

Stability & Palatability of Flavor Excipients

*A Winning Combination for
Veterinary Drug Formulation*

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INTEGRATING
Delivery Science
ACROSS DISCIPLINES





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)

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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...

¹Data on file, PF LLC, Melbourne, FL

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)

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



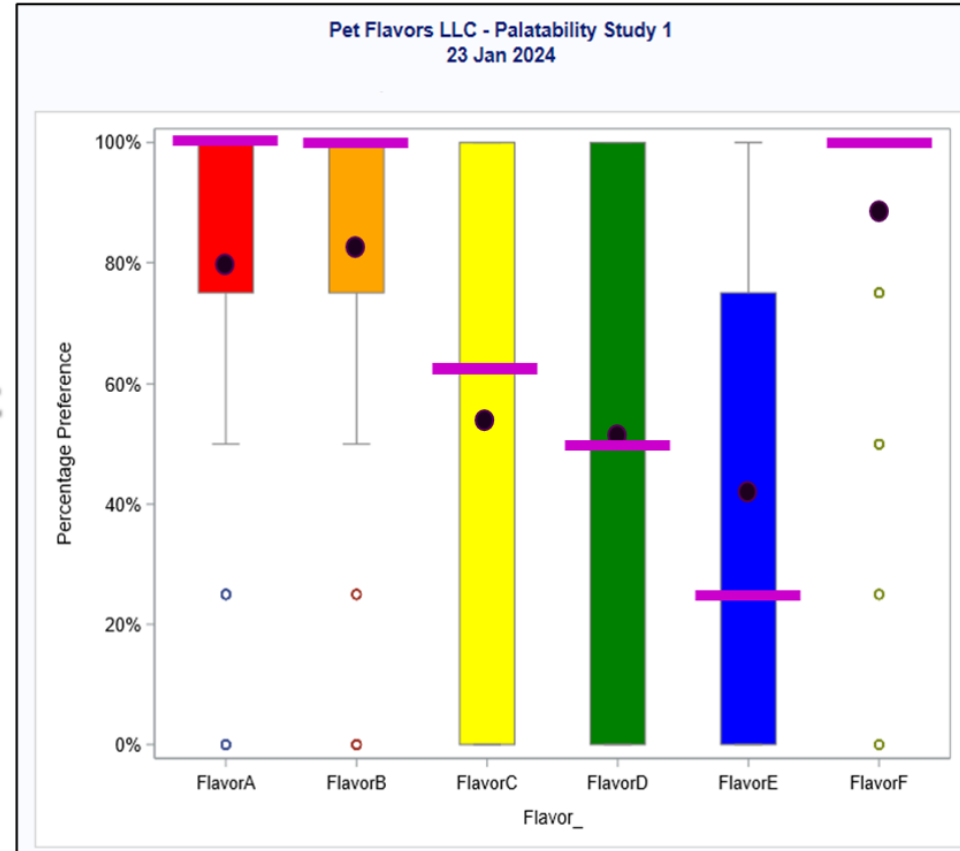
Sample	Product	Palatability %
A	Artificial Powdered Beef Flavor; PC-0125 (Mfr. date: August 2022)	77%
B	Artificial Powdered Beef Flavor; PC-0125 (Mfr. date: August 2013)	79%
C	Control	50%
D	Artificial Powdered Meat Flavor; PC-0170 (Mfr. date: September 2022)	46%
E	Artificial Powdered Meat Flavor; PC-0170 (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	Meets Description	Meets Description	Meets Description	Meets Description	Meets Description	Meets Description	Meets Description	Meets Description	Meets Description
Organoleptic Evaluation	Characteristic to standard when evaluated at 10 grams in 90 grams of powdered sugar	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	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	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected
Total Yeast Count	Not greater than 100 cfu/g	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected
Total Mold Count	Not greater than 100 cfu/g	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected
E.Coli	Negative	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected
Salmonella	Negative	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected	None Detected





Palatant Stability & Quality Requirements *ed* *by a reputable company*

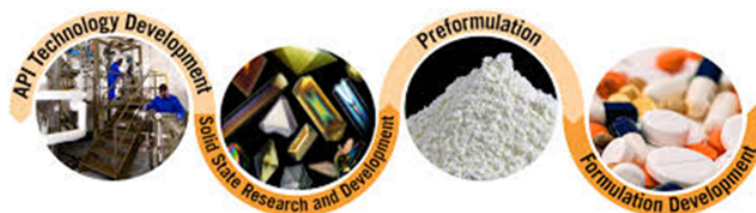


- **Flavor stability should be 3-5 years**
- **Adhere's to stringent quality control measures**
- **Complies with USDA regulations**
- **cGMP certified and compliant**
- **Follows all international regulations**



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” Phycos® HA HypoAllergenic Soft Chews/Small Bites
 - “B” Phycos® 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

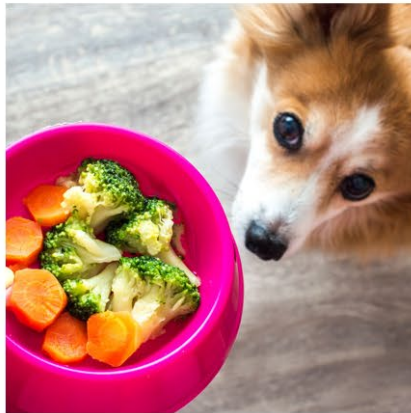


Sample	Product	Palatability %
A	Phycox® HA Soft Chews	81%
B	Phycox® Soft Chews	77%
C	Natural Liver Powdered Flavor; PC-0150	80%
D	Artificial Powdered Beef Flavor; PC-0125	67%
E	Artificial Powdered Meat Flavor; PC-0170 (Hypo-Allergenic)	34%
F	Control	54%

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!

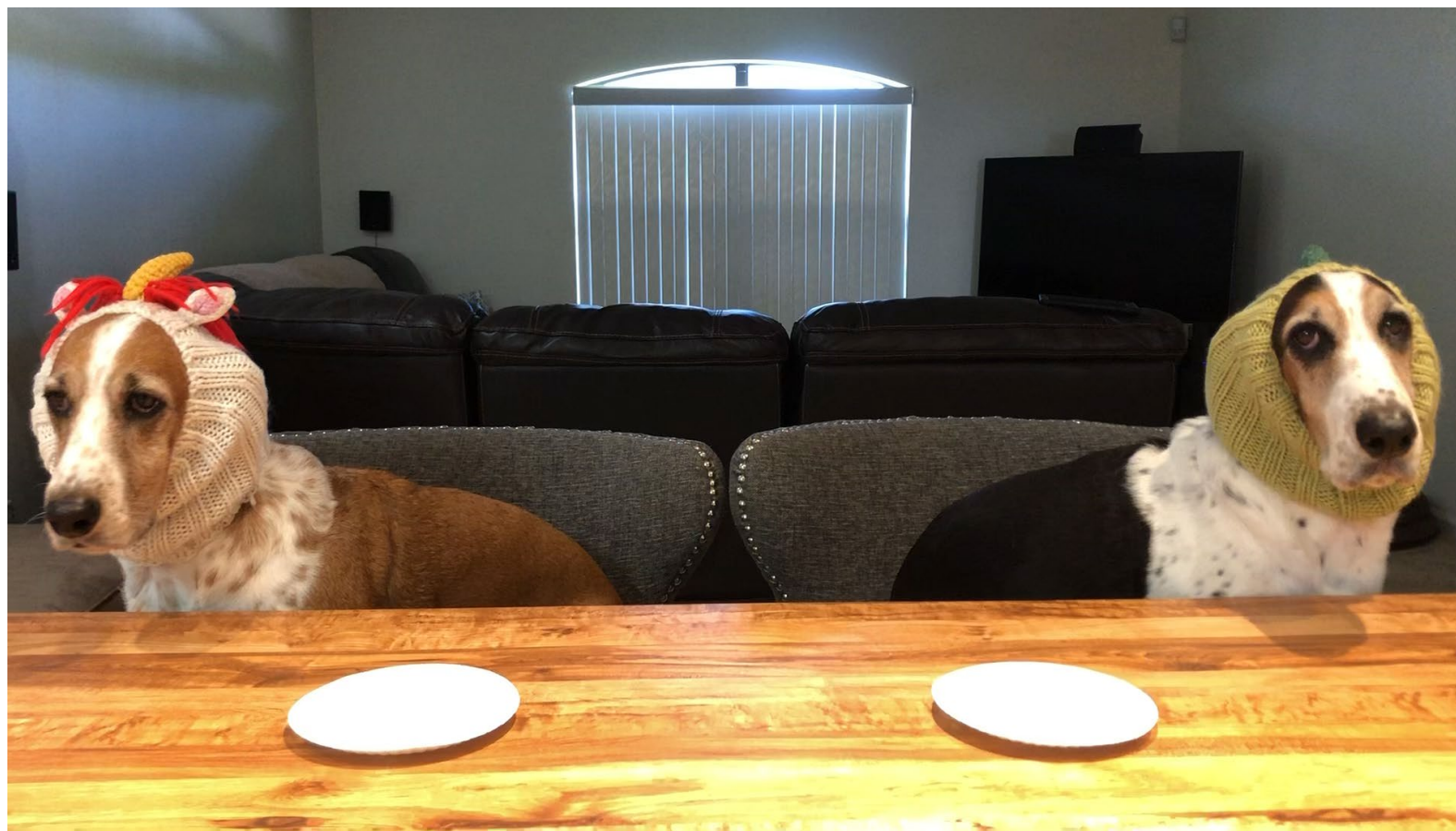


A feline participant taste testing our new Fish Flavor!



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Thank You!



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