

Stability & Palatability of Flavor Excipients

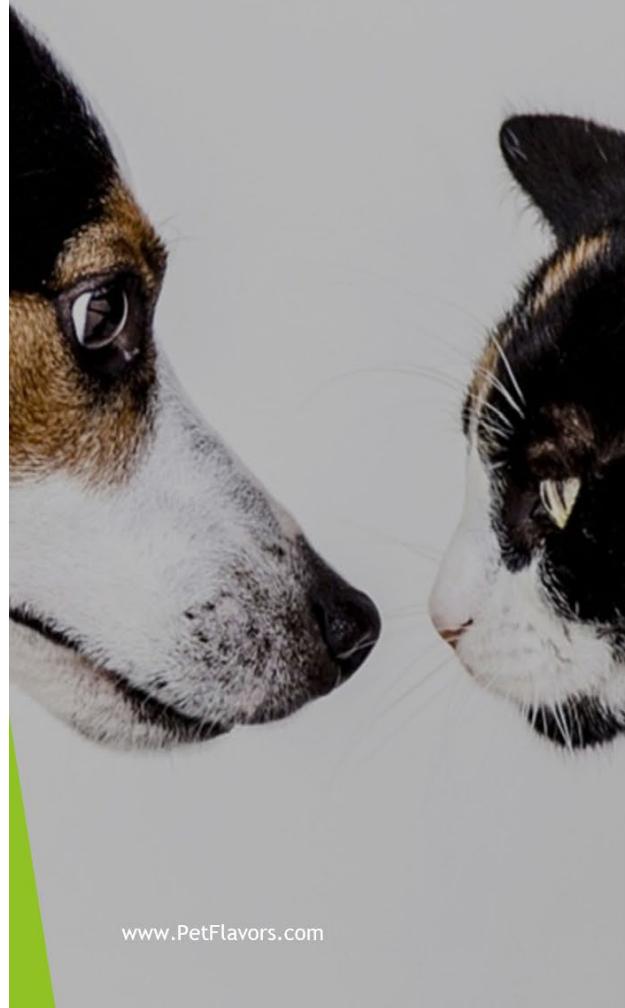
*A Winning Combination for
Veterinary Drug Formulation*

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INTEGRATING
Delivery Science
ACROSS DISCIPLINES





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Pet Flavors

At a Glance...

- Developer & manufacturer of quality powdered flavor bases
- Sold worldwide
- Only palatant manufacturer **focused on pet pharmaceuticals**
- Over **30 years** in business
- Flavor bases used in over 30 different New Animal Drug Approvals (NADAs)
- Human food-grade ingredients
- **USDA licensed and inspected facility**, follows FDA and European Union standards for pharmaceutical ingredients
- Based in Melbourne, Florida (USA)

The Veterinary Market At A Glance

Industry Size & Trends

- ▶ Global companion animal pharmaceuticals market is valued at **\$15.6 Billion** USD and is expected to reach \$27.16 Billion USD by 2032¹
- ▶ Veterinary pain management market was valued at **\$1.2 billion** USD in 2020 and it is expected to reach \$1.9 billion in 2026²
- ▶ Global market growth estimated at 5.9%³



¹Spherical Insights and Consulting

²Mordor Intelligence

³Brakke Consulting

The Animal Health Industry Continues to Expand & Advance

► Pharmaceutical

- Injectables (mAbs to treat OA pain, allergies; pancreatitis)
- Liquid oral dosage forms (diabetic cats, giardia)
- Solid oral dosage forms (diabetic cats, allergies)

► Nutritional

- Allergies, Arthritis
 - ❖ Plant Based

► Diagnostics

- Cancer Detection

► Technology

- Artificial Intelligence
- Remote Assistance



What are the **KEY Elements** for Pet Pharmaceuticals, Nutraceuticals?



#1 = Safety

The drug must be safe!



#2 = Efficacy

The drug must work!



#3 = Palatability

The drug must be acceptable!

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Measuring An Excipient's Palatability...

A blinded, random, crossover study in 162 client owned dogs (August 2023)¹

Study Protocol:

- Healthy dogs, ages 2-10 years of age ✓ Variety of breeds, sexes
- Each dog sampled ~ 1 gram of 5 different flavor excipients plus a control twice daily for 12 days
- Random groups (#1-6) dictated the flavor, day and time (am/pm) given
- Each dog tasted each sample 4 times during the study duration
- Pet owners recorded all results, observations, pet's acceptance

Study duration: 60 days

Location: Melbourne, Florida (USA)

¹Data on file, PF LLC, Melbourne, FL

Samples



- A: Artificial Powdered Beef Flavor; PC-0125 (Mfr. date: August 2022)*
- B: Artificial Powdered Beef Flavor; PC-0125 (Mfr. date: August 2013)*
 - 10 years post manufacture!
- C: Control (Mfr. date: October 2022)
- D: Artificial Powdered Meat Flavor; PC-0170 (Mfr. date: Sept 2022)**
- E: Artificial Powdered Meat Flavor; PC-0170 (Mfr. date: April 2015)**
 - 8 years post manufacture!
- F: PF Custom Flavor (Mfr. date: October 2021)**

Mfr. date = Date of Manufacture

* 5 years shelf life

**3 years shelf life



Key Points...

- ✓ Study was conducted using RAW MATERIALS
- ✓ Samples were not in a final dosage form
- ✓ NO active ingredients (APIs)



➤ European Medicines Agency

“To be granted a palatability claim, the overall voluntary acceptance rates should at least reach the threshold of **80% in dogs** and 70% in all other species.”¹

¹23 July 2021 EMA/CVMP/EWP/206024/2011-Rev.1* Committee for Medicinal Products for Veterinary Use (CVMP)



Palatability Data Results



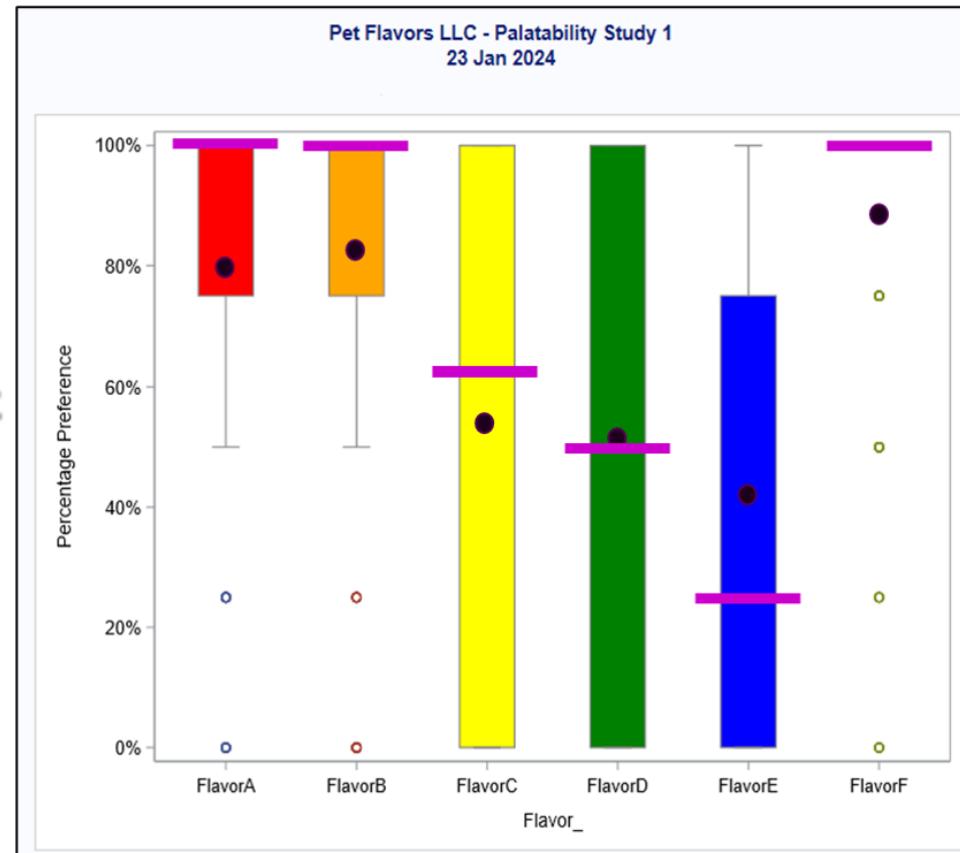
Sample	Product	Palatability %
A	Artificial Powdered Beef Flavor; PC-0125 (Mfr. date: August 2022)	77%
B	Artificial Powdered Beef Flavor; PC-0125 (Mfr. date: August 2013)	79%
C	Control	50%
D	Artificial Powdered Meat Flavor; PC-0170 (Mfr. date: September 2022)	46%
E	Artificial Powdered Meat Flavor; PC-0170 (Mfr. date: April 2015)	34%
F	PF Custom Flavor (Mfr. date: October 2021)	87%



Statistical Analysis¹

Key Highlights²:

- While Flavor A and B (PC-0125, different ages) showed some numerical difference in palatability, it was not a significant difference ($p = 0.276$)³
 - ✓ **Shelf life does not have a significant impact on palatability for PC-0125, and it is highly palatable**
- Flavor F (Custom) was also highly palatable, with 80% of dogs exhibiting preference 4 out of 4 times



¹All data provided by Kellie M. Hogan, PhD, Phoenix Feather Statistics LLC

²Kruskal-Wallis Test used to compare distributions; Pairwise comparisons were further evaluated using the Dwass-Steel-Critchlow-Fligner Test

³Significance was evaluated at p -value of ≤ 0.05

Study Results...



All flavor bases (excipients) proved highly

PALATABLE & STABLE in their raw, powdered formulation

Of special note:

Flavor Excipient (Artificial Powdered Beef Flavor; PC-0125)

- *Proven 5-year shelf life*
- *Tested **10 years** post manufacture*
- *Study findings¹:*
 - **STABLE & PALATABLE**
 - *Stability test results all within normal limits*
 - *79% free choice acceptance rate*

Demonstrated the combined palatability and stability of an excipient

¹Data on file, PF LLC, Melbourne, FL

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Stability

An integral part of the drug development and approval process!



► Stability Testing:

- The objective should be to provide evidence that the excipient is stable under the likely storage conditions (i.e., temperature, humidity, light)
 - Typically conducted using long term ambient storage conditions (25°C)
 - Three (3) validation batches placed under a formal stability study

► Shelf Life Evolves

- Provides evidence about the **QUALITY** of materials over time

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Stability Study Results PC-0125 (10Kg)
May 2016 - May 2021
600460

Time		0 months	3 months	6 months	9 months	12 months	18 months	24 months	36 months	48 months	60 months
Description	Brown powder with very fine white particles and a roast beef & liver flavor and odor	Meets Description									
Organoleptic Evaluation	Characteristic to standard when evaluated at 10 grams in 90 grams of powdered sugar	Passes									
Protein %w/w	Not less than 25% by weight	51.0%	50.8%	50.7%	50.7%	51.0%	50.5%	50.9%	50.7%	50.2%	50.4%
Fat %w/w	Not less than 2% by weight	6.7%	7.0%	7.1%	6.4%	6.6%	6.9%	6.9%	6.5%	6.1%	5.9%
Moisture %w/w	Not more than 15% by weight	4.1%	4.4%	4.0%	4.1%	4.8%	4.8%	5.0%	5.6%	6.1%	5.7%
Total Aerobic Bacterial Count	Not greater than 1000 cfu/g	None Detected									
Total Yeast Count	Not greater than 100 cfu/g	None Detected									
Total Mold Count	Not greater than 100 cfu/g	None Detected									
E.Coli	Negative	None Detected									
Salmonella	Negative	None Detected									



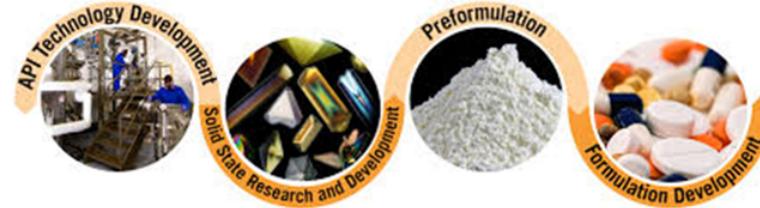
Palatant Stability & Quality Requirements

by a reputable company

- Flavor stability should be 3-5 years
- Adheres to stringent quality control measures
- Complies with USDA regulations
- cGMP certified and compliant
- Follows all international regulations

Formulation Development

- Formulation is one of the most **critical aspects** of pharmaceutical development
- No longer can excipients be regarded as simply inert or inactive ingredients
 - Most surprises during drug product stability come from excipients, particularly from impurities
- Adding excipients, such as palatants, can change a drug's qualities
 - Quality becomes critical such that an end-product **doesn't degrade** during shipment or storage



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Novel Palatant Research

Soluble Flavors

- Poultry & Pork
- Completely water-soluble powder
- Soluble in glycerin and forms homogenous, microfine suspension in PEG, propylene glycol and fixed oils
- Heat stable and accepted in EU
- 100% natural

Plant-Based Meats

- 100% vegan and GMO free
- Hypo-allergenic flavor: no animal protein, corn, wheat or gluten
- No diluents or cutting agents
- 100% natural

Custom Flavor Development



✓ Market Exclusivity & Unique Product Differentiation

Work with a manufacturer that has developed formulations including

- ❖ Chewable tablets, soft chews, granules, pastes
- ❖ Assisted in pre-formulations:
 - Oral thin films
 - Oil and water-soluble suspensions
 - Solutions
 - Emulsions
 - Dry powders
 - Wet and dry granulations
- ❖ Palatability Studies ★

Pet Flavors Ongoing Palatability Studies... What Have We Done & What's Next?



An average of 150 dogs & cats are used for each study!

- Previous Studies
 - Newly **customized** flavorings for top animal health companies
 - **Raw** formulation w/excipient **vs Final** formulation w/excipient
 - **Feline** Studies
- Current Studies
 - **Hypo-allergenic**, plant-based flavors
 - **Feline** studies
 - **Soluble** flavors (aqueous solutions)



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Palatability Field Trial: *Hypo-Allergenic Flavors*



September 2023

A field study with 178 client owned dogs was conducted to test the palatability of our raw flavor bases compared to their palatability in final formulation...

Study Overview

- A blinded, random, crossover study
- Healthy dogs, ages 2-10 years of age, all breeds, sexes, weights
- **6 samples were tested twice daily for 12 days (~1 gram, 1 chew)**
 - "A" Phycox® HA HypoAllergenic Soft Chews/Small Bites
 - "B" Phycox® Original Formula Soft Chews/Small Bites
 - "C" Natural Liver Powdered Flavor; PC-0150
 - "D" Artificial Powdered Beef Flavor; PC-0125
 - "E" Artificial Powdered Meat Flavor; PC-0170 (Hypo-Allergenic)
 - "F" (Control)



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Palatability Data Results (HA Study)¹



Sample	Product	Palatability %
A	Phycox® HA Soft Chews	81%
B	Phycox® Soft Chews	77%
C	Natural Liver Powdered Flavor; PC-0150	80%
D	Artificial Powdered Beef Flavor; PC-0125	67%
E	Artificial Powdered Meat Flavor; PC-0170 (Hypo-Allergenic)	34%
F	Control	54%

¹Data on File, PF LLC, Melbourne, FL

Hypo-Allergenic Palatability Study:

Comparing the palatability of the Artificial Powdered Meat Flavor; PC-0170 in both raw & final formulation using the Phycox® brand of soft chews for dogs



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- ✓ Most flavor bases proved highly palatable
- ✓ Artificial Powdered Meat Flavor; PC-0170 (Hypo-Allergenic) was **highly palatable** in its final formulation (Phycox® HA small bites/soft chews)
- ✓ Hypo-Allergenic & Palatable – a winning combination for new pharmaceutical product line and customized formulations!



A feline
participant
taste testing
our new
Fish Flavor!



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Thank You!



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