# STUDY TO ASSESS VISUAL ELIMINATION OF A NOVEL OTIC GEL (FLORFENICOL, TERBINAFINE, BETAMETHASONE ACETATE) IN COMPARISON TO AN OTIC SOLUTION (FLORFENICOL, TERBINAFINE, MOMETASONE FUROATE) AND AN OTIC SUSPENSION (GENTAMICIN SULFATE, CLOTRIMAZOLE, MOMETASONE FUROATE MONOHYDRATE) IN DOGS IMMEDIATELY AFTER APPLICATION TO THE EAR CANAL

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## Introduction

The Otic Gel is a gel formulation containing florfenicol, terbinafine and betamethasone acetate (Osurnia™), approved in the EU for the treatment of acute otitis externa (OE) and acute exacerbations of OE associated with *Staphylococcus pseudintermedius* and *Malassezia pachydermatis*.

The gel formulation has specific rheological properties allowing it to have low viscosity during application and high viscosity once applied to the ear. In theory, these properties should reduce the amount of product eliminated from the ear if a dog shakes its head after application, a frequent and messy occurrence with traditional products for the treatment of OE.

The Otic Solution is intended as a single administration only. The Otic Suspension is intended as a daily administration for 7 days. Both products are registered by the Food and Drug Administration (FDA) in the US; they are not registered in the UK.

## Objective of the study

To quantify the spontaneous elimination of the Otic Gel and two liquid formulations from the external ear canal of dogs as measured by surface area covered by product shaken from the ear immediately after application.

## Methods

Nine healthy dogs with clinically normal ears were randomly allocated to three treatment groups in a crossover non-blinded design. Dogs were administered each product bilaterally once with two days washout between treatments. Prior to administration, external ear canals and pinnae were cleaned with saline and dried, and tympanic membranes were assessed. Products were applied per FDA labeled instructions for administration methodology. Dose volume for the Otic Gel and the Otic Solution were 1 ml; dose volume for the Otic Suspension was eight drops. Dogs were immediately placed into individual paper-lined crates with remote video monitoring for up to two minutes post-administration. The dog and lining paper were removed from the crate. Cleaning of external ear canals and medial pinnae was repeated after exiting the treatment crate. Areas of paper with eliminated product were immediately encircled with blue ink and photographed. Photographs were analyzed to estimate visible elimination, calculated as total area of paper covered by product.

| Group | Number of dogs | Day 0 | Day 2 | Day 4 |
|---|---|---|---|---|
| 1 | 3 | Otic Gel | Otic Suspension | Otic Solution |
| 2 | 3 | Otic Solution | Otic Gel | Otic Suspension |
| 3 | 3 | Otic Suspension | Otic Solution | Otic Gel |

Table 1. Treatment Groups and Product Administration Order

Statistical methodology included the calculation of mean and median of area covered for each product. A linear mixed model was also fitted to the log transformed data to give model-based back-transformed mean estimates of the total area of cover.

## Results

Data from all nine dogs was included in the analysis.

The overall total area of product cover was significantly larger for the Otic Solution (mean 16.22 $cm^2$; median 5.25 $cm^2$; model-based estimate 8.06 $cm^2$) than for either the Otic Gel (mean 0.67 $cm^2$; median 0.09 $cm^2$; model-based estimate 0.35 $cm^2$, p = 0.0015) or the Otic Suspension (mean 0.18 $cm^2$; median 0.06 $cm^2$; model-based estimate 0.15 $cm^2$, p = 0.0010); Figure 1 and Table 2. There was no significant difference in the total area covered between the Otic Gel and the Otic Suspension (p = 0.4564).

| Treatment | Least Squares Mean | Back-Transformed Least Squares Mean | Lower 95% Confidence Limit | Upper 95% Confidence Limit |
|---|---|---|---|---|
| Otic Solution | 2.20 | 8.06 | 2.49 | 22.52 |
| Otic Suspension | .014 | .015 | 0.00 | 0.40 |
| Otic Gel | 0.30 | 0.35 | 0.00 | 1.09 |

Table 2. Model-based Estimates of Total Area ($CM^2$) and Confidence Intervals

## Conclusion

The Otic Gel (1 ml) demonstrated a significantly lower visual elimination of the administered dose shaken from the ear canal compared to the Otic Solution (1 ml), with no significant differences to the Otic Suspension (8 drops), as determined by area. This supports the hypothesis that the unique gel formulation of the Otic Gel results in less of the intended dose being eliminated from the ear canal immediately after application as determined by surface area. The impact of repeated dosing on product elimination were not investigated in this study.

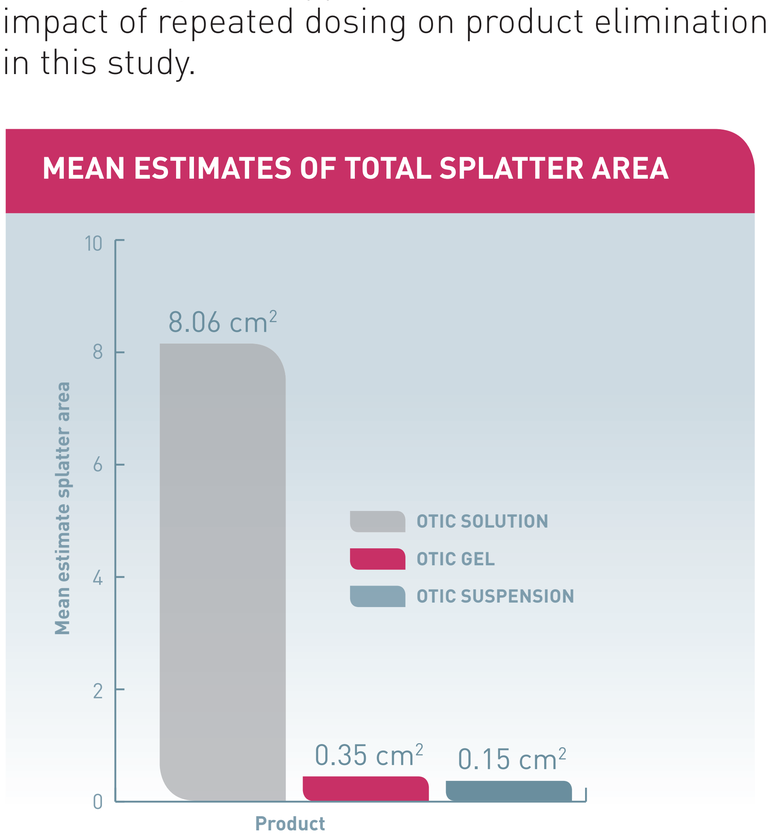


Figure 1.