UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

April 27, 2021

Jennifer Schofield, DVM
Elanco Animal Health
12707 Shawnee Mission Pkwy
Shawnee, KS 66216, USA

Subject: Information Concerning Seresto Collars That Must Be Reported Pursuant to FIFRA section 6(a)(2)

Dear Dr. Schofield:

As discussed during the virtual meeting on 3/23/21, the Environmental Protection Agency (EPA or the Agency) is concerned about the numerous reports of adverse incidents the Agency has received related to the use of Seresto collars (EPA Registration Number 11556-155). As a registrant of pesticide products registered under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), you are required to notify EPA pursuant to FIFRA section 6(a)(2) of any "additional factual information regarding unreasonable adverse effects on the environment."

EPA's implementing regulations at 40 CFR Part 159 identify the types of information that registrants must submit to the Agency pursuant to FIFRA section 6(a)(2). Under 40 CFR § 159.195(a), registrants are required to submit information that "the registrant knows, or reasonably should know, that if the information should prove to be correct, EPA might regard the information alone or in conjunction with other information about the pesticide as raising concerns about the continued registration of a pesticide or about the appropriate terms and conditions of registration of a product." Under 40 CFR § 159.195(c), the same types of information must be submitted if "the registrant has been informed by EPA that such additional information has the potential to raise questions about the continued registration of a product or about the appropriate terms and conditions of registration of a product." By this letter, the Agency is reminding you of your general obligations under 40 CFR 159.195(a), and is informing you of certain specific types of information that it considers reportable under 40 CFR 159.195(c).

If Elanco, any subsidiary of the company, or any consultant, attorney, or agent who acquired such information while acting as a consultant, attorney, or agent for Elanco has any information relating to Seresto collars that falls into the categories identified below, such information must be made available to the Agency within 30 days of the date of this letter. You must respond in writing within 10 days from the date of this letter and describe the information you intend to submit in response to this letter. To the extent the specific information listed in this letter overlaps with information specified in 40 CFR §§ 159.165 through 159.188, the deadline for submitting the information is either 30 days from the date of this letter or the applicable standard

deadline in 40 CFR 159.155, whichever is sooner.[1] Please note that we are not asking attorneys to provide any opinions or conclusions rendered as the professional legal judgment of an attorney, as defined in the Model Code, as part of this letter. However, any factual information in the possession of attorneys that attorneys acquired while working for Elanco that falls into the categories identified below, including any applicable expert opinions of non-attorneys, must be submitted pursuant to this letter.

At this time, any of the information listed below, in the possession of Elanco or any of its consultants, attorneys, or agents, must be reported to EPA under section 6(a)(2). Any information or studies that falls into the categories below that has previously been submitted to EPA's Office of Pesticide Programs is excluded and need not be provided to the Agency again in response to this letter. We request that you include a document index with your submission.

1) Any information concerning the annual incident rate (e.g., incidents per million units sold) for Seresto collars stratified by clinical severity including, if available, by collar size/type (e.g., cat, small dog, large dog). Provide any supporting data, and criteria used to develop this response, in addition to any calculations (e.g., Reporting Odds Ratios (ROR) or Incident Rate Ratios (IRR)) that Elanco may have performed to address this question.

2) Any information concerning the adverse reactions/advisories that are listed on the Seresto collars labels in the European Union and their prevalence, including any supporting data that was reviewed by EU regulatory authorities to determine that these adverse reaction could happen and are rare/very rare cases (based on frequency of adverse reactions per 10,000 collars sold).

3) Any information concerning your global pharmacovigilance program for Seresto collars and other veterinary medical products, including a summary of any specific pharmacovigilance activities that have been performed by Elanco on suspected adverse reactions in the U.S. and other major global markets. The summary must include information on reported adverse reactions to Seresto collars, analysis of the incident rate of more serious adverse reactions, and investigation of specific clinical signs that have been identified as potential safety signals of concern by global regulatory authorities. Additionally, should include existing comparative analysis of Seresto collars and related pet products that marketed by Elanco and part of its global pharmacovigilance program.

4) All available sales data and detailed/enhanced incident data for Seresto collars. Please provide the incident information, in electronic format, using the EPA's spot-on reporting templates (https://www.epa.gov/pesticides/use-standardized-templates-report-pet-spot-incidents-conclusion-pilot-and-implementation).

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[1] Pursuant to 40 CFR § 159.155(c), "EPA may, in its discretion, notify a registrant in writing of a different reporting period that will apply to specific types of reportable information . . . . Such notification supersedes otherwise applicable reporting requirements set forth in [Part 159]."

5) All available pre-market data for Seresto collars that has not previously been submitted (e.g., FDA requirement Guideline No: 85 (VICH GL9)).

6) All information concerning incident analyses, including supporting data/incident reports, that has been previously shared with PMRA or other regulatory bodies.

7) All information concerning the underlying data supporting your own analyses of the incidents, including those analyses on neurological effects.

8) Any reports and supporting information, including incident and market data, to support the following assertions made by Elanco and its representatives during the March 23, 2021 meeting, convened between Elanco and EPA convened to discuss Elanco's review of the safety profile of Seresto collars:
    a. From 2013-2020, the overall annual rate of reported incidents has decreased while the number of Seresto collars distributed in the U.S. has increased
    b. Based on causality assessment of pet deaths reported during 2013-2020, there is no established link between death and exposure to the active ingredients in Seresto collars.
    c. The incident rate of reported neurological signs in pets is "very rare" and may reflect the background prevalence of seizures/convulsions in pets.

Moreover, the requirements to report information to the Agency pursuant to section 6(a)(2) continue as long as the product is registered. Any information that falls into the categories identified above, that Elanco, any subsidiary, or any consultants, attorneys, or agents thereof, receives subsequent to the receipt of this letter, must be made available to the Agency.

In addition, when assessing the reported incidents, EPA intends to compare the rates of incidents for comparable products. To assist that comparison EPA requests you provide incident rates for your other pet products, including the Advantage II and K9 Advantix product lines.

If you have any questions about this letter, or whether particular pieces of information fall within the scope of the letter, please feel free to call Dr. Jennifer Saunders at (703) 347-0156.

Sincerely,

MARIETTA ECHEVERRIA

Digitally signed by MARIETTA ECHEVERRIA
Date: 2021.04.27 16:35:37 -04'00'

Marietta Echeverria, Acting Division Director
Registration Division
Office of Pesticide Programs
United States Environmental Protection Agency