Health Canada Santé Canada

Evaluation Report for Category B, Subcategory 2.1, 2.3, 2.4, 3.13 Application

Application Number: 2010-4843
Application: Product chemistry - guarantee, identity and proportion of formulants; Product labels - precautions
Product: Citrobug Insect Repellent Oil
Registration Number: 25797
Active ingredients (a.i.): Lemon oil, Eucalyptus oil, Pine needle oil, Geranium oil and Camphor oil
PMRA Document Number: 2285141

Purpose of Application

The purpose of this application is to amend the specifications of the formulation of Citrobug Insect Repellent Oil.

Chemistry Assessment

Citrobug Insect Repellent Oil is a solution containing lemon, eucalyptus, pine needle, geranium and camphor oils at nominal concentrations of 0.64%, 0.64%, 0.64%, 0.64% and 0.21%, respectively. This product has a density of 0.883 g/mL and pH of 3.75. The chemistry requirements for Citrobug Insect Repellent Oil have been completed.

Health Assessments

The active ingredients in the end-use product (EP), Citrobug Mosquito Repellent Oil, are essential oils that are currently used and have a history of use as flavouring agents in foods, and as ingredients in cosmetics, natural health and drug products, many with a similar topical, “leave on” use pattern as personal insect repellents. In addition, the concentration of each of the oils in the EP is < 1%. A review of the toxicity of the EP was conducted taking into consideration the history of use of the essential oils, their presence at very low concentrations in the EP, the toxicity of the TGAI, a submitted summary of acute toxicity information on the EP, and toxicity data submitted for the previous formulation of the EP.

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The EP is considered to be of low acute oral and dermal toxicity, and non-irritating to the eyes and skin. Because the EP is a personal insect repellent likely to be applied in small amounts via a plastic spray bottle and spread in a thin film on the skin, toxicity from acute inhalation exposure is not considered to be relevant. Although no skin sensitization reactions were reported in a human volunteer study using the previous formulation of the EP, the study was not acceptable due to limitations in the protocol. Since reports from the published literature indicate that several of the active ingredients in the EP and some of their components are potential skin sensitizers, a precautionary statement is included on the label for the EP indicating that it may cause skin reactions on sensitive individuals.

In 2004, the PMRA re-evaluated citronella oil as an active ingredient in personal insect repellents. It was noted that methyleugenol can be naturally occurring in citronella oil and has been reported to be mutagenic and to induce tumours in rats and mice. As a result, the PMRA established a limit on the concentration of methyleugenol in personal insect repellents of 0.0002%. In response to the PMRA re-evaluation, the EP has been re-formulated so that citronella oil is no longer an active ingredient.

Because the EP is a personal insect repellent intended for direct application to human skin, the extent of dermal exposure is potentially high. However, as indicated previously, the concentration of each of the active ingredients is < 1%, and personal insect repellents are generally used by consumers intermittently, when biting insects are active (e.g., from May to August), and only when insects are present. To limit dermal exposures, label directions for the EP limit applications to twice per day with a two hour re-application interval, and advise against application to the eyes, mouth, wounds, and sensitive, irritated or sun-burned skin. Only a thin film of the product is to be used, it is to be applied sparingly and not under clothing, the EP is to be rubbed on the face after spraying on the hands and treated skin, and contaminated clothing should be washed after returning indoors. Consequently, it is expected that use of the re-formulated EP including adherence to label directions will not significantly increase dermal exposure to or health risks from the active ingredients.

As noted above, the EP is to be applied via a plastic spray bottle and spread in a thin film on the skin, and label directions limit the application rate and the amount of product to be applied to the skin. Also, personal insect repellents are generally used when a person is outdoors, exposed to ambient air. Therefore, it is unlikely that volatilization of any of the active ingredients in the EP will result in the inhalation of concentrated vapours, so use of the EP according to label directions is not expected to significantly increase inhalation exposure to or health risks from the active ingredients.

Although toddlers can ingest insect repellents through hand-to-mouth transfers, the low concentrations of the active ingredients in the EP, and label directions that limit the amount and rate of application, suggest that any hand-to-mouth transfers would not result in the ingestion of any significant amounts of the active ingredients. Potential hand-to-mouth transfers are also mitigated by label precautionary statements advising that the EP be kept out of the reach of children and not used on children under 2 years of age. In addition, label directions note that applications to children be supervised and that the EP not be applied to the hands of young children. Therefore, if label precautionary statements and directions are followed it is unlikely that use of the EP will significantly increase oral exposures to or human health risks from the active ingredients in toddlers.

Environmental Assessment

An environmental assessment was not required for this application.

Value Assessment

The applicant submitted a scientific rationale to support the claim that the change in formulation is not expected to have an effect on the duration of protection from mosquitoes provided by Citrobug Insect Repellent Oil. This rationale is acceptable, and based on the provided information the new formulation of Citrobug Insect Repellent Oil is expected to biologically equivalent to the previous formulation, therefore is expected to provide the same level of performance.

Conclusion

The PMRA has completed an assessment of the available information and is able to support the amendment to the specifications of the formulation of Citrobug Insect Repellent Oil.

References

PMRA No.	Reference
2224133	2011, 2.13.3 Data #1., DACO: 3.2.3,3.4.2 CBI
2224135	2011, 2.13.3 Data #2., DACO: 3.2.3,3.4.2 CBI
1963153	Tableau CODO 0.8 for commercial product
1756714	1998, CIO-FAS-2 Product Chemistry for Citrobug Formule HE-F-5000, DACO: 2.0
1181375	1996, Evaluation de la Toxicite du Produit "Chasse-Moustique" HE-F-5000 (Sub No 95-1668) et Citrobug (Sub No 95-1505), [HE-F-5000;Citrobug;Sub No 95-1505;95-1668], DACO: 4.2.1, 4.2.4, 4.2.5, 4.6.1, 4.6.4, 4.6.5
1181382	1995, Rapport D'une Etude de Sensibisation Chez L'humain avec Citrobug Huile, [Citrobug Huile;HE-F-5000;Sub No 95-1505;95-1668], DACO: 4.6.6
1963125	New registration application for the active ingredients, DACO: ` 10.1,10.2.1,10.2.2,10.2.3.4,10.3,10.6,10.7.2,3.5,4.1,5.1
1963152	Rationale for amended registration application for the commercial product, DACO: 10.1,10.2.1,10.2.2,10.2.3.4,10.3,10.6,10.7.2,3.5,4.1,5.1
2224141	biological properties of essential oils, DACO: 10.2.3.3
2280693	2013, Lettre Recapitulative, DACO: 10.2.3.3
1181380	1996, Field study report on the efficacy of Heloise Laboratoires Inc. (Ctirobug) oil based lotion as mosquito repellent, DACO: 10.2.3.3

Additional Information Considered

Published Information

PMRA No.	Reference
2348315	2012, Fahlbusch, K-G., Hammerschmidt, F-J., Panten, J., Schatkowsi, D., Bauer, K., Garbe, D., and Surburg, H., 2012, Flavors and Fragrances, Ullman's Encyclopedia of Industrial Chemistry Wiley-VCH Verlag GmbH & Co, DACO: 12.5.5
2348316	Health Canada, 2013, Lemon Oil, Licensed Natural Health Products Database, accessed on September 30, 2013, http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/start-debuter.do?lang=eng, DACO: 5.2
2348515	US Department of Health and Human Services, 2013, Lemon Oil, accessed on September 12, 2013, http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=8008-56-8&tbl=TblChemicals&prodcat=all, DACO: 12.5.5
2348519	CCOHS, 2013, Lemon Oil, Registry of Toxic Effects of Chemical Substances (RTECS) Canadian Centre for Occupational Health (CCOHS), DACO: 12.5.4
2348522	Opdyke, D.L.J., 1974, Lemon Oil Expressed Fragrance Raw Materials Monographs, Food and Cosmetics Toxicology 12(5-6): 725-725, DACO: 12.5.4
2348524	Health Canada, 2013, Eucalyptus Oil, Licensed Natural Health Products Database, accessed on September 30, 2013, http://webprod3.hc-sc.gc.ca/Inhpd-bdpsnh/start-debuter.do?lang=eng, DACO: 5.2

2348525 US Department of Health and Human Services, 2013, Eucalyptus Oil, Household Products Database, accessed on September 23, 2013 http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=8000-48-4&tbl=TblChemicals&prodcat=all, DACO: 12.5.5

2348532 Opdyke, D.L.J., 1975, Eucalyptus Oil Fragrance Raw Materials Monographs, Food and Cosmetics Toxicology 13: 107-108, DACO: 12.5.4

2348533 Devleeschouwer, V., Roelandts, R., Garmyn, M., and Goossens, A., 2008, Allergic and Photoallergic Contact Dermatitis from Ketoprofen: Results of (Photo) Patch Testing and Follow-up of 42 Patients, Contact Dermatitis 58: 159-166, DACO: 4.2.6

2348537 CCOHS, 2013, Eucalyptus Oil, Registry of Toxic Effects of Chemical Substances (RTECS) Canadian Centre for Occupational Health (CCOHS), DACO: 12.5.4

2348539 Health Canada, 2013, Camphor Oil, Licensed Natural Health Products Database, accessed on September 30, 2013, http://webprod3.hc-sc.gc.ca/Inhpd-bdpsnh/index-eng.jsp, DACO: 5.2

2348540 Health Canada, 2013, Camphor, Drug Products Database Online Query, accessed on September 30, 2013, http://webprod5.hc-sc.gc.ca/dpd-bdpp/previous-precedent.do?lang=eng&page=2, DACO: 5.2

2348542 Opdyke, D.L.J., 1973, Camphor Oil White Fragrance Raw Materials Monographs, Food and Cosmetics Toxicology 11:1047, DACO: 12.5.4

2348547 Krauze-Baranowska, M., Mardarowicz, M., Wiwart, M., Poblocka, L., and Dynowska, M., 2002, Antifungal Activity of the Essential Oils from Some Species of the Genus Pinus, Z. Naturforsch. 57c: 478-482, DACO: 12.5.5

2348549 Health Canada, 2013, Pine Oil, Licensed Natural Health Products Database, accessed on September 30, 2013, http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/start-debuter.do?lang=eng, DACO: 5.2

2348552 US Department of Health and Human Services, 2013, Pine oil, Household Products Database, accessed on September 30, 2013, http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=8002-09-3&tbl=TblChemicals&prodcat=all, DACO: 12.5.5

2348553 Health Canada, 2013, Pine Oil, Drug Product Database Online Query, accessed on September 30, 2013, http://webprod5.hc-sc.gc.ca/dpd-bdpp/dispatch-repartition.do?lang=eng, DACO: 5.2

2348591 CCOHS, 2013, Pine Oil, Registry of Toxic Effects of Chemical Substances (RTECS) Canadian Centre for Occupational Health (CCOHS), DACO: 12.5.4

2348592 Opdyke, D.L.J., 1976, Pinus Pumilio Oil, Fragrance Raw Materials Monographs Food and Cosmetics Toxicology, 14: 843-844, DACO: 12.5.4

2348593 Health Canada, 2013, Geranium Oil, Licensed Natural Health Products Database, accessed on September 30, 2013, http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/index-eng.jsp, DACO: 5.2

2348594 US Department of Health and Human Services, 2013, Geranium Oil, Household Products Database, accessed on September 30, 2013, http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=8000-46-2&tbl=TblChemicals&prodcat=all, DACO: 12.5.5

2348595 Opdyke, D.L.J., 1976, Geranium Oil Algerian Fragrance Materials Monographs, Food and Cosmetics Toxicology 14: 781-782, DACO: 12.5.4

2348596 CCOHS, 2013, Geranium Oil, Registry of Toxic Effects of Chemical Substances (RTECS) Canadian Centre for Occupational Health (CCOHS), DACO: 12.5.4

2350749 Lapczynski, A., Bhatia, S.P., Letizia, C.S. and Api, A.M., 2008, Fragrance material review on dl-citronellol, Food and Chemical Toxicology 46: S103-S109, DACO: 12.5.4

2350751 International Programme on Chemical Safety, 1998, Limonene, Concise International Safety Assessment No. 5, World Health Organization, DACO: 12.5.4

2351094 US Department of Health and Human Services, 2013, Pine Oil, Household Products Database, accessed on October 9, 2013, http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=8002-09-3&tbl=TblChemicals&prodcat=all, DACO: 12.5.5

ISSN: 1911-8082

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