



OCT 28 2016

Dawn M. Cleaver, D.V.M.  
Associate Director, Regulatory Affairs  
Zoetis, Inc.  
333 Portage Street  
Kalamazoo, Michigan 49007

Ms. Jaana Mero  
Senior Manager, Regulatory Affairs  
Orion Corporation  
Orionintie 1A, FI-02200 Espoo  
P.O. Box 65, FI-02101 Espoo  
FINLAND

**Re: NADA 141-456**  
SILEO (dexmedetomidine oromucosal gel)

Dear Dr. Cleaver and Ms. Mero:

The U.S. Food and Drug Administration (FDA), Center for Veterinary Medicine (CVM), Division of Surveillance has reviewed the following promotional materials for SILEO (dexmedetomidine oromucosal gel):

- the website (<https://www.zoetisus.com/products/dogs/sileo/canine-noise-aversion.aspx>);
- a bag insert entitled "*The buzz about canine noise aversion*" (NA-00820), and "*SILEO 2016 Paid Search Recommendations*" (SIL-00111), both of which were submitted by you to CVM on July 29, 2016;
- screen shots from the "Sileo Pet Owner Website" (NA-00112), a display advertisement (NA-00113), and a consumer press release (NA-00120) all of which were submitted by you to CVM on July 8, 2016;
- a brochure for dog owners entitled "*Loud noises don't have to be scary anymore*" (SIL-00006), submitted by you to CVM on April 15, 2016;
- a press release, dated May 16, 2016 (<http://news.zoetis.com/press-release/companion-animals/zoetis-announces-launch-sileo-treatment-noise-aversion-dogs>).

These promotional materials are misleading because they omit material facts, contained in the Precautions section of the approved labeling for SILEO, that communicate information regarding the lack of effectiveness data for SILEO for treatment of aversion

behaviors to thunderstorms. These materials therefore cause SILEO to be misbranded under sections 502(a) and (n) of the Food, Drug, & Cosmetic Act (FD&C Act) [21 U.S.C. § 352(a) and (n)]. The introduction of a misbranded drug into interstate commerce is a violation of section 301(a) of the FD&C Act [21 U.S.C. § 331(a)].

## Background

According to the FDA-approved product labeling, SILEO is an oromucosal gel containing 0.09 mg dexmedetomidine (equivalent to 0.1 mg dexmedetomidine hydrochloride) per mL. SILEO is indicated for the treatment of noise aversion in dogs. The approved package insert for SILEO contains important risk information in the Precautions section as follows:

***“PRECAUTIONS:***

*...SILEO has not been evaluated for aversion behaviors to thunderstorms...”*

## Omission of Material Facts

The materials cited above all include thunder as an example of noise that may elicit noise aversion in dogs. For example:

The website that discusses canine noise aversion (<https://www.zoetisus.com/products/dogs/sileo/canine-noise-aversion.aspx>) includes “thunder” in a list of “common triggers for noise aversion.”

The press release published by Zoetis, Inc., dated May 16, 2016, (<http://news.zoetis.com/press-release/companion-animals/zoetis-announces-launch-sileo-treatment-noise-aversion-dogs>) opens with the statement “Dogs that experience fear and anxiety in response to loud noise such as fireworks, thunder, and ...”

The bag insert entitled “*The buzz about canine noise aversion*” states that thunder is a noise aversion trigger in 73% of dogs.

The SILEO 2016 paid search recommendations focused on four ad groups. The leading group was thunder and the headline was “Dog Afraid of Thunder?”

However, none of the promotional materials cited include the precautionary statement “*SILEO has not been evaluated for aversion behaviors to thunderstorms.*”

Dogs’ aversion behavior to thunderstorms can be elicited by phenomena other than thunder that are commonly associated with thunderstorms, including changes in barometric pressure, a darkening sky, bright flashes of lightening, and sounds of wind

and rain, among others.<sup>1</sup> Because the materials cited above include thunder as an example of noise that may elicit noise aversion in dogs, but fail to disclose that SILEO has not been evaluated for aversion behaviors to thunderstorms, they are misleading.

## Conclusion and Requested Action

Because the promotional materials cited above include thunder as an example of noise that may elicit noise aversion in dogs, the omission of the Precautions statement concerning the lack of efficacy data for thunderstorms from your promotional materials causes SILEO to be misbranded within the meaning of sections 502(a) and 502(n) of the FD&C Act [21 U.S.C. 352(a) and (n)].

CVM requests that Zoetis, Inc. immediately cease the dissemination of the SILEO promotional items described above and any other materials that fail to disclose the Precautions statement regarding aversion behavior to thunderstorms.

Please submit a written response within thirty calendar days of receipt of this letter describing whether you intend to comply with this request. Please direct your response to Dr. Neal Bataller at the Food and Drug Administration, Center for Veterinary Medicine, Division of Surveillance, HFV-216, 7519 Standish Place, Rockville, Maryland 20855.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that the promotional materials for SILEO, as well as other Zoetis, Inc. products, comply with the requirements of the FD&C Act and applicable FDA regulations.

If you have any questions, please contact Dr. Dorothy McAdams at the address above, or by phone at (240) 402-5763.

Sincerely,

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Neal Bataller, ME, DVM  
Director, Division of Surveillance  
Office of Surveillance & Compliance  
Center for Veterinary Medicine

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<sup>1</sup> Cottam, N., and Dodman, NH. (2009) Applied Animal Behaviour Science 119:78-84.  
doi:10.1016/j.applanim.2009.03.014.