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SUBSTANCES

September 21, 2009

MEMORANDUM

SUBJECT: Study Review – Lisi, P. (1992) Sensitization risk of pyrethroid insecticides.
Contact Dermatitis 26:349

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*Rec'd in PR
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Objective: The study aim is to establish the irritation and sensitization potential of seven of widely used pyrethroids: allethrin, cypermethrin, deltamethrin, fenothrin (assumed phenothrin), fenvalerate, permethrin, resmethrin.

Study Design: Experimental, intentional dosing study.

Methods: Volunteer subjects (230 total, 162 males and 68 females, between the ages of 19-78 years old) were patch tested with each of the 7 pyrethroids. The patch tests were performed on the upper back and read after 2 or 3 days and three different concentrations were used (1%, 2%, and 5%) for each pesticide for each participant. The participants were classified into three groups: agricultural workers (n=82), ex-agricultural workers (n=28), and others (n=120). The author stated 54 subjects had irritant or allergic contact dermatitis of the hands, 18 of which were correlated with agricultural activities. The author stated 176 of the participants had non-allergic skin disorders and 16 of these participants were also atopic.

Statistical Analysis: No statistical analysis was performed. Simple counts and proportions were used to compare irritation and sensitization effects across the three groups.

Results: There were 2 cases of irritant reactions to the pesticide resmethrin reported, and 3 cases of allergic reactions to other pyrethroids reported. Of these 3 cases of allergic reactions, 2 were in association with fenvalerate, and 1 with cypermethrin.

Of the 2 irritant reactions observed, both were in non-atopic participants with venous leg ulcers. According to the author, the allergic reaction observed in a participant after cypermethrin skin patch testing was not clinically relevant (no further detail was provided).

Of the 2 participants with allergic reactions to fenvalerate, both had chronic contact dermatitis of the hands. One of these participants was a farmer with previously observed sensitization to potassium dichromate and mercaptobenzothiazole, and the other participant was a gardening hobbyist.

The author concludes that pyrethroids are only very slightly cutaneous irritants or sensitizers.

Study Observations and Limitations:

1. While published as a short communication, the author did not adequately describe the methodology employed to conduct the study including criteria for enrollment, if any; the dosing regimen (order); working definition of the outcomes under study, irritation and sensitization; and, protocol used to evaluate all participants. These factors severely limit the interpretation and utility of the study.
2. The author did not clearly articulate the purpose of including individuals with pre-existing skin disorders, including contact dermatitis; and how the author defined pre-existing skin disorders among the volunteers. As designed, the results, if considered, would be applicable to persons with existing dermal hypersensitivity.

3. The author is not clear about the dosing regimen, although the Agency assumes that each participant was simultaneously dosed with 3 concentrations of the 7 pyrethroids under study. Additionally, the author is not clear what is meant by “cross-reactions” among the pyrethroids, and whether a ‘cross reaction’ (presumably some type of combined effect) would be expected or could be identified using the dosing regimen employed in this study.
4. In general, it would have been helpful to include the other pesticides to which agricultural workers may have been exposed to understand qualitatively the cumulative exposure experienced in this population.
5. There was a lack of information to clarify the difference between ‘agricultural workers’ and ‘ex-agricultural workers.’ For example, approximately how long since employment as an agricultural worker among ex-agricultural workers?

Reviewer Conclusion: The study provides qualitative information regarding the potential relationship between human exposure to pyrethrins/pyrethroids and human dermal irritation and sensitization. It should be considered in a qualitative weight of evidence approach. There are enough questions about the design and implementation of this study, however, particularly concerning the investigators’ distinction between sensitization and irritation effects, such that the study should receive little weight.



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Chemical Name: Allethrin
Cypermethrin
Cypermethrin
Deltamethrin
Phenothrin
Fenvalerate
Permethrin
Resmethrin

PC Code: 004001

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