

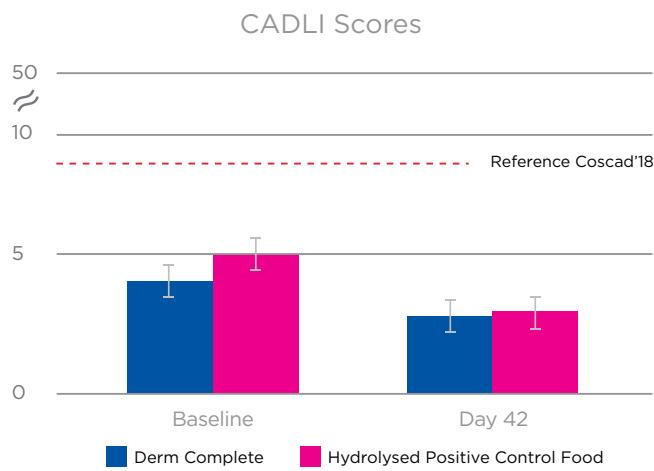
# Clinical Evidence Report 1

In a multi-centre, blinded, controlled, longitudinal study, client-owned dogs with well-controlled food sensitivities fed **Hill's Prescription Diet Derm Complete** demonstrated continued control of clinical signs.

Hill's Pet Nutrition, Inc. Data on file

## Results:

### Veterinarian-Reported Canine Atopic Dermatitis Lesion Index (CADLI) Scores Were No Different from Baseline = Continued Control\*



\*Veterinarian assessments over times were not significantly different vs baseline or compared with control food ( $P>0.05$ )

\*\*CADLI (Figure 1) score less than or equal to 8 (dotted line above) is normal (COSCAD, 2018).

Error bars: standard error

These results demonstrate that **Prescription Diet Derm Complete** maintained control of clinical signs of food sensitivities in dogs previously well controlled on a dietetic novel or hydrolysed food and was as effective as a hydrolysed protein dietetic food when fed to food-allergic dogs in a 21-day study.

## Additional Significant Findings:

- Dogs with dermatological clinical signs noted, once transitioned from original novel or hydrolysed protein dietetic foods were few and similar in number between groups.
- There were no significant differences between foods or over time in the activity data collected from Hill's wearable collars, including no significant increases in scratching, shaking or worsening of sleep quality behaviours.
- There were no differences in owner-reported control of scratching using the Pruritus Visual Analog Scale (PVAS, Figure 2), sleep and stool quality when food-allergic dogs were fed Derm Complete compared with a dietetic hydrolysed protein food.
- There was a significant improvement in veterinarian-reported skin healing scores in the United Kingdom study dogs fed Derm Complete after 21 days compared with dogs fed the hydrolysed protein dietetic positive control food ( $P<0.05$ ).

## Implications for Practice

These results demonstrate that Derm Complete provides excellent control of clinical signs of food sensitivities in dogs and therefore is an excellent first choice for dogs with suspected food or environmental allergies. Additionally, Derm Complete was associated with significant skin healing in food-allergic dogs in as little as 21 days.

## Supplementary Study Information

### Subjects

- 57 client-owned dogs
- Mean age 6 years

### Methods

Dogs with a food sensitivities were recruited for two identical, randomised, double-blinded, controlled studies in the United States and United Kingdom to evaluate the effect of a test food (Prescription Diet Derm Complete), on food sensitivities-related signs over a 42-day period compared with a positive control food. The results of the two studies were similar and have been combined for analysis. The test food contained egg, omega-3, 6 and 9 fatty acids, and the control food a hydrolysed animal protein. Dogs had been diagnosed by a food elimination trial, managed in general veterinary practice and were consuming a novel or hydrolysed protein dietetic food at the time of enrollment. Veterinary-reported canine atopic dermatitis lesion index (CADLI) scores (Figure 1) and owner pruritus visual analog scale (PVAS, Figure 2) values were performed at study entry to assess dermatologic clinical signs and conformed with the 2018 COSCAD (Core Outcome Set for Canine Atopic Dermatitis trials) guidelines outlined by the veterinary dermatology profession (Olivry, 2018). Dogs consumed their usual diet for the 21-day study and then CADLI and PVAS values were repeated. Dogs wore a collar-mounted activity monitor throughout the study. Machine learning-based behaviour recognition

- Previously diagnosed with food sensitivities, well-controlled on a dietetic novel or hydrolysed protein dietetic food

algorithms quantified the total duration of scratching (sec/day), shaking (sec/day), resting (hrs/day) and sleeping (hrs/day); sleep quality was evaluated with an algorithm based on the absence of night-time disturbance (0: highly disturbed sleep, 100: undisturbed sleep). The validated scratching and shaking algorithms have an accuracy >99%. Behaviours, CADLI and PVAS values were analysed in SAS using linear mixed-models with diet, time, and diet x time as fixed-effects and a significance threshold of  $P < 0.05$ . On Day 22 (end of baseline), dogs were randomly assigned to either Test Food (Prescription Diet Derm Complete dry food) or a positive control hydrolysed protein dietetic food (Royal Canin Ultamino canine dry food) until study day 42. Upon study completion, veterinarian-reported CADLI, owner-reported PVAS and behavioural assessments collected by the activity monitors were evaluated and compared with baseline. Analysis was linear mixed-models with diet, time, and diet x time as fixed-effects in SAS and was appropriately powered to detect significant differences between groups ( $P < 0.05$ ) with 80% power if any differences were to have existed. There were no significant differences between groups for all relevant measures.

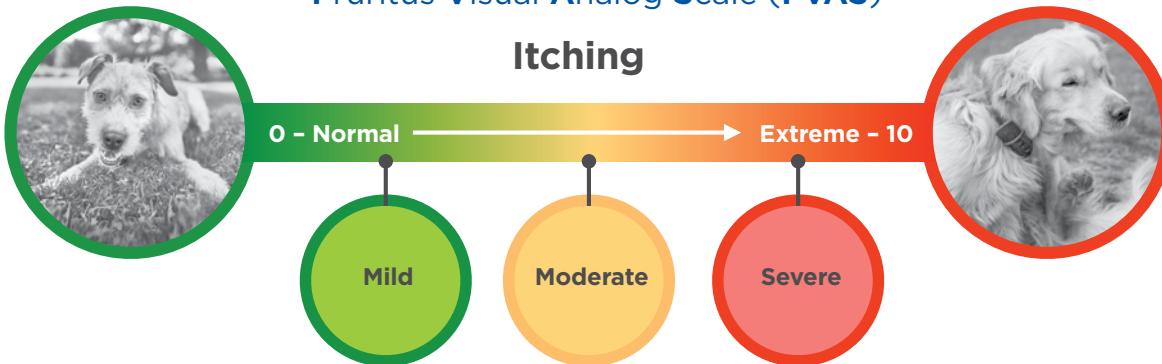
Figure 1

### Veterinary Evaluations: The Canine Atopic Dermatitis Lesion Index (CADLI)

Body Region	Erythema Excoriation Erosion 0-5	Alopecia Lichenification Hyperpigmentation 0-5
Head & Pinnae		
Forefeet		
Hind Feet		
Ventral Thorax & Axillae		
Ventral Abdomen & Inguinal		
Sub-totals 0-25		
Totals 0-50		

Figure 2

### Pruritus Visual Analog Scale (PVAS)



### Key Conclusions

**Prescription Diet Derm Complete** is as effective as a dietetic hydrolysed protein food in maintaining control of clinical signs of food sensitivities in a 42-day study in food-allergic dogs as assessed by veterinarians, owners and use of objective wearable data.

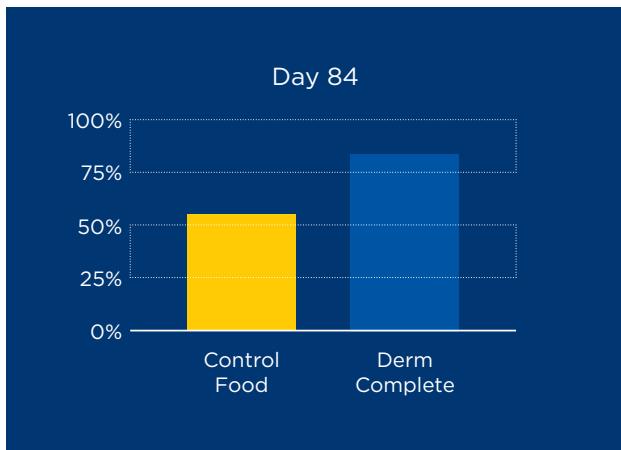
# Clinical Evidence Report 2

Client-owned dogs with canine atopic dermatitis fed **Prescription Diet Derm Complete** in a multi-centre, blinded, controlled, longitudinal study demonstrated significant improvements in owner-reported clinical signs and sleep quality.

Hill's Pet Nutrition, Inc. Data on file.

## Results:

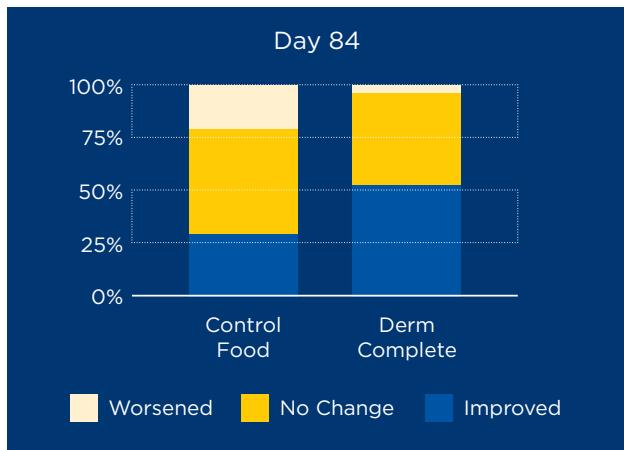
**Significantly More Owners Reported Lower (Improved) Pruritus Visual Analog Scores (PVAS) After Feeding Derm Complete Compared with Control Food**



### Percentage of Lower Owner-Reported PVAS Scores Upon Study Completion

A significantly greater proportion of owners (82% vs 60%) who fed Derm Complete to their dogs with canine atopic dermatitis reported lower scratching scores (PVAS, Figure 1) on a 0-10 scale of severity at the end of the study compared with study start than owners of dogs fed a control food ( $P<0.05$ ).

**Owners Reported Significantly Improved Sleep in Dogs Fed Derm Complete Compared with Dogs Fed the Control Food**



### Sleep Quality of Dogs Reported by Owners at Study Completion

A significantly greater proportion of owners (59% vs 32%) who fed Derm Complete to their dogs with canine atopic dermatitis reported an improved score for the question "my dog sleeps well" at study end compared with study start than owners of dogs fed a control food ( $P<0.05$ ).

These results demonstrate that **Prescription Diet Derm Complete** provides significant benefits to dogs with atopic dermatitis when used as part of multimodal therapy.

## Additional Significant Findings:

- There was a significant improvement in owner-reported score for "how much does your dog's condition interfere with your or a member of your family's sleep" after 2 months in dogs with atopic dermatitis fed Derm Complete compared with dogs fed a control food ( $P<0.05$ ).
- At study completion, 8/10 veterinarians reported that they would recommend Derm Complete to a colleague.

## Implications for Practice

These results demonstrate that Derm Complete is an important component of multimodal therapy for canine atopic dermatitis.

## Supplementary Study Information

### Subjects

- 47 client-owned dogs
- Mean age 6.4 years

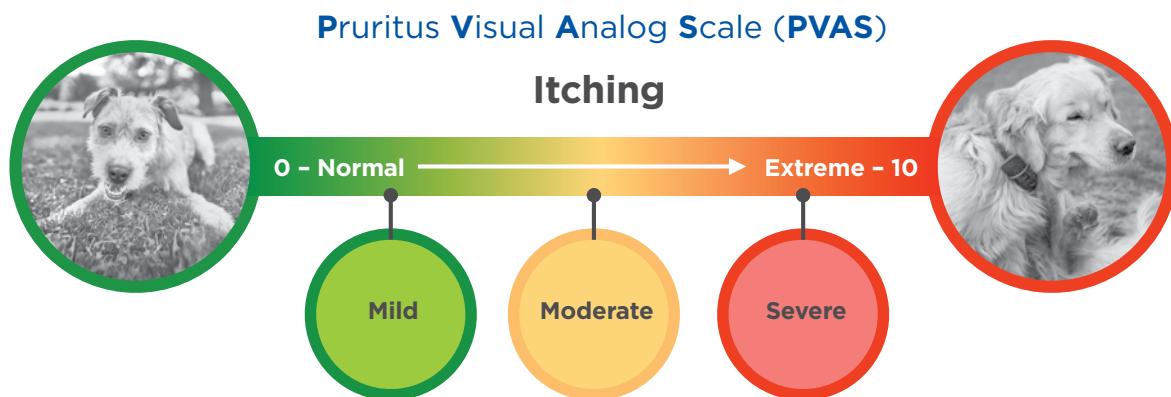
- Previously diagnosed with atopic dermatitis and experiencing an active episode

### Methods

Dogs with seasonal pruritus diagnosed by their attending veterinarian, at least 1-year-old, under veterinary care for canine atopic dermatitis and currently exhibiting clinical signs were recruited from general and specialty practices in 12 states throughout the USA for participation in an 84 day, randomised, double-blinded controlled study. Veterinary-reported canine atopic dermatitis lesion index (CADLI) scores (Figure 2) and owner pruritus visual analog scale (PVAS, Figure 1) were performed at study entry to assess dermatologic clinical signs and the study conformed with the 2018 COSCAD (Core Outcome Set for Canine Atopic Dermatitis trials) guidelines outlined by the veterinary dermatology profession (Olivry, 2018). Dogs had a veterinarian-assessed canine atopic dermatitis lesion index (CADLI) score  $>8/50$  (Figure 2, less than 8 is considered normal) and an owner-reported Pruritus Visual Analog Score (PVAS) of  $>3.5/10$  at enrollment (Figure 1, 1-10 scale where

0 represents no pruritus, 10 extreme pruritus), had to be free of infectious pyoderma, and not receiving monoclonal antibody therapy. Other medications were allowed provided they remained unchanged during the study period. Dogs were followed for a 21-day baseline period and then CADLI and PVAS were repeated. Dogs were then blocked based on CADLI scores and randomised to Test Food (Prescription Diet Derm Complete) or Control Food for 63 days. The test food contained ingredients rich in polyphenols with reported antioxidant and anti-inflammatory properties as well as egg, omega-3, 6 and 9 fatty acids. The control food was an adult maintenance food. Upon study completion, veterinarian-reported CADLI and owner-reported PVAS values were collected and compared with baseline. Analysis was linear mixed-models with diet, time, and diet x time as fixed-effects and a significance threshold of  $P<0.05$  in SAS.

**Figure 1**



**Figure 2**

### Veterinary Evaluations: The Canine Atopic Dermatitis Lesion Index (CADLI)

Body Region	Erythema Excoriation Erosion 0-5	Alopecia Lichenification Hyperpigmentation 0-5
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Forefeet		
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Ventral Thorax & Axillae		
Ventral Abdomen & Inguinal		
Sub-totals 0-25		
Totals 0-50		

### Key Conclusions

**Prescription Diet Derm Complete** is an effective component of multimodal therapy for canine atopic dermatitis and results in significant improvements in owner-reported scratching and sleep quality compared with the control food.

# Clinical Evidence Report 3

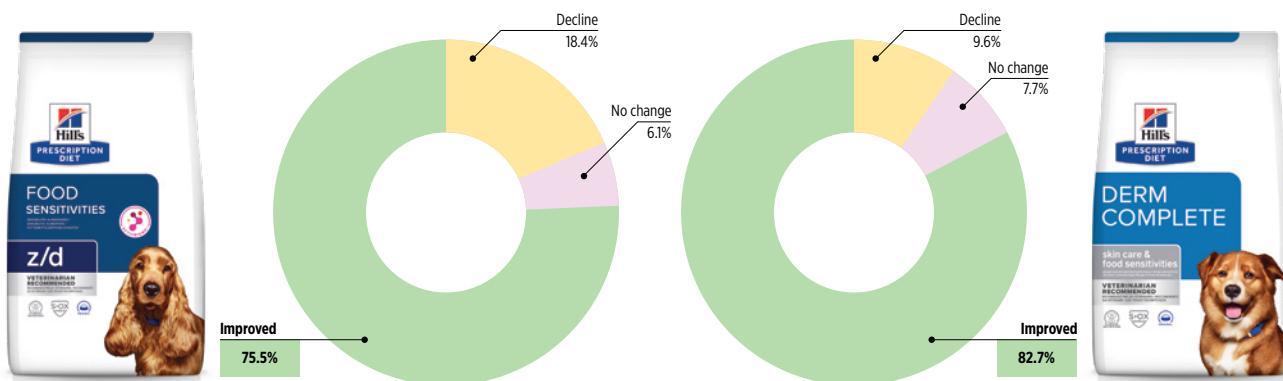
In a prospective, matched pair, longitudinal clinical trial, Hill's **Prescription Diet Derm Complete** resulted in improved pruritus scores and showed equivalent results to Hill's Prescription Diet z/d in managing itchy dogs without a known primary cause.

Hill's Pet Nutrition, Inc. Data on file.

## Results:

When fed to pruritic dogs, both Hill's Prescription Diet z/d and Derm Complete resulted in improved owner-reported pruritus scores and veterinarian-reported Canine Atopic Dermatitis Extent and Severity Index (CADESI) -4 Scores. There was no significant difference in the percent of dogs with clinical improvements in the z/d vs. Derm Complete fed groups.

**Significant decreases in veterinary-assessed CADESI-4 scores occurred in the pruritic dogs fed both Prescription Diet z/d and Derm Complete ( $p < 0.05$ ).**



Of the dogs fed z/d, 75.5% (n = 37/49) had a reduction in CADESI-4 score with an average CADESI score of 19.9 at the start of the program and 10.9 at the end (45% reduction). Of the dogs fed Derm Complete, 83% (n = 43/52) had a reduction in CADESI-4 score, with an average CADESI-4 score of 13.8 at the start to 7.2 at the end (47% decrease).

**Owner-reported pruritus decreased in both the dogs fed Derm Complete and z/d during the study period.**



Of the dogs fed Prescription Diet z/d, 71% (n = 35) reported improvements from the first consultation to the last. Of the dogs fed Prescription Diet Derm Complete, 73% (n = 37) reported improvements from the first consultation to the last.

These results demonstrate that **Prescription Diet Derm Complete** managed dogs with undefined pruritic skin conditions as well as z/d.

## **Additional Significant Findings:**

- Improvements in the owner-reported quality of life score was seen in 42% (n = 20/49) of dogs fed z/d and in 48% (n = 25/52) of participants fed Derm Complete.
- Of dogs that had head-shaking symptoms at the start of the trial, improvements were seen in 60% (n = 15/25) of dogs fed z/d and 81% (n = 17/21) in dogs fed Derm Complete.
- Improvements in erythema were observed in 67% (n = 33) of dogs fed z/d and 75% (n = 39) of dogs fed Derm Complete.

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## **Implications for Practice**

Dietetic nutrition can help reduce clinical signs associated with pruritus and skin disease in a majority of dogs. Derm Complete should be considered when managing dogs with atopic dermatitis and those that have not yet undergone a full workup for their pruritus.

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## **Supplementary Study Information**

### **Subjects**

- 101 client-owned adult dogs
- Mean age 5 years

### **Methods**

Dogs with clinical signs of pruritus were prospectively recruited from a pet insurance database for a 12 week, prospective clinical trial in the United Kingdom to evaluate the effects of 2 different foods (Prescription Diet z/d and Derm Complete) on clinical signs associated with pruritic skin disease. A total of 101 dogs were enrolled in the study with 49 in the z/d group and 52 in the Derm Complete group. The dogs were between 2-13 years (mean 5 years) with 50 males and 51 females representing numerous breeds as well as crossbreeds. Participants were excluded from the trial if they were under one year of age, had previously been placed on a controlled dermatological food trial, or had concurrent chronic disease comorbidities.

Participants were randomly assigned to a feeding group. Data pertaining to owner assessed clinical signs and veterinarian assessed clinical parameters (BCS and CADESI-4) were collected via interactions on the smartphone application at day 0, weeks 2, 4, 8, and 12 of the study. Owners were provided with food at the start of the study and had a choice of dry, wet or combination wet and dry of the assigned food for their dog. Owners were instructed to feed nothing except the food and hydrolyzed protein treats provided for the duration of the study. Participants were managed as normal in their home environments, and continued any routine additional medical management of their pruritic skin disease.

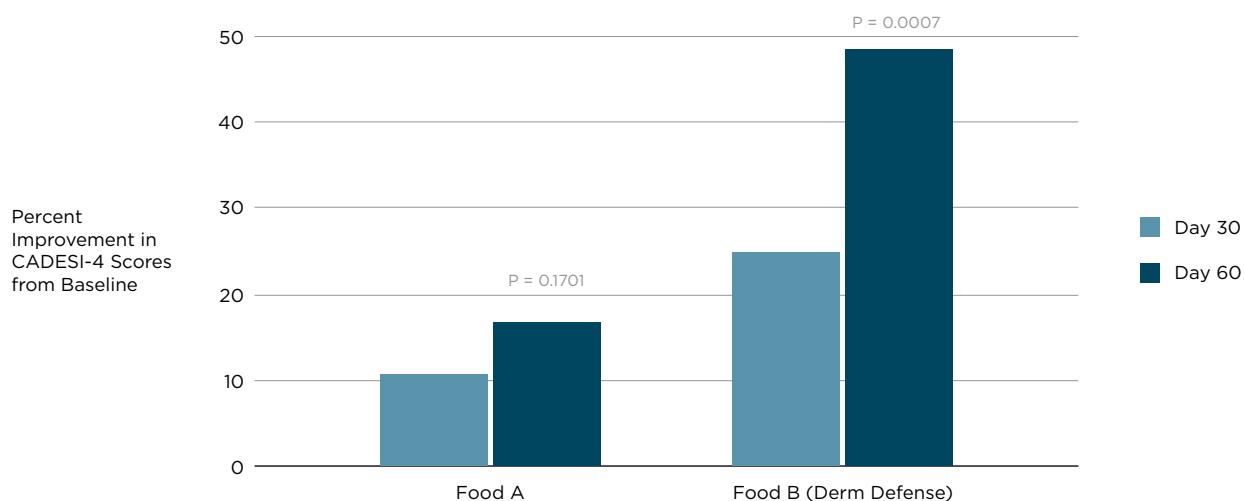
# Clinical Evidence Report 4

In a randomise, double-blind, placebo-controlled clinical trial, nutrition containing the **HistaGuard Complex** significantly reduced CADESI-4 and owner-reported pruritus scores in dogs with atopic dermatitis.

de Santiago, M.S., Arribas, J.L.G., Llamas, Y.M. et al. Randomized, double-blind, placebo-controlled clinical trial measuring the effect of a dietetic food on dermatologic scoring and pruritus in dogs with atopic dermatitis. *BMC Vet Res* 17, 354 (2021). <https://doi.org/10.1186/s12917-021-03063-w>

## Results:

**The Percent Improvement in CADESI-4 Scores was Significantly Greater When Dogs Were Fed Derm Defense Compared to a Control Food.**



There was a 48.5% decrease in CADESI-4 Index Scores for the Derm Defense group but only a 16.8% decrease in the control group. The percent change in the Derm Defense Group was statistically significant both over time and compared to Food A.

**Owner-Reported Pruritus Scores Decreased Significantly on Derm Defense**

	Food A	Food B (Derm Defense)
Day 0	8.0 (6.0-10.0)	8.0 (4.0-10.0)
Day 30	5.0 (1.0-9.0)	4.0* (1.0-10.0)
Day 60	6.0 (1.0-10.0)	3.5* (0.0-9.0)

Significant decrease with Derm Defense

\* The change in pruritus scores over time in the Derm Defense Group was statistically significant vs. day 0 ( $p < 0.0001$ ).

There was a 48.5% decrease in median CADESI-4 Index Scores for the Derm Defense group but only a 16.8% decrease in the control group. The percent change in the Derm Defense Group was statistically significant over time vs. day 0 ( $p < 0.0001$ ).

## Implications for Practice

These results demonstrate that dietetic nutrition including the HistaGuard Complex as part of multi-modal management for atopic dermatitis can help reduce pruritus and clinical signs associated with atopic dermatitis. Derm Defense and Derm Complete, both containing the HistaGuard Complex, can be used to aid in the management of dogs with atopic dermatitis.

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## Supplementary Study Information

### Subjects

- 40 client-owned adult dogs (18 male, 22 female)
- All enrolled dogs completed the study

### Methods

Dogs diagnosed with atopic dermatitis at Complutense University of Madrid were enrolled in this 2 month trial. Dogs were diagnosed with AD based on history, clinical signs and fulfillment of Favrot's criteria. They also had to be free of ectopic parasites and have received parasite preventative medications for at least 2 months prior to enrollment. All enrolled dogs underwent an 8-week dietary elimination trial with a hydrolyzed protein food (Hill's Prescription Diet z/d) to rule out food allergic dermatitis. Oclacitinib was not permitted prior to enrollment but was started for all dogs at the start of the study. No dietary supplements, treats or topical medication medications were allowed during the study but flea and tick preventative collars were encouraged.

Dogs were randomly assigned to a control food (Purina ProPlan OptiNutrition Adult, dry) or a test food (Derm Defense, dry) for 60 days. The foods had similar macronutrient profiles but the test food had higher levels of omega-3 fatty acids, polyphenols, and vitamin C and E. Veterinary assessments using the CADESI-4 index occurred at days 0, 30 and 60 by a single blinded investigator. Owner assessments of the intensity of their pet's pruritus occurred on days 0, 15, 30, 45, and 60 using the Pruritus Visual Analog Scale (PVAS).