EFFECT OF LABORATORY TEMPERATURE ON THE VOLATILITY OF [^{14}C]-PRIRIMIPHOS-METHYL DURING *IN VITRO* SKIN ABSORPTION STUDIES

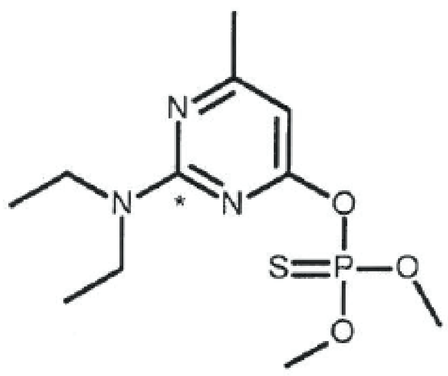
T Kerin[1], F Toner[1], E Lessmann[2] and J Fernandes[2]
[1]Charles River Laboratories Edinburgh Ltd, Edinburgh, EH33 2NE, UK
[2]Syngenta Ltd, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK

1 Introduction

Following an *in vitro* skin absorption assessment of [^{14}C]-Pirimiphos-methyl in 3 concentrations (formulation concentrate and highest and lowest concentration in-use spray dilutions), the mass balances were 99.0, 96.3 and 94.0%, respectively. EFSA 2017[1] states "if overall recovery is consistently low (mean over all animals/replicates < 95% for radiolabelled studies), as a worst-case assumption, the missing material should be considered absorbed and added to the absorbed amount, unless it can be justified that the missing material is unlikely to have been absorbed". A volatility assessment was undertaken to investigate whether volatility was a contributory factor for the observed under-recovery during the dermal absorption experiment.

The relevant physiochemical properties of Pirimiphos-methyl are: molecular weight 305, melting point: 20.8°C, Henry 0.608 Pa.m^{-3}.mol^{-1}.

Figure 1. The Structure and Site of Labelling of [^{14}C]-Pirimiphos-methyl



2 Materials and Methods

Sections of Parafilm® covered with aluminium foil were mounted onto a static diffusion cell containing phosphate buffered saline. The temperature of the membranes in the cells was maintained at 31.6°C to 32.8°C (target 32°C). A static diffusion cell system (PermeGear Inc) was used (Figure 2).

[^{14}C]-Pirimiphos-methyl in the lowest concentration in-use spray dilution was applied (6.4 µL, 10 µL/cm^2) evenly over the exposed area of foil (0.64 cm^2). The donor chambers of the cells were not occluded. Triplicate samples were terminated and assessed for recovery immediately after dosing (*i.e.* at 0 h post-dose), 6 and 24 h post dose. This experiment was conducted at 2 different ambient laboratory temperatures (Table 1).

Figure 2. Photographs of a Static Diffusion Cell

3 Results and Discussion

For volatility assessment 1 (Table 2 and Figure 3), the average laboratory temperature was *ca* 6°C lower than the original absorption experiment. The recovery for this volatility assessment was 96.96% at 24 h post dose. This was higher than the recovery for the original absorption experiment at 24 h post dose (93.96%). Based on this volatility assessment, the losses in the recovery for the original absorption experiment could not be attributed to volatility.

For volatility assessment 2 (Table 2 and Figure 3), the average laboratory temperature was within 1°C of the original absorption experiment. The recovery for this volatility assessment was 90.15% at 24 h post dose. This was lower than the recovery for the original absorption experiment at 24 h post dose (93.96%). Based on this volatility assessment, the losses in the recovery for the original absorption experiment could be attributed to volatility under the representative experimental conditions.

Table 1. Laboratory Temperature For Each Experiment

	Average Laboratory Temperature (°C)	Maximum Laboratory Temperature (°C)	Minimum Laboratory Temperature (°C)
Absorption Experiment	22.17	23.04	19.70
Volatility Assessment 1	15.70	19.47	13.00
Volatility Assessment 2	21.91	23.08	19.35

Figure 3. Total Percentage Recovery (Mean + SD) For Each Experiment

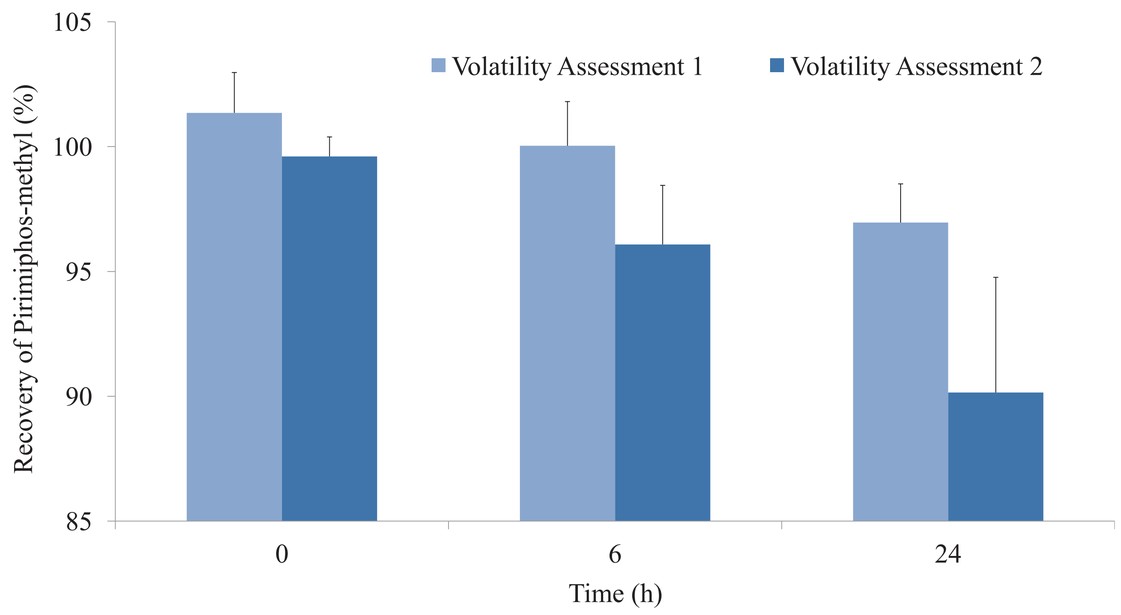


Table 2. Total Percentage Recovery (Mean + SD) For Each Experiment

	Total Recovery at 0 h		Total Recovery at 6 h		Total Recovery at 24 h	
	Mean (%)	SD (%)	Mean (%)	SD (%)	Mean (%)	SD (%)
Absorption Experiment	N/A	N/A	N/A	N/A	93.95	2.45
Volatility Assessment 1	101.35	1.62	100.03	1.77	96.96	1.55
Volatility Assessment 2	99.61	0.78	96.08	2.37	90.15	4.61

4 Conclusion

Based on limited evidence from this volatility assessment, it can be concluded that the ambient laboratory temperature may be an important factor influencing the volatility of certain pesticides in dermal absorption studies.

5 Reference

Guidance on Dermal Absorption (EFSA Journal, 2017, 15(6): 4873).