



Government
of Canada

Gouvernement
du Canada

RISK MANAGEMENT SCOPE

for

Benzene, 1,2-dimethoxy-4-(2-propenyl)-

Methyl Eugenol

Chemical Abstract Service Registry Number (CAS RN):
93-15-2

Environment Canada
Health Canada

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Canada

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SUMMARY OF PROPOSED RISK MANAGEMENT

1. The Government of Canada will propose notification regarding any potential changes in the use pattern of methyl eugenol.
2. The Government of Canada will propose a phase out plan for insect repellents containing citronella oil, which contains methyl eugenol, if further information to support their continued safety is not provided.
3. It is proposed that pure methyl eugenol will not be authorized for use in natural health products.

Note: This summary is an abridged list of the instruments and tools proposed to manage risks associated with this substance. Please see section 3 of this document for a complete explanation of risk management.

1. ISSUE

1.1 Draft Screening Assessment Report Conclusion

The substance benzene, 1,2-dimethoxy-4-(2-propenyl)-, Chemical Abstract Service Registry Number (CAS RN)¹ 93-15-2, referred to throughout this document as “methyl eugenol”, is included in Batch 9 of the Challenge under the Chemicals Management Plan. The Ministers of the Environment and of Health (the Ministers) have conducted an assessment under section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999)² to assess whether the substance meets one or more of the criteria as set out in section 64 of CEPA 1999.

A notice summarizing the scientific considerations of the draft screening assessment report was published for methyl eugenol by Environment Canada and Health Canada in the *Canada Gazette*, Part I, on March 20, 2010, under paragraphs 68(b) and 68(c) of CEPA 1999. The report proposes that methyl eugenol, on the basis of its carcinogenic potential, for which there may be a probability of harm at any level, is entering or may be entering the environment in a quantity or a

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² A determination of whether one or more of the criteria of section 64 are met and whether risk management may be required is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes but is not limited to exposures from ambient and indoor air, drinking water, foodstuffs and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) Challenge Batches 1-12 is not relevant to nor does it preclude an assessment against the hazard criteria specified in the Workplace Hazardous Materials Information System [WHMIS] *Controlled Products Regulations* for products intended for workplace use.

concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Based on the information available, the draft screening assessment report proposes that methyleugenol is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

The report also proposes that methyl eugenol does not meet the criteria for persistence or the criteria for bioaccumulation, as defined in the *Persistence and Bioaccumulation Regulations* made under CEPA 1999. The presence of methyl eugenol in the environment results primarily from human activity.

For further information on the proposed report conclusion for methyl eugenol, refer to the report, available from <http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/batch-lot-9/index-eng.php>. Please note that the conclusions described in this document and in the report are preliminary and are subject to change.

1.2 Current Uses and Exposure Sources/Pathways of Concern

Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards.

Methyl eugenol is a naturally occurring substance found in the essential oils of several plant species. The oils are extracted from plants for use as flavour or fragrance ingredients. The amount of methyl eugenol in an essential oil extracted from a given type of plant varies with variety, plant maturity at harvest, harvesting method, storage conditions and extraction method (Smith et al 2002). Internationally methyl eugenol is also produced synthetically in small quantities. Annual production in the United States in 1990 was estimated to be 25,000 lb (11,400 kg) (U.S. Dept. Health and Human Services 2005); in a more recent report, annual production in the United States was given as 77 kg (WHO 2009). There are currently four manufacturers of methyl eugenol in the United States and three manufacturers elsewhere, but none in Canada (2009 email from SRI Consulting to Risk Assessment Bureau, Health Canada; unreferenced). In response to the section 71 notice pursuant to CEPA 1999, in 2006 it was not reported to be manufactured in Canada, and there was less than 100 kg of the substance imported into the country in the same calendar year.

In Canada, flavouring ingredients can be added to any food that does not have a standard of identity and composition in the Food and Drug Regulation and to those foods that have a standard of identity and composition that allows for the addition of flavours to the food. Methyl eugenol, essential oils and plant materials such as leaves, stems, and seeds containing methyl eugenol may be added to foods without a regulatory standard and to those having a standard where there is provision for the addition of spices or seasoning. Some examples of common culinary herbs and spices that contain methyl eugenol are basil, tarragon, lemon grass, bay leaf, nutmeg, allspice, cloves and mace. Methyl eugenol is also reported to have been found in oranges, bananas and grapefruit juice (Johnson and Abdo 2005; Smith et al 2002). Commercially prepared foods in which methyl eugenol may be found include ice cream; baked goods such as

cookies, pies, pastries and buns; puddings and other gelatin-based desserts; condiments, soups and sauces, especially pesto; various meat products; candy and chewing gum; and beverages made with spices and herbs containing methyl eugenol (Council of Europe 2001).

The concentration of methyl eugenol in basil is highly variable and the use of basil to make pesto may occasionally result in the ingestion of a large amount of methyl eugenol.

There is no evidence to show that the presence of methyl eugenol in food, and beverages, whether added as a flavour ingredient or naturally present, poses a risk to Canadians.

Methyl eugenol is a component of several essential oils sold to individuals who choose to make their own preparations for use in aromatherapy, massage oils and in alternative medicine practices (Stanfill et al 2003).

Methyl eugenol is considered ubiquitous in air and water at very low concentrations in the order of parts per trillion. Exposure to methyl eugenol is dominated by ingestion of food and beverages with smaller contributions from the use of personal care products, cosmetics, and citronella-based insect repellents. Methyl eugenol is not intended to be used as an intentional ingredient in personal care products and is present only as a naturally occurring component of essential oils which are used in the formulation of thousands of personal care products in Canada (CNS 2009).

While there is evidence to suggest that pure methyl eugenol is a multi-site carcinogen, there is no available data to assess the toxicological potential of the mixtures most commonly found in foods or consumer products. A 2009 WHO/FAO report suggested that the toxicity data may not relate to the presence of methyl eugenol in natural spices based on recent data that indicates that other components of natural spices might modulate bioactivation and/or act as detoxifying agents.

There is not yet any epidemiological evidence associating the natural presence of methyl eugenol in spices and spice oils, which are likely to be the main sources of methyl eugenol in the diet, with liver cancer in humans (WHO 2009).

With respect to noncancer effects, comparison of the critical effect level with upper-bounding estimates of exposure to the general population from presence of methyl eugenol in use of personal care products and citronella-based insect repellents results in margins of exposure that are considered adequate.

2. OVERVIEW OF EXISTING RISK MANAGEMENT

2.1 Existing Canadian Risk Management

Methyl eugenol is listed on the Cosmetic Ingredients Hotlist (which is an administrative tool to help manufacturers satisfy the cosmetic safety provisions of section 16 of the *Food and Drugs Act*) for use as a naturally occurring component in botanical extracts at concentrations equal to or less than 0.01% in fine fragrances, 0.004% in eau de toilette, 0.002% in a fragrance cream, 0.0002% in other leave-on products and in oral hygiene products, and 0.001% in rinse-off products.

Certain therapeutic products which have drug identification numbers (DINs) and contain methyl eugenol may be regulated as natural health products (NHPs) under the *Natural Health Products Regulations*.

The Government of Canada does not authorize the use of pure methyl eugenol for either medicinal or non-medicinal purposes in oral and topical Natural Health Products.

The Pest Management Regulatory Agency's (PMRA) re-evaluation of citronella oil-based personal insect repellents is ongoing pending additional data to refine the proposed risk assessment published on September 17, 2004. Following the report from an "Independent Science Panel on Citronella Oil as an Insect Repellent", the PMRA required producers of citronella oil-containing skin application products to provide confirmatory data that the levels of methyl eugenol do not exceed 0.0002% of the product formulation. If this requirement is satisfied, producers will then be required to provide additional toxicology data within a specified timeframe. Review of these data will determine the eligibility for continued registration of citronella oil-based personal insect repellents (PMRA 2008).

There is not yet any epidemiological evidence associating the natural presence of methyl eugenol in spices and spice oils, which are likely to be the main sources of methyl eugenol in the diet, with liver cancer in humans (WHO 2009). Canadians should consume a variety of foods from each food group according to *Eating Well With Canada's Food Guide*.

2.2 Existing International Risk Management

European Union:

EC Regulation 1334/2008, which applies from January 2011, prohibits the addition of methyl eugenol to foods and restricts the concentration of methyl eugenol in compound foods that have been prepared with flavourings or food ingredients with flavouring properties.

Methyl eugenol is permitted in cosmetics as a component of plant extracts only. The permitted concentrations are as follows: 0.01% in fine fragrances, 0.004% in eau de toilette, 0.002% in a fragrance cream, 0.0002% in other leave-on products and oral hygiene products, and 0.001% in rinse-off products. Methyl eugenol may not be added as a pure chemical to cosmetics.

As a result of re-evaluation activities in the European Union (EU), data was requested to support the continued registration of citronella containing products, with a deadline of September 1, 2006. The citronella industry declined to provide the requested data and, therefore, all registrations in the EU were cancelled as of September 1, 2006.

USA:

Methyl eugenol was affirmed as GRAS (generally recognized as safe) by the Food and Drug Administration as a food additive under 21 CFR §172.515.

The EPA has registered methyl eugenol as a pesticide active ingredient to attract fruit flies to lure traps.

Australia:

Australia permits methyl eugenol in drugs at concentrations of equal to or less than 1% (DECISION 2005/45-4, Schedule 6).

3. PROPOSED RISK MANAGEMENT

As a result of an assessment of a substance under section 68 of CEPA 1999, the substance may be found to meet one or more of the criteria under section 64 of CEPA 1999. In that case, either Minister can provide information and make recommendations respecting any matter in relation to the substance. While not subject to section 74 to 77, the Ministers may choose to do such actions as, add the substance to the Priority Substances List (PSL) for further assessment, or recommend the addition of the substance to Schedule 1 of the Act or take no further action. In this case, the Ministers proposed to recommend the addition of methyl eugenol to Schedule 1. If methyl eugenol is added to Schedule 1 of CEPA 1999, the Ministers may develop a regulation or instrument respecting preventive or control actions to protect the health of Canadians and the environment from the potential effects of exposure to this substance.

In accordance with the Government of Canada's *Cabinet Directive on Streamlining Regulation*³, the proposed risk management regulation(s), instrument(s) and/or tool(s) would be selected using a thorough, consistent and efficient approach and take into consideration the information that has been received and other information available at this time.

As a result of the risk management activities on methyl eugenol undertaken by the Chemicals Management Plan, the Government of Canada has proposed to change the listing for methyl eugenol on the Natural Health Products Ingredients Database from a restricted substance to a substance which will not be authorized for use in natural health products. This change has now been made to the database with the following wording: "Use of methyl eugenol as an isolate for

³ Section 4.4 of the *Cabinet Directive on Streamlining Regulation* states that "Departments and agencies are to: identify the appropriate instrument or mix of instruments, including regulatory and non-regulatory measures, and justify their application before submitting a regulatory proposal."

either medicinal or non-medicinal purposes is prohibited in oral and topical NHPs due to toxicity concerns. Oral use of methyl eugenol present as a component of essential oils should not exceed 200 µg/kg bw/day. Oral use of methyl eugenol when naturally present in plant materials such as basil, tarragon, lemon grass, bay leaf, nutmeg, allspice, cloves, mace, orange, grapefruit and banana is not restricted as it is likely not a significant risk to health.” Topical use of methyl eugenol present as a component of essential oils should be in accordance with the current restrictions set out on the *Cosmetic Ingredient Hotlist*, available at <http://www.hc-sc.gc.ca/cps-sp/person/cosmet/info-ind-prof/hot-list-critique/prohibited-eng.php>.

As no Canadian data were available to estimate exposure to methyl eugenol, Health Canada’s Food Directorate will follow up with its stakeholders to gather information about the use of methyl eugenol as a flavour and/or the use of essential oils or plant parts such as leaves, stems and seeds that naturally contain methyl eugenol as flavouring ingredients in foods offered for sale in Canada.

If the final report concludes that methyl eugenol meets one or more of the criteria under section 64 of CEPA 1999, three options for risk management would focus on **(1) the Government of Canada will propose a requirement for notification regarding any potential changes in the use-pattern of methyl eugenol, (2) the Government of Canada will propose a phase out plan for insect repellents containing citronella oil, which contains methyl eugenol, if further information to support their continued safety is not provided and (3) not authorizing the use of pure methyl eugenol in Natural Health Products.**

4. NEXT STEPS

Industry and other interested stakeholders are invited to submit comments on the content of this risk management scope or other information that would help to inform decision making. Please submit comments prior to May 19, 2010, since the risk management of methyl eugenol will be moving forward after this date. If applicable, the proposed risk management approach will be released approximately six months after the release of the risk management scope. This would coincide with the publication of the final assessment report under section 68 of CEPA 1999. At that time, there would be opportunity for further consultation. Comments and information submissions on the risk management scope should be submitted to the address provided below:

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Gatineau QC K1A 0H3
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Fax: 819-953-7155
Email: Existing.Substances.Existantes@ec.gc.ca

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