

# A review of recommendations on the safe and effective use of topical mosquito repellents

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## Article history

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## Key points

- Topical insect repellents are recommended by health authorities to avoid mosquito bites and prevent mosquito-borne disease
- Products purporting to repel mosquitoes must be registered by the Australian Pesticides and Veterinary Medicines Authority
- Safe and effective active ingredients in topical repellent formulations are diethyltoluamide (DEET), picaridin and p-menthane-3,8-diol (PMD)
- The provision of recommendations on the use of commercially available formulations in light of current research is critical to the effectiveness of topical insect repellents

## Abstract

Mosquito-borne disease is an annual problem in Australia, with endemic pathogens such as Ross River virus infecting thousands of people each year. The recent emergence of Zika virus in South America and the Pacific, together with ongoing outbreaks of dengue viruses in Southeast Asia, generated great community interest in the most effective strategies to avoid mosquito bites. Large-scale mosquito control programs are not common in Australia and are limited in New South Wales (NSW).

The use of topical insect repellents is a key recommendation by health authorities to prevent mosquito-borne disease. All products sold in Australia purporting to repel mosquitoes must be registered with the Australian Pesticides and Veterinary Medicines Authority. Despite around 100 commercial products registered as repelling mosquitoes, there are relatively few active ingredients used across these formulations. The most common are diethyltoluamide (DEET), picaridin, p-menthane-3,8-diol (PMD) and a range of plant-derived products (e.g. melaleuca, eucalyptus, citronella oils). Research has shown that each of these active ingredients varies in the duration of protection provided against biting mosquitoes.

Recommendations by health authorities are informed by this research, but inconsistencies between recommendations and available repellent formulations and their concentration of active ingredients can cause confusion in the community. There are conflicts between the data resulting from scholarly research, marketing promotion by manufacturers and recommendations provided by overseas health authorities. A review was undertaken of NSW Health's current recommendations on choosing and using insect repellents, taking into consideration recent research and currently registered topical repellents.

## Introduction

In addition to their nuisance-biting impacts, mosquitoes have the potential to transmit a range of pathogens of medical importance in Australia. Ross River virus, Barmah Forest virus, Murray Valley encephalitis virus, Kunjin virus and dengue viruses are all mosquito-borne pathogens associated with human disease in various regions of Australia.<sup>1</sup> The threat of small local outbreaks of chikungunya virus and Zika virus, triggered by returning travellers, is of increasing concern.

The most commonly reported mosquito-borne disease in New South Wales (NSW) is caused by Ross River virus, with infection causing an illness typified by rash, fever, headache and joint pain. The severity of these symptoms is often debilitating and can persist for many weeks or months.<sup>2</sup> It is difficult to predict outbreaks of Ross River virus<sup>3</sup> and there is no vaccine. The largest outbreak of this disease in almost 20 years was reported in 2015, with a total of 9551 cases reported from across Australia, 81.8% of those from Queensland and NSW.<sup>4</sup>

Surveillance of mosquito populations and activity of mosquito-borne pathogens throughout NSW informs decisions by local health authorities to issue public health warnings above and beyond the routine seasonal mosquito-borne disease awareness programs. Promoting personal protection measures, including avoiding mosquito habitats, limiting outdoor activities at times of the day when mosquitoes are most active and covering up exposed skin with clothing, remain at the core of public health messages. The use of topical insect repellents is one of the strongest recommendations by health authorities.<sup>5</sup>

Although insect repellents have been shown to provide protection against biting mosquitoes, for this approach to be effective at preventing mosquito-borne disease, it is important that health authorities provide recommendations on safe and effective use of these products.<sup>6,7</sup> Health authorities across Australia provide general information on recommended active ingredients, but the advice often does not reflect the wide range of commercial repellents available, the differences between them and the correct use of the formulations.<sup>5</sup>

In 2016, NSW Health reviewed the recommended personal protection measures that were included in fact sheets, media releases and other public health communications. This review included revising the insect repellent information provided in light of currently available commercial formulations and recently published mosquito repellent research.

## Mosquito repellent formulations and their active ingredients

All products claiming to provide protection from biting mosquitoes must be approved and registered by the Australian Pesticides and Veterinary Medicines Authority

(APVMA), which assesses their effectiveness and safety. There are currently around 100 individual products registered as mosquito repellents, including topical insect repellents, spatial repellents (e.g. mosquito repellent wrist bands and patches) and insecticides (e.g. mosquito coils, sticks and plug-in devices).

Spatial repellents such as mosquito coils are used commonly and, although there is evidence that they provide some protection against biting mosquitoes, their role in reducing disease is less well studied.<sup>6,7</sup> The growing community interest in spatial repellents and new insecticide technologies warrants further investigation. However, for the purpose of this review, we are only considering topical insect repellents.

Once registered, repellents are labelled with active ingredient(s) and their concentration, and recommended reapplication times and safety warnings. However, this information is not consistent across formulation types, including those containing the same active ingredient(s). This is likely to cause confusion among consumers, and the lack of definitive information means local health authorities are left to make general statements about repellent use (e.g. "Always check the label for reapplication times" or "Always follow the product label instructions"). This deficiency in labelling of topical insect repellents has been identified by the US Environmental Protection Agency (EPA). The EPA has introduced a program to include a "repellency awareness graphic", based on standard scientific testing, on topical repellent formulations to help consumers easily assess repellency time for biting arthropods.<sup>8</sup> A similar program here in Australia would be useful.

### Diethyltoluamide (DEET)

One of the most widely recommended mosquito repellents internationally is N,N-diethyl-3-methylbenzamide (commonly known as diethyltoluamide, or DEET). There are many and varied registered DEET formulations available, ranging from less than 10% through to 80% concentration. There is a considerable body of scientific work supporting their safety and effectiveness<sup>7,9</sup>, with laboratory and field investigations demonstrating that DEET effectively protects against a range of nuisance-biting and vector mosquito species in Australia.<sup>10</sup>

### Picaridin

Picaridin has been shown in laboratory and field investigations to provide protection from biting mosquitoes.<sup>9,10</sup> Registered formulations range in concentration from 9% to 20%. Alongside DEET, it has been widely recommended by health authorities internationally. Picaridin-based formulations are generally considered cosmetically more pleasant to use and, in Australia, this active ingredient is currently more commonly available than lower-dose (<20%) DEET-based commercial repellent formulations.

## Oil of lemon eucalyptus (p-menthane-3,8-diol, PMD)

Repellent formulations containing p-menthane-3,8-diol (PMD) are becoming widely available and, given their effectiveness<sup>11,12</sup>, are increasingly included in lists of recommended products.<sup>13</sup> However, this product should not be confused with eucalyptus-based essential oil formulations, which generally do not provide long periods of protection against biting mosquitoes.<sup>14</sup> In Australia, PMD is registered as “extract of lemon eucalyptus, being acid modified oil of lemon eucalyptus (*Corymbia citriodora*)” as it is a byproduct of the hydrodistillation process rather than the essential oil itself. It is available in 26–40% formulations and, although not tested widely in Australia, laboratory studies have demonstrated that a 30% PMD formulation provided comparable duration of protection against biting mosquitoes to low-dose (5–10%) DEET- and picaridin-based repellents.<sup>11,14</sup> Following the 2016 review, PMD is now included in the list of repellents recommended by NSW Health.<sup>15</sup>

## Botanical extracts

A number of registered topical mosquito repellents contain plant-derived active ingredients including one or more of citronella, melaleuca, eucalyptus, leptospermum and lavender extracts. These formulations typically range from <1% through to approximately 8.5%, representing relatively low active ingredient concentrations compared with other repellents. Although there is evidence that repellents containing plant-derived extracts will repel biting insects for short periods<sup>14</sup>, they would need to be reapplied far more frequently than DEET-, picaridin- or PMD-based repellents to provide comparable protection.<sup>5</sup>

## Health and safety considerations of mosquito repellents

There are inconsistencies in the advice included on registered labels in Australia. Although some provide specific age-related warnings on repellent use, others only contain general warnings about use on children, so it is difficult for health authorities to be specific in warnings about particular active ingredients and their concentrations.

There is often a perception that DEET is unpleasant to use or may pose a health risk. However, a number of studies that investigated health risks associated with use of topical DEET-based repellents found that, if used as recommended, it poses minimal health risk.<sup>9,16</sup> Although the safety of picaridin has not been investigated to the same extent as DEET, it is also considered a safe product to use.<sup>17</sup> DEET and picaridin are considered safe to use for pregnant and breastfeeding women.<sup>18,19</sup> Recommendations are included on registered products safe for use on children older than 3 months.

There are some inconsistencies relating to the recommended use of PMD by health authorities internationally. The US Centers for Disease Control and Prevention (CDC) recommends PMD-based repellents not be used on children younger than 3 years.<sup>19</sup> However, in Australia, registered products carry an advisory from the APVMA not to use the repellent on children younger than 12 months. A review of recommendations by NSW Health concluded that there was no evidence to support recommendations differing from the advisory registered by the APVMA.

Botanical-based repellents are often perceived as being ‘natural’ and may be preferred by many in the community because of perceived risks associated with other topical repellents.<sup>14</sup> However, essential oils have the potential to cause adverse skin reactions<sup>20</sup>, an important consideration when discouraging use of unregistered repellents, or ‘homemade’ mixtures, that may contain relatively high doses of these products.

## Effective use of mosquito repellents

Irrespective of the inherent effectiveness of active ingredients in mosquito repellents, the best bite protection is achieved by thorough application to all exposed skin. Recommendations about how to use topical repellents are typically absent from public health messages.<sup>5</sup> However, following the NSW Health review, more specific information was provided in its fact sheet, highlighting the need to follow label instructions and reapplication requirements following swimming, vigorous exercise and during hot weather.<sup>14</sup>

## Summary

Regardless of future changes to mosquito-borne disease risks, topical mosquito repellents will remain an essential component of recommended personal protection measures. Although it is unlikely there will be substantial changes in the active ingredients used in registered mosquito repellents in Australia, the landscape of commercial formulations will continue to evolve. Together with the emergence of new technologies for mosquito bite prevention (i.e. clip-on insecticide devices or insecticide-treated clothing), it will be important that local health authorities routinely review academic studies of mosquito repellent effectiveness and safety, particularly for picaridin- and PMD-based repellents, to provide the most informed public health messages to reduce the burden of mosquito-borne disease.

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## Competing interests

NSW Health Pathology has been commissioned by a range of companies that develop and market insect repellents to test mosquito repellent formulations, and to provide expert advice about mosquito biology and mosquito-borne disease risks. No external funding was received from these companies for the preparation of this manuscript.

## Author contributions

Both authors contributed to the paper's conception and made substantial intellectual contributions to draft versions.

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