ABSTRACT
A one-year field study was carried out in 45 households in Cairns, North Queensland to evaluate the efficacy of three topical or systemic treatment programs in controlling cat flea (Ctenocephalides felis) infestations within the residence and on dogs and cats. Homes were randomly assigned to one of three treatments. In the first group of homes, lufenuron was administered orally to all household pets according to label recommendations for the study duration, and nitenpyram was administered orally once per week for the first 6 weeks. After 6 weeks, all pets in the household received a single dose of nitenpyram if fleas were observed on any animal. Treatments in the second group of homes were identical to those for the first group except that all pets in the household received two doses of nitenpyram per week. In the final group, imidacloprid was applied topically to all household pets once every 4 weeks for the duration of the study, and no other flea-control measures were applied. Flea populations on the pets of all treatment groups were assessed; environmental flea numbers were assessed only for Groups 1 and 3. The combination of lufenuron and nitenpyram provided superior control of flea populations on the animals and in the environment compared with using imidacloprid alone.

INTRODUCTION
Traditional recommendations for flea control have been to take a two-tiered approach to the problem, using one product to control fleas on the animal and another to control flea stages in the environment. This approach was successful in controlling most infestations; however, during the last decade several new flea-control products have been introduced...
which have dramatically changed flea-control practices and recommendations. The orally administered insect-development inhibitor lufenuron (Program®, Novartis Animal Health, Greensboro, NC) was the first of these new products and enabled pet owners to achieve environmental flea control without using insecticides in the home. The topical insecticides imidacloprid and fipronil also have provided excellent flea control on pets and are noted for their ease of application. In studies carried out on imidacloprid and fipronil, it was concluded that environmental control is not required with the use of these products.

Nitenpyram (CapstarTM, Novartis Animal Health), a member of the neonicotinoid chemical group, was introduced to the Australian market in January 1999. Nitenpyram is rapidly absorbed from the gut before entering into the bloodstream, and the half-life is short—around 3 hours in the dog7 and 7.7 hours in the cat. Effective blood concentrations are only maintained for about one day after administration. The pharmacokinetics of nitenpyram suggest it is an excellent ‘knock-down’ agent to partner with lufenuron, which has excellent long-term efficacy but can take a few weeks to impact existing flea infestations.

In the present field study, flea control achieved by oral administration of lufenuron and nitenpyram was compared with results obtained using imidacloprid applied topically to all resident pets once every 4 weeks for 52 weeks.

**MATERIALS AND METHODS**

**Trial Sites**

This study was carried out in Cairns, North Queensland, Australia. Annual average daily temperature is 27.5 °C and the average humidity is 73% (range, 66% to 78%; 9 AM; source: Australian Bureau of Meteorology Web site). These conditions make it an ideal location for field studies on the cat flea, *Ctenocephalides felis*, because weather conditions approximate the ideal for flea development. The study was started in February 1999 and continued for 52 weeks.

Forty-five private households in Cairns were identified and selected by referral from veterinary clinics or by advertising in local media for inclusion in the study. Households and pets were selected based on the following criteria: One to four healthy, nonfractious dogs and/or cats lived at the residence; a minimum of ten adult fleas were observed on at least one dog or cat; and owners were willing to participate in the study for one full year.

All households meeting the minimum requirements for inclusion in the study were asked to complete a questionnaire, which included the treatment history of the animals and the environment. Households were rejected if they had used lufenuron, fipronil, imidacloprid, any consumer flea-control products containing an insect growth regulator, or had a professional pest-control treatment within the previous 3 months.

Owners were instructed not to restrict pets’ normal activity in any way, except to allow the scheduled flea counts and the application of the various flea-control products. Most houses had fenced yards, but no restrictions were placed on the movement of the animals outside the house or in the neighborhood. All pets had free access to any areas the owners thought appropriate for them. This method of pet management was used to give a true reflection of how these flea-control products would be used in actual household situations.

**Allocation and Treatment**

Homes meeting the selection criteria above were randomly allocated to three treatment groups (15 households per group). Households were assigned to treatment groups based on a randomized block design, which ensured that
each treatment group had an equivalent spread of pretreatment flea populations on the animals. No attempt was made to match for other factors, although there was a similar number of cats (0 to 2) and dogs (0 to 3) per household in each treatment group.

Products were obtained from commercial sources for the study. Care was taken to ensure the products had not reached their expiration dates. Nitenpyram tablets contained either 11.4 mg or 57 mg each, and lufenuron tablets contained 67.8 mg, 204.9 mg, or 409.8 mg each. Lufenuron injectable suspension, containing 10 mg lufenuron/ml, was also used in some households (i.e., those with cats). Imidacloprid was provided in a liquid formulation containing 100 g active ingredient/L. All products were administered according to label instructions.

Group 1: All dogs and cats in each household received treatment with lufenuron. Dogs were treated orally at a minimum dosage rate of 10 mg/kg once every 4 weeks; cats were given lufenuron by injection at a minimum dosage of 10 mg/kg at the start of the study and then once every 6 months. Nitenpyram tablets were administered orally to all dogs and cats at a minimum dosage of 1 mg/kg once per week for the initial 6 weeks. After the initial 6-week period, any animal having five or more fleas counted received another single dose of nitenpyram.

Group 2: All dogs and cats in the household were administered lufenuron as described for Group 1. Nitenpyram tablets were administered orally to all dogs and cats twice per week for the initial 6 weeks. After the initial 6-week period, any animal having five or more fleas counted received two doses of nitenpyram 3 or 4 days apart.

Group 3: All dogs and cats in the household were treated with topical imidacloprid according to label directions at the start of the trial and then every 4 weeks during the trial period irrespective of flea counts.

All pets were weighed at the start of the study to determine doses. Any pet that appeared to the investigator to have changed body weight significantly at a scheduled assessment was weighed again to assure accuracy of treatment dose. The trial investigator carried out all oral and topical dosing. A licensed veterinarian administered all injections, thus eliminating any inconsistencies in dosing due to poor owner compliance. No other topical or environmental flea treatments were used during the study. Due to practicalities and resources available for the trial, there was no attempt at blinding the treatments or assessment.

**Evaluations**

Fleas were counted using the method described by Dryden and coworkers in which 1-minute counts were made in each of five areas of the pet (left lateral, right lateral, inguinal, dorsal midline, and tailhead). On-animal flea counts were conducted at the start of the trial (immediately prior to the initial application of the flea-control products) and then once every 2 weeks for the initial 12 weeks, then every 4 weeks until completion of the trial. Subsequent counts were carried out just prior to the scheduled reapplication of the flea-control products. Flea counts for each household were expressed as the mean of the counts for all animals in the residence.

Environmental flea counts were assessed for all homes one or two days prior to initiation of treatments. Thereafter, environmental flea assessments were made (only for Groups 1 and 3) every 2 weeks for the initial 12 weeks and then every 4 weeks until completion of the trial. Only on-animal flea counting was done for households in Group 2.

Environmental flea numbers were determined using intermittent-light flea traps. These traps consist of a green light that flashes intermittently to attract fleas hatching from
pupae. Attracted fleas are trapped on an adhesive card fixed in front of the light source. The trapped fleas can then be counted in situ under hand-lens magnification. Environmental trap counts were conducted over a 20- to 24-hour period in two rooms of each house. Traps were placed in rooms where the pets spent the majority of their time or where homeowners observed fleas. The same two rooms were used for trap collections during the entire study.

**Data Analysis**

Flea populations per household were calculated as the arithmetic mean of the counts from all animals in the household. Reductions in flea counts on the animals and from the environment were calculated for each treatment in each household using the formula:

\[
\text{Percentage reduction} = \frac{\text{Pretreatment flea count} - \text{Posttreatment flea count}}{\text{Pretreatment flea count}} \times 100
\]

Overall percentage reductions for each treatment were calculated by averaging the percentage reduction of each household. On-animal flea counts for Groups 1 and 3 were compared using a Wilcoxon rank sum test to determine if there were significant differences at any of the evaluation times. This test was chosen as the most suitable for nonparametric data (i.e., the number of properties in each treatment group did not remain constant over the study period). Differences were declared significant when \( P < .05 \).

**RESULTS**

Some households were not able to complete their participation in the study. This occurred for a variety of reasons, including relocation by the family to a new home. From the original sample size of 15 properties per treatment group, each of the three treatment groups had nine properties remaining in the study at the final 52-week assessment. Evaluations were carried out for whatever properties were still in the study at each time point throughout the study.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Pretreatment</th>
<th>2 wk</th>
<th>4 wk</th>
<th>6 wk</th>
<th>8 wk</th>
<th>10 wk</th>
<th>12 wk</th>
<th>16 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–Lufenuron</td>
<td>26.3 ± 2.47</td>
<td>2.47 ± 0.27</td>
<td>0.4 ± 0.33</td>
<td>0</td>
<td>0</td>
<td>0.73 ± 0.53</td>
<td>0.3 ± 0.77</td>
<td>1.23 ± 0.83</td>
</tr>
<tr>
<td>plus nitenpyram*</td>
<td>15.5</td>
<td>3.7</td>
<td>0.59</td>
<td>0.83</td>
<td>1.29</td>
<td>0.33 ± 0.5</td>
<td>1.09 ± 0.38</td>
<td>1.42 ± 1.45</td>
</tr>
<tr>
<td>2–Lufenuron</td>
<td>28.0 ± 2.73</td>
<td>2.73 ± 0.43</td>
<td>0</td>
<td>0</td>
<td>0.43 ± 0.57</td>
<td>0.5 ± 0.5</td>
<td>0.5 ± 0.17</td>
<td>0.17 ± 0.33</td>
</tr>
<tr>
<td>plus nitenpyram†</td>
<td>24.2</td>
<td>3.35</td>
<td>1.09</td>
<td>1.24</td>
<td>1.45</td>
<td>1.07 ± 1.79</td>
<td>1.76 ± 1.76</td>
<td>2.69 ± 2.65</td>
</tr>
<tr>
<td>3–Imidacloprid‡</td>
<td>28.7 ± 4.0</td>
<td>4.0 ± 1.73</td>
<td>1.47 ± 2.4</td>
<td>1.4 ± 0.93</td>
<td>0.93 ± 0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Lufenuron administered per label directions to all dogs and cats in household, plus nitenpyram tablets administered orally to all dogs and cats once per week for 6 weeks, then another single dose of nitenpyram per week if needed for re-infestation.

† Lufenuron administered per label directions to all dogs and cats in household plus nitenpyram tablets administered orally to all dogs and cats twice per week for 6 weeks, then two doses of nitenpyram per week if needed for re-infestation.
Flea Populations on Animals

In households of Group 1, which had their animals treated with lufenuron (monthly for dogs and every 6 months for cats) plus nitenpyram (once per week for 6 weeks), flea counts on animals were generally reduced by 90% to 100% (Table 1, Figure 1). Little additional intervention using nitenpyram was required after the initial 6-week treatment program (one household each at Weeks 8, 16, and 36 and three households at Week 40).

Animals from households in Group 2 were treated with lufenuron the same as for Group 1 but were allowed two treatments per week with nitenpyram. As would be expected, flea counts (Table 1) and percentage reductions (Figure 1) for animals in this group were quite similar to those for Group 1. Once again, there was only occasional use of nitenpyram after the initial 6-week period. Additional nitenpyram was used at four of the nine properties, including one each at Weeks 12, 20, and 24, two households at Week 32, and one household at Week 40. In each case, the animal with fleas was given two doses of nitenpyram three or four days apart, as directed by the study protocol.

In Group 3, flea counts on pets treated with imidacloprid (Table 1) and reductions (86.1% to 97.2%) were relatively similar to those obtained with lufenuron plus nitenpyram for the first 16 weeks; however, results were variable thereafter, ranging from a high of 92.8% at Week 24 to a low of 35.2% at Week 36 (Figure 1). This coincided with the start of the wet season in Cairns (October). Arithmetic mean flea counts were significantly \((P < .05)\) higher for Group 3 (imidacloprid) than for Group 1 (lufenuron plus nitenpyram) at Weeks 4, 8, 10, 20, 28, 32, 36, 40, 44, and 52 (Table 1).

Environmental Flea Populations

Mean environmental flea counts for Groups 1 (lufenuron and nitenpyram) and 3 (imidacloprid) are shown in Table 2. The percentage of homes with fleas present in the environment is displayed in Figure 2. At 2 weeks after the start

<table>
<thead>
<tr>
<th>20 wk</th>
<th>24 wk</th>
<th>28 wk</th>
<th>32 wk</th>
<th>36 wk</th>
<th>40 wk</th>
<th>44 wk</th>
<th>48 wk</th>
<th>52 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.53 ±</td>
<td>0.77 ±</td>
<td>0.15 ±</td>
<td>1.23 ±</td>
<td>0.83 ±</td>
<td>2.8 ±</td>
<td>0.3 ±</td>
<td>0.3 ±</td>
<td>0.44 ±</td>
</tr>
<tr>
<td>0.83</td>
<td>1.09</td>
<td>0.38</td>
<td>1.42</td>
<td>1.64</td>
<td>4.21</td>
<td>0.67</td>
<td>0.67</td>
<td>0.88</td>
</tr>
<tr>
<td>1.0 ±</td>
<td>1.0 ±</td>
<td>0.6 ±</td>
<td>1.33 ±</td>
<td>0.33 ±</td>
<td>1.0 ±</td>
<td>0 ±</td>
<td>0.33 ±</td>
<td>0.11 ±</td>
</tr>
<tr>
<td>1.79</td>
<td>1.76</td>
<td>1.07</td>
<td>2.69</td>
<td>1.0</td>
<td>2.65</td>
<td>1.0</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>3.53 ±</td>
<td>2.08 ±</td>
<td>7.0 ±</td>
<td>13.1 ±</td>
<td>18.6 ±</td>
<td>7.3 ±</td>
<td>3.75 ±</td>
<td>5.13 ±</td>
<td>2.33 ±</td>
</tr>
</tbody>
</table>

³Imidacloprid administered topically every 4 weeks to all dogs and cats in household.

‡Significantly greater than Group 1 (lufenuron plus nitenpyram) \((P < .05)\).
of the study, the environmental flea population was reduced by 85.5% in the homes with pets treated with lufenuron and nitenpyram (Group 1) compared with a reduction of only 21.7% in homes using imidacloprid for their pets (Group 3). Throughout the remainder of the year, environmental flea counts in Group 1 were reduced by 94.5% to 100%. In Group 3, reductions in environmental flea counts ranged from 0% to 93.7% throughout the year.

All homes in Group 1 were free of environmental fleas from Week 8 through Week 52 with the exception of one home found to be infested at Week 40 (Figure 2). Conversely, all homes in Group 3 had fleas in the traps at various times during the study. The infestation rate for homes in Group 3 ranged from 16.7% to 100%. Rates were highest  

### TABLE 2. Mean Environmental Flea Counts

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Pretreatment</th>
<th>2 wk</th>
<th>4 wk</th>
<th>6 wk</th>
<th>8 wk</th>
<th>10 wk</th>
<th>12 wk</th>
<th>16 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–Lufenuron plus nitenpyram*</td>
<td>5.5 ± 8.6</td>
<td>0.80 ± 1.27</td>
<td>0.27 ± 0.59</td>
<td>0.13 ± 0.52</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3–Imidacloprid†</td>
<td>5.2 ± 13.2</td>
<td>4.07 ± 4.52</td>
<td>1.20 ± 1.42</td>
<td>1.80 ± 1.90</td>
<td>1.47 ± 2.29</td>
<td>0.87 ± 1.13</td>
<td>0.80 ± 1.21</td>
<td>1.07 ± 1.44</td>
</tr>
</tbody>
</table>

*Lufenuron administered per label directions to all dogs and cats in household, plus nitenpyram tablets administered orally to all dogs and cats once per week for 6 weeks, then another single dose of nitenpyram per week if needed for reinestation.

†Imidacloprid administered topically every 4 weeks to all dogs and cats in household.
for this group from Week 28 to Week 48, coinciding with the area's wet season.

**DISCUSSION**

As a result of the biology and prodigious reproductive potential of the cat flea, the majority of the flea populations are present in the surroundings of the host, with all stages represented there. Only 5% to 10% of the flea population is found on the animal.\(^1\) With an understanding of this biology, traditional flea-control procedures have included environmental and on-animal flea-control strategies used concurrently.\(^2\) During the past 10 years lufenuron, fipronil, and imidacloprid have given veterinary practitioners dramatically better flea control than rinses and powders had previously. As a result, veterinarians are less inclined to consider additional environmental flea control to be essential.\(^3\) This strategy may give adequate control in the short term but will allow development of flea infestations to continue in the environment of the pet. Results of recent laboratory studies\(^4\) suggest that imidacloprid can pass from treated dogs into the environment and thus can prevent larval development. In this field study, environmental flea numbers were estimated by the number of fleas caught in flea traps over a 24-hour period. If no fleas were trapped in either of the flea traps placed in each household, then it was assumed this household had zero or very low numbers of environmental fleas. There was no attempt to quantify numbers of fleas trapped with total numbers of environmental fleas in the household. However, a number of houses in Group 3 (imidacloprid) always had environmental fleas present, and during the period of heavy flea activity in spring and early summer (Weeks 28 through 48), all of the households evaluated in this group had fleas present in the environment. This suggests that if imidacloprid leaves the animals and enters the environment, as suggested by Hopkins and coworkers, this method of environmental control was not completely effective in the present study, despite treatment of all pets in the household every 28 days.

**CONCLUSION**

There are currently no published studies on the use of an insect-development inhibitor combined with a short-acting insecticide to provide short- and long-term flea control in a field trial setting. This trial, conducted in one geographical region with data from all time points collected from up to 45 households,
demonstrated definite benefits in terms of re-
ducing on-animal and environmental flea pop-
ulations with the use of lufenuron concurrently
with nitenpyram for household pets when
compared with the use of topical imidacloprid
as the only means of flea control.

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