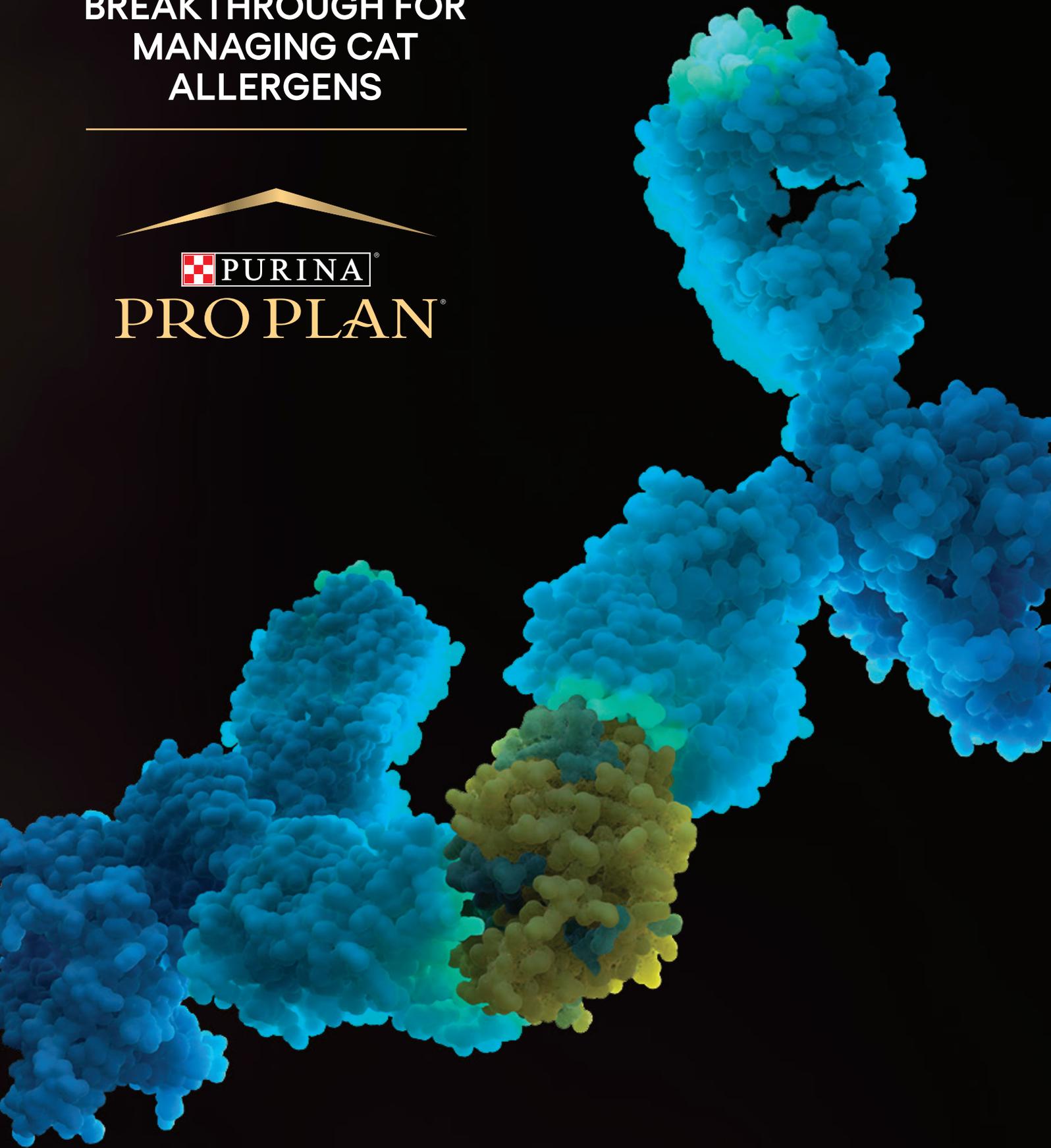


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**A FELINE-FRIENDLY  
BREAKTHROUGH FOR  
MANAGING CAT  
ALLERGENS**

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# Contents

Sensitisation to **cat allergens** is a global health concern, affecting approximately **1 in 5 adults** around the world. The commonly recommended methods for reducing these allergens—constant house cleaning, bathing the cat, or medications that ease symptoms for people with cat allergen sensitivity—all have limited effectiveness. Human allergists note that the best line of defense against this sensitisation is to avoid having any cats in the home, even as they recognize that many cat owners will not comply with this recommendation. None of these options improve the bond between cats and the people who love them.

Now there is a **feline-friendly approach** for managing these allergens. This breakthrough enables people who love cats to reduce their exposure to the allergens—while keeping cats in their homes and on their laps.

Up to 95% of people sensitised to cat allergens are affected by Fel d 1, a protein produced by cats mainly in their salivary and sebaceous glands. Through grooming, **cats transfer salivary Fel d 1 onto the hair coat** and then shed this allergen, stuck to hair and dander, into the environment.

Inspired by pet allergen sensitivities in my own family, our research team discovered a way to safely **neutralise the active Fel d 1 in cats' saliva** before it can trigger allergen sensitivities in people. This revolutionary method was developed after **more than a decade of research**, beginning with proof-of-concept benchtop studies that demonstrated how the Fel d 1 allergen could be effectively blocked by naturally occurring anti-Fel d 1 antibodies, and culminating with a complete and balanced diet containing an **egg product ingredient with anti-Fel d 1 antibodies** that was proven to reduce salivary active Fel d 1 levels in cats and on the hair coat and dander. Importantly, this method neutralises the active allergen but it **does not interfere with a cat's natural Fel d 1 production**.

This monograph provides the information you need to understand the breakthrough science behind this innovative method for neutralising Fel d 1, the primary cat allergen, at its source in cats' saliva. Feeding Purina® Pro Plan® LiveClear® can help keep cats and people closer together.

  
Dr. Ebenezer Satyaraj, PhD  
Director, Molecular Nutrition  
Nestlé Purina Research

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## Fel d 1 – The Primary Cat Allergen

The global incidence of cat allergies has been reported to be rising sharply, with increasing rates of allergy being recorded as posing a major public health problem.<sup>12</sup> Eight cat-origin allergens (Fel d 1 – to Fel d 8) have been registered to date through the World Health Organization/International Union of Immunological Societies (WHO/IUIS) Allergen Nomenclature Sub-Committee.<sup>2-4</sup> **Fel d 1**, a secretoglobulin, is the **primary cat allergen**, accounting for up to 95% of all adults who are sensitised to cat allergens.<sup>2,5</sup>

**All cats produce Fel d 1** regardless of breed, age, hair length or color, sex, housing (indoors vs outdoors), or body weight.<sup>2,5-9</sup> Importantly, despite a very common misconception, there are no allergen-free or ‘hypoallergenic’ cat breeds.<sup>2,5,7-11</sup> Fel d 1 production can vary widely among individual cats and in the same cat can fluctuate throughout the year.<sup>5,9,11,12</sup> In a recent study, Bastien *et al*<sup>12</sup> observed an 80-fold difference in salivary Fel d 1 levels between the lowest-producing and highest producing cats in a group of 64 cats, and up to a 76-fold difference between the lowest and highest salivary Fel d 1 levels in individual cats. Studies have also shown that **male cats produce 3-5 times less Fel d 1 after neutering**.<sup>13,14</sup> These findings, combined with observations that Fel d 1 production can be restored to pre-neutering levels with the administration of exogenous testosterone, suggest an influential role of

testosterone on Fel d 1 production.<sup>14</sup> **Fel d 1 is produced primarily in the salivary and sebaceous glands** and in lesser amounts in the lacrimal and anal glands.<sup>2,9</sup> Typically Fel d 1 is transferred and spread throughout the cat’s hair as the cat grooms and is then shed into the environment with hair and dander.<sup>2,9</sup>

**Fel d 1’s biological function for the cat is still unknown**, but a pheromone/chemical signaling role has been suggested.<sup>2,9,15</sup>

Since Fel d 1 is light it easily becomes and remains airborne in dander and dust particles.<sup>2,5</sup> **Up to 60% of Fel d 1 is carried by particles <5 microns in diameter.**<sup>2,5</sup> It is transferred on clothing<sup>2,5,11,16</sup> and as a result, the allergen is ubiquitous and has been found in homes without cats, and on public transportation and buildings at levels ( $\geq 8 \mu\text{g}$  Fel d 1 per gram of dust), that exceed the threshold value associated with sensitisation.<sup>2,5,16,17</sup> Although Fel d 1 levels in schools are detectable, they are often low and may not induce a response.<sup>18</sup>



## Impact of cat allergen sensitivities on cat welfare and the human-animal bond

Pets and pet ownership confers numerous positive health benefits to humans, including positive physical benefits such as influences on blood pressure and cardiovascular health and weight management, as well as improvements in mental health relating to loneliness and depression.<sup>19</sup>

When presented with a cat-allergic, cat-owning patient, **allergists are often compelled to recommend removal of the cat from the home** in order to reduce the environmental allergen load and relieve clinical responses to the allergen.<sup>5</sup> However, this recommendation is often met with resistance because cat owners consider their cats to be members of the family and understandably are not willing to re-home or relinquish their cat.<sup>5,11,20-22</sup>

For cat owners with sensitivities, their interactions with their cat can **directly impact the human-animal bond**. Physical contact plays an important role in the strength and longevity of the human-cat bond.<sup>23,24</sup> Allergists’

recommendations to keep the cat outside, out of the bedroom or keep them restricted to a certain part of the house can also result in increased levels of stress for the cat. Several studies have shown that stress in cats can increase the incidence of feline interstitial cystitis, upper respiratory infections and susceptibility to infectious agents.<sup>25</sup>

Although many owners with cat sensitivities will keep their cats, unfortunately, there is a direct impact on cat welfare because this is a commonly cited reason for relinquishment of cats to shelters,<sup>26-30</sup> as well as a **barrier to cat adoption and ownership**.<sup>30,31</sup>

## Current methods to reduce environmental allergens have limitations

Many cat owners value their cat's cleanliness and **grooming as an important aspect of cleanliness**.<sup>32</sup> However, it is also a primary method for dispersion of cat allergens throughout the cat's hair and subsequently into the environment, and can actually facilitate allergen exposure for cat allergen sensitised individuals.

**Environmental control measures to reduce environmental allergen levels in cat-sensitised households can be extensive**, and can include the following: use of HEPA (High Efficiency Particulate Air) filters in vacuum cleaners,<sup>5,11,33</sup> removal of carpets,<sup>33-35</sup> using pillow and mattress covers,<sup>5,35</sup> and removal or covering of upholstered furniture,<sup>5,34</sup> and extensive and regular cleaning of surfaces and fabrics.<sup>34,35</sup>

Allergists' recommendations may include washing the cat to physically remove allergens from the hair. However, this recommendation typically has poor compliance,<sup>35</sup> largely due to the feline species' aversion to bathing. But in addition, although immersion bathing is effective for lowering allergen levels on the cat's hair, the actual effects of bathing are transient; studies

have shown that **allergen levels return to baseline within 24 hours of bathing**.<sup>2,36,37</sup>

Although the **various measures may reduce the allergen load**, they mostly require significant effort, can be costly, and may be difficult to sustain long term.<sup>38</sup> In addition, the effects may be transient. Multifaceted interventions are recommended for best results.<sup>5,33</sup> Since **Fel d 1 is such a ubiquitous allergen**, sensitised individuals that successfully reduce the allergen load in their own homes will still be exposed to potentially high levels of cat allergens at work, in homes of cat-owning family members or friends, and in public places.

**Pharmaceutical interventions** such as preventing the onset of symptoms by using medications before cat exposure and immunotherapy are a common approach which also have limitations relating to both side effects and efficacy.

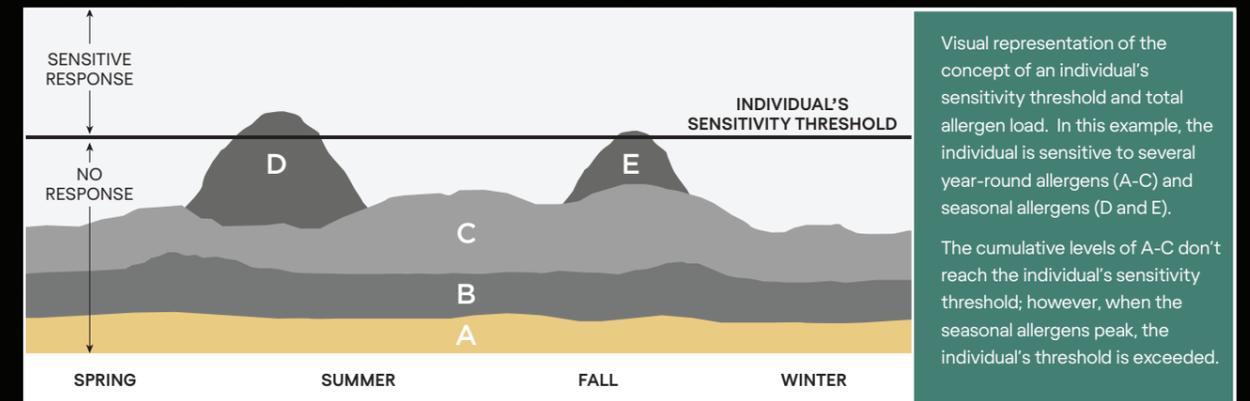
## Allergen Load Reduction

Typically humans are sensitive to a number of allergens and allergens have an additive effect<sup>39,40</sup> —this is the concept known as the **'total allergen load'** which represents the **sum of the individual allergens in the environment at that time**. If the total allergen load exceeds an individual's allergic threshold, that individual will develop a response. **High exposure of one allergen may be sufficient** to trigger mast cell degranulation and mediator release, while lower levels do not. However **multiple allergens** present at subthreshold levels may have a cumulative effect that exceeds the threshold

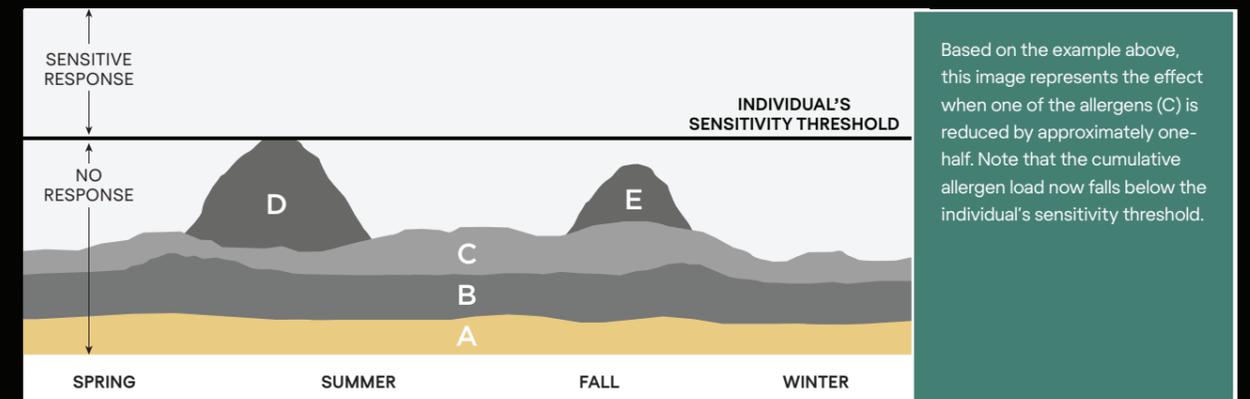
and triggers the chain of events leading to a response. If the allergen load can be reduced by avoiding or reducing the level of exposure to one or more of the contributing allergens, the cumulative level of allergen response may fall below an **individual's threshold** and improve or prevent a response.

Having an additional management tool that can help manage Fel d 1 to reduce the allergen load is much needed.

THE CONCEPT OF TOTAL ALLERGEN LOAD



EFFECT OF REDUCING TOTAL ALLERGEN LOAD



## A breakthrough and clinically proven method to reduce Fel d 1 on cats' hair and dander

Over a decade of research has resulted in a scientifically proven, innovative method that is feline friendly and can transform the way to manage allergens to cats: by reducing exposure to the allergen, but not to the cat.

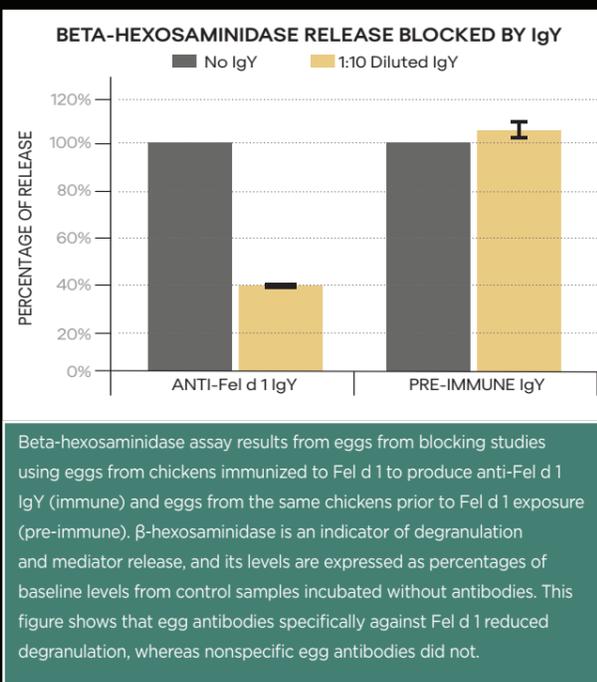
Since the biological function of Fel d 1 for the cat is currently unknown,<sup>2,9,15</sup> the potential health and welfare concerns of interfering with or stopping the production are also unknown.

Thus foundational to our research was to develop an approach that did not **alter the cat's production of Fel d 1** or affect the cat's overall physiology.

Our proof of efficacy research started with the **development of an antibody** that could be delivered as a coating on nutritious cat food and that would work directly in the mouth, as the cat chewed her kibble.

## Anti-Fel d 1 IgY effectively neutralises active Fel d 1 *in vitro* and *ex vivo*

Based on the findings that polyclonal binding is necessary to neutralise Fel d 1's allergenicity, Satyaraj *et al*<sup>41</sup> evaluated the efficacy of avian **egg yolk-derived immunoglobulin Y (IgY)** directed against Fel d 1. IgY is an avian equivalent to mammalian IgG and is found in chicken serum and egg yolks. Chickens naturally produce IgY against environmental antigens or pathogens, and transfer the IgY into their eggs to provide passive immunity to their offspring.<sup>42,43</sup> Anti-Fel d 1 IgY can be developed by exposing hens to Fel d 1. Based on this principle, anti-Fel d 1 IgY were produced using well established methods.<sup>41</sup> Our studies demonstrated that **anti-Fel d 1 IgY blocked the binding of salivary Fel d 1** to Fel d 1-specific IgE *in vitro* in a dose-dependent manner similar to a standardized polyclonal antibody in both the modified chimeric ELISA and basophil activation assay<sup>41</sup>.



## Feline test diet with added anti-Fel d 1 IgY reduces active Fel d 1 in saliva

Based on the *in vitro* and *ex vivo* study results, it was hypothesized that feeding cats anti-Fel d 1 IgY would reduce immunologically active Fel d 1 in cat saliva.

In a pilot study, saliva was collected from six healthy, adult domestic shorthair cats before their morning feeding and at 1, 3 and 5 hours post-feeding. All of the cats received a control diet (without anti-Fel d 1 IgY) for a two-week baseline period, followed by six weeks on the test diet (control diet with added anti-Fel d 1 IgY). **A significant decrease in salivary active Fel d 1 was detected** within two weeks of starting the test food, and the average decrease over the 6-week test period was 29.6%.<sup>44</sup>

In the second trial in the study, saliva was collected from twenty healthy, adult domestic shorthair cats five hours after their morning feeding, five days a week for the duration of the

5-week study. Cats were fed a control diet for a one-week baseline period, followed by either the control diet (control group) or the control diet with an egg product containing anti-Fel d 1 IgY (test group) for four weeks. **Salivary active Fel d 1 was significantly reduced by Week 3** in the cats receiving the anti-Fel d 1 IgY in their diet, with a mean reduction of 24%, while the control group did not show a significant reduction in active Fel d 1 with a mean reduction of only 4%. This reduction was likely attributable to normal variation in Fel d 1 production.<sup>44</sup>

This study demonstrated that a diet with an egg product ingredient containing anti-Fel d 1 IgY effectively reduced salivary active Fel d 1 levels of cats.



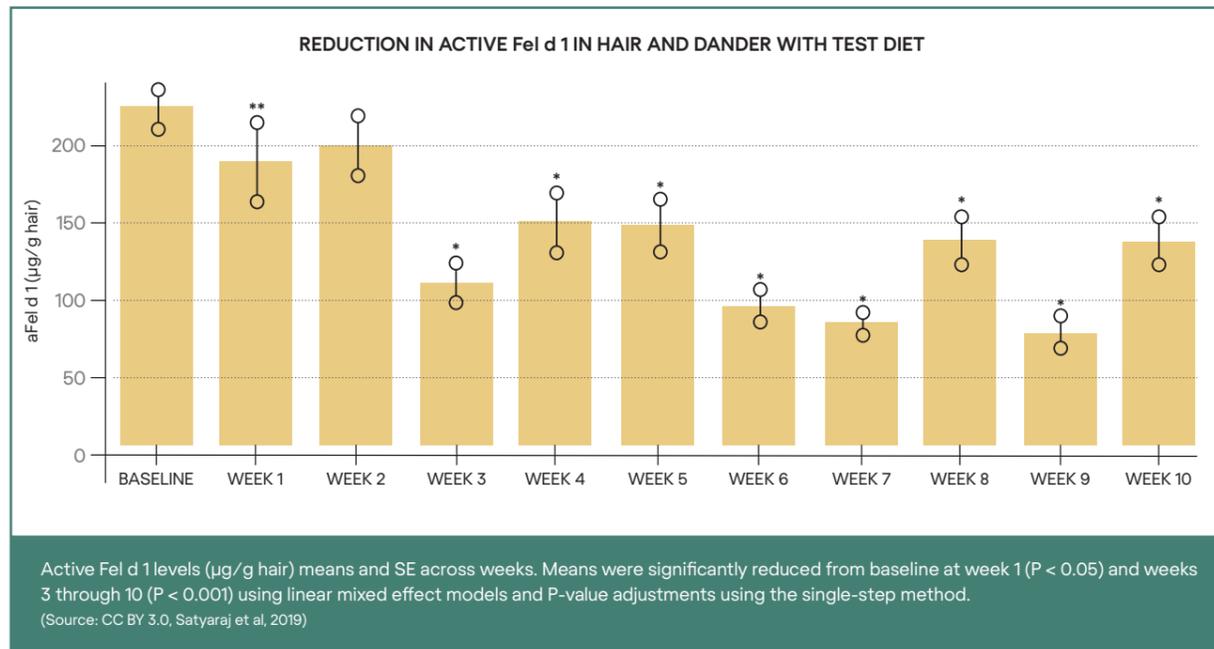
# Feline diet with added anti-Fel d 1 IgY reduces active Fel d 1 on hair and dander

Previous studies<sup>41,44</sup> demonstrated that anti-Fel d 1 IgY blocked IgE-mediated degranulation *in vitro* and *ex vivo* and **significantly reduced salivary active Fel d 1 levels in cats *in vivo***. Fel d 1 enters the environment through shed hair and dander and therefore, the next step in the validation process was to determine the effects of anti-Fel d 1 IgY on active Fel d 1 levels on the cat's hair and dander.

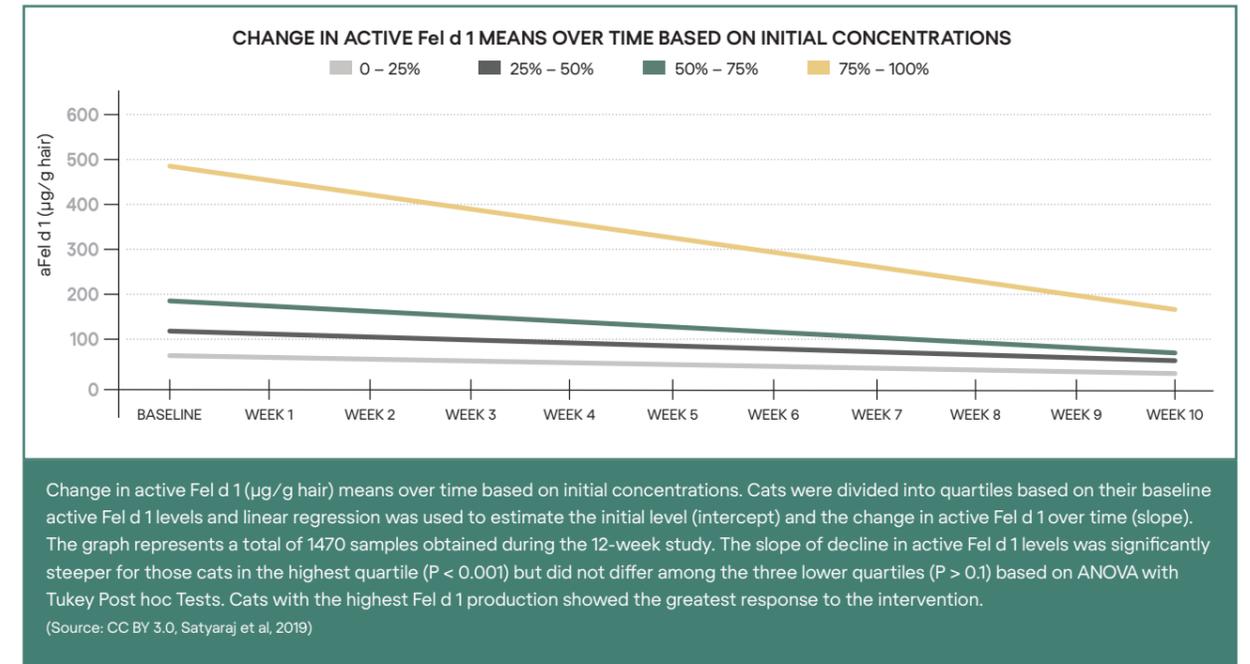
product ingredient containing anti-Fel d 1 IgY. **Active Fel d 1 levels on the hair and dander collected by brushing were significantly reduced** starting from 3 weeks of the treatment period, and remained at reduced levels for the remainder of the treatment period. The active Fel d 1 reduction ranged from 31-77%, starting in the third week, with an average active Fel d 1 reduction of 47%.<sup>45</sup>

Hair was collected by brushing from 105 healthy domestic shorthair cats four times over a two week baseline period, then weekly during a 10-week treatment period during which the cats received a food with an egg

This study demonstrated that a diet with egg product ingredient containing anti-Fel d 1 IgY effectively reduced active Fel d 1 levels on the hair and dander of cats starting in week 3.



Cats with the highest baseline Fel d 1 levels showed the greatest decrease in active Fel d 1 during the treatment period.



## Anti-Fel d 1 IgY is safe for cats

Many cat owners view their cats as part of the family<sup>46-48</sup> and will often go to great lengths to keep their cat in the home despite being sensitive to the allergens. However, although many allergic owners will compromise their own well-being to keep their cat, they are unlikely to accept approaches that they feel may put their cat's health and well-being at risk.

All egg products with egg yolk contain IgY. Egg products containing specifically targeted IgY have been used safely for decades.<sup>49-52</sup> **The anti-Fel d 1 IgY has been shown to be safe for cats**, based on a comprehensive safety study that fed an egg product ingredient with multiple levels of anti-Fel d 1 IgY, including levels many times higher than those used in the efficacy studies.<sup>53</sup>

Based on the principle of allergen load

reduction, complete elimination of Fel d 1 production is not necessary. Our approach does not neutralise 100% of the cat's Fel d 1. In essence, it **converts cats with moderate and high levels of active Fel d 1 to cats with low or moderate levels** of active Fel d 1.

This innovative and efficacious approach offers healthcare providers an opportunity to reframe their conversations with cat-sensitised patients, allowing a focus on proactive measures without the emotional toll associated with recommending the removal of a beloved cat from the home.



**NEW**



## THE FIRST ALLERGEN-REDUCING CAT FOOD

Pro Plan® LiveClear® is a revolutionary cat food shown to reduce the allergens on cat hair and dander by an average of 47% starting in the third week of daily feeding.<sup>45</sup>

Covers all life stages:

- KITTEN Rich in Turkey (1.4kg)
- STERILISED ADULT Rich in Turkey (1.4kg, 2.8kg)
- STERILISED ADULT Rich in Salmon (1.4kg, 2.8kg)
- STERILISED SENIOR Rich in Turkey (2.8kg)

### Feeding and Administration

It is important that you feed Pro Plan® LiveClear® throughout the day, rather than as just a single feeding at only mealtime. Follow the feeding guidelines for each product. Feeding quantities required to maintain ideal body condition will vary, depending on age, activity and environment, so they need to be adapted accordingly. Clean, fresh drinking water should always be available.

As for any change in diet, please recommend to your clients to allow 7 - 10 days to ease the transition from their cat's current food to Pro Plan® LiveClear®. The gradual transition will help avoid dietary upsets.

Pro Plan® LiveClear® is formulated to be fed to cats every day for sustained benefits. While Pro Plan® LiveClear® should remain as the primary diet, providing occasional wet cat food or treats is acceptable.



All cats produce a common allergen, Fel d 1 in their saliva



When cats eat Pro Plan® LiveClear®, a key protein sourced from eggs binds to the Fel d 1 in cat saliva and neutralises it



And when fed daily, ProPlan® LiveClear® significantly reduces the allergens on cat hair and dander



Simply and safely<sup>53</sup>

### Kitten < 1 year

(Rich in turkey)

RECOMMENDED DAILY AMOUNT (g/day)	
Age (weeks)	Grams
4	30
12	55
26	65
52	70

Feed the diet daily for sustained benefits and store in a cool, dry place.

Key nutrient values	
Protein	40%
Fat	20%
Crude ash	7.5%
Crude fibre	1.5%
DHA	0.5%
Metabolisable energy (ME)*	4.23kcal/g

\*calculated with NRC 2006 equation

#### Composition

Turkey (16%), rice, dried turkey protein, soya protein powder, pea protein, pork fat, corn protein meal, corn starch, dried chicory root (2%), minerals, dried egg, digest, egg yolk powder, fish oil, yeast.

#### Key Nutritional Benefits

- Supports a healthy immune system thanks to high protein level and vitamins C and E
- Proven to promote digestive health thanks to natural prebiotics
- Helps support healthy vision and brain development thanks to DHA

### Sterilised Adult 1+ year

(available Rich in Turkey or Rich in Salmon)

RECOMMENDED DAILY AMOUNT (g/day)	
Cat Weight	Grams
3 kg	40
5 kg	65
7kg	90

Feed the diet daily for sustained benefits and store in a cool, dry place.

Key nutrient values	
Protein	41%
Fat	14%
Crude ash	7.5%
Crude fibre	4.0%
DHA	0.5%
Metabolisable energy (ME)*	3.85kcal/g

\*calculated with NRC 2006 equation

#### Composition

##### Turkey Flavour

Turkey (17%), dried poultry protein, rice, corn protein meal, wheat gluten, cellulose, wheat middlings, corn, pork fat, minerals, dried egg, fish oil, digest, egg yolk powder, yeast.

##### Salmon Flavour

Salmon (18%), dried poultry protein rice, corn protein meal, wheat gluten, wheat middlings, cellulose, pork fat, minerals, dried egg, corn, digest, egg yolk powder, yeast, fish oil.

#### Key Nutritional Benefits

- Maintains urinary health in neutered cats thanks to balanced minerals
- Promotes healthy kidneys thanks to a special combination of nutrients including anti-oxidants, arginine and omega-3 fatty acids
- Helps maintain an ideal body weight thanks to a high protein level, added fibre and low carbohydrate level

### Sterilised Senior 7+ years

(Rich in Turkey)

RECOMMENDED DAILY AMOUNT (g/day)		
Cat Weight	Grams (7-11 years old)	Grams (from 12 years old)
3kg	40	45
5kg	65	75
7kg	90	105

Feed the diet daily for sustained benefits and store in a cool, dry place.

Key nutrient values	
Protein	40%
Fat	15%
Crude ash	6.5%
Crude fibre	3.0%
DHA	3.1%
Metabolisable energy (ME)*	3.97kcal/g

\*calculated with NRC 2006 equation

#### Composition

Turkey (14%), dried poultry protein, corn protein meal, rice, soya meal, wheat gluten, wheat, pork fat, corn starch, dried egg, wheat middlings, chicory (2%), minerals, soybean oil, cellulose, fish oil, digest, egg yolk powder, yeast.

#### Key Nutritional Benefits

- Supports key vital functions (immune, renal, digestion) for a longer, healthier life thanks to a proprietary combination of prebiotics, anti-oxidants, omega 3 and 6 fatty acids
- Maintains urinary health in neutered cats thanks to balanced minerals
- Helps maintain an ideal body weight thanks to a high protein level, added fibre and low carbohydrate level

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