD-ROM.

13. Opdyke, D.L.J. (1974) Monographs on Fragrance Raw Materials: Clary Sage Oil. *Food and Cosmetics Toxicology* 245-255.

14. Moreno, O.M. (1972b) Report to RIFM, 31 May.

15. Moreno, O.M. (1972a) Report to RIFM, 19 July.

16. Katz, A.E. (1946) Dermal irritating properties of essential oils and aromatic chemicals. *The Spice Mill* 69:46-51.

17. Kligman, A.M. (1972) Report to RIFM, 19 July.

18. PM USA (2003a) P&T/GC/MS Analysis of Clary Oil. Request 20031157. Scan TH073LSB.D. Unpublished Internal Report.

19. PM USA (2003b) Pyrolysis GC/MS Analysis of Clary Oil. Request 20031157. Scan P031157A.D. Unpublished Internal Report.

20. Carmines, E.L. (2002) Evaluation of the potential effects of ingredients added to cigarettes. Part 1: Cigarette design, testing approach, and review of results. *Food and Chemical Toxicology* 40:77-91.

21. Roemer, E.; Tewes, F.J.; Meisgen, T.J.; Veltel, D. and Carmines, E.L. (2002) Evaluation of the potential effects of ingredients added to cigarettes. Part 3: *In vitro* genotoxicity and cytotoxicity. *Food and Chemical Toxicology* 40:105-111.

22. Rustemeier, K.; Stabbert, R.; Haussmann, H.J.; Roemer, E. and Carmines E.L. (2002) Evaluation of the potential effects of ingredients added to cigarettes. Part 2: Chemical composition of mainstream smoke. *Food and Chemical Toxicology* 40:93-104.

23. Vanscheeuwijck, P.M.; Teredesai, A.; Terpstra, P.M.; Verbeek, J.; Kuhl, P.; Gerstenberg, B.; Gebel, S. and Carmines E.L. (2002) Evaluation of the potential effects of ingredients added to cigarettes. Part 4: Subchronic inhalation toxicity. *Food and Chemical Toxicology* 40:113-131.