UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Pet Spot-On Enhanced Reporting Implementation

Registration Division

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(Updated August 2019)

SCOPE

This Pet Spot-On Enhanced Reporting Implementation document explains the Pilot program for use of standardized templates, which was concluded in 2018, and the associated, tiered approach to data analysis. In addition, this document serves to describe the implementation process for using EPA's standardized templates for submitting enhanced reporting and sales data, which affects all Spot-On products with registrations that require the submission of quarterly enhanced reporting. Pet spot-on registrants may currently request a change to annual (versus quarterly) enhanced reporting if using the templates issued following the conclusion of the Pilot in 2018. This document has been updated since its original release to describe a process for also requesting removal of the conditional registration expiration date when the standardized templates are used.

BACKGROUND

In 2008-2009 a notable increase in the number of reports of adverse health effects from pet spot-on flea and tick control products was identified in EPA's Incident Data System (IDS). The IDS system incorporates data submitted by registrants under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) section 6 (a)(2) in aggregate form on a quarterly basis. Aggregate reports include information such as the number of incidents reported per quarter, severity of incidents, and the products involved.

As a result of the increase, EPA required registrants of these products to submit enhanced incident data for the year of 2008. Enhanced incident reporting includes more detailed information such as exposure scenarios and associated clinical signs. The data were reviewed by EPA in 2009 with the resultant report being released in 2010. As a result of the increased incident reports and data analysis, EPA responded with mitigation measures including:

- 2-year time-limited conditional registrations
- Label mitigation to clarify instructions for safe use and provide clear indicators to prevent misuse
- Limitation of Confidential Statements of Formulations (CSFs) to one formulation
- Enhanced quarterly incident reporting with corresponding sales data

For additional and related information see EPA Evaluation of Pet Spot-on Products: Analysis and Plans for Reducing Harmful Effects at https://www.epa.gov/pets/epa-evaluation-pet-spot-products-analysis-and-plans-reducing-harmful-effects.

Although these mitigation measures have been implemented, screening level analysis demonstrated inconsistencies in the data submissions. Meaningful analysis of the data was not achievable with these inconsistencies making it difficult to use for regulatory purposes. Lack of standard data fields, standard terminology, and inconsistent formats are the deficiencies that facilitated the development of the Pet Spot-On Enhanced Reporting Pilot.

PILOT SUMMARY

The objective of the Pilot was to determine if use of standardized enhanced incident reporting and sales templates would provide the data in a format that could be more readily analyzed which would allow the Agency to review incidents more efficiently providing the necessary information on which to act should concerns be raised. In addition, through the Pilot, EPA sought feedback from Pilot participants and other interested stakeholders on the usability and feasibility of the templates which was used to modify the templates as needed.

The Pilot was introduced on the web in May of 2016[1] and via open stakeholder webinar in June of 2016[2]. EPA asked for up to nine volunteer registrants to submit one year of enhanced incident reporting data using the draft standardized reporting templates. Five registrants volunteered to participate in the Pilot program submitting data for the 2016 year using the draft excel-based templates.

The first data submission was made by August 29, 2016 which included data for Q1 and Q2 of 2016 (January-June 2016). A teleconference was held pre-submission to facilitate initial use of the templates and post submission to exchange feedback regarding the templates. Individual webinars were also held to provide a more individualized forum for each registrant to discuss concerns, feedback, and data sets. The final data submission for Q3 and Q4 of 2016 (July-December 2016) was made by February 28, 2017 completing the submission of one year of data using the draft templates provided by EPA.

Pilot results demonstrate that use of the standardized templates is feasible, and analysis by the health Effects Division (HED) confirms that use of the templates does provide data in a format that can be analyzed in a meaningful way.

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[1]Introduction of Pilot on the web in May of 2016 https://archive.epa.gov/epa/pesticides/epa-plans-standardize-manufacturers-enhanced-incident-reporting-pet-spot-products-seeks.html

[2]Open stakeholder webinar in June of 2016 https://www.epa.gov/pesticides/pilot-test-new-template-enhanced-pet-spot-product-incident-reporting

DATA ANALYSIS

As outlined in the Memorandum drafted by HED dated January 23, 2018, EPA will adopt a tiered approach for this analysis as described below:

Tier	Data Source	Description
Level 0: Aggregate Incident Data System Query	OPP's Incident Data System	Descriptive analysis will be performed using OPP's Incident Data System (IDS). IDS captures data on domestic animal (pet) incidents received under FIFRA 6(a)(2) from registrants and is reported in aggregate form on a quarterly basis. IDS data includes the number of incidents reported for quarter, severity of the incidents, products implicated, but does not include species or any narrative information regarding exposure scenario or symptoms.
Level 1: Reporting Odds Ratio (ROR), by Severity Outcome	Spot-on Enhanced Reporting Data	RORs will be calculated using enhanced reporting data to compare the odds of a given outcome (or event) for one product to odds of (same) outcome to another. This analysis will likely evaluate the ROR of Death (or Death+Major) incidents for each product *vs*. all other products combined, by species.
Level 2: Incident Rate Ratio (IRR), by Severity Outcome	Spot-on Enhanced Reporting Data	IRRs will be calculated using enhanced reporting data to compare the rate of a given outcome (or event) for one product to the rate of (same) outcome to another. This will likely evaluate the IRR of Death (or Death+Major) incidents for each product *vs*. all other products combined, by species. Rates will be estimated using sales data submitted as part of enhanced reporting.
Level 3: Signal-Based Case-by-Case Review & Causality Analysis	Spot-on Enhanced Reporting Data	This signal-based case-by-case review evaluates cases on an individual basis and incorporates information in the submitted narrative. This may involve investigating IRR on a symptom rather than a product basis and may incorporate causality analysis.

EPA understands that – for all levels or tiers described above – that signals are signals only, representing simple "disproportionalities" (sometimes referred to as SDR (signals of disproportionate reporting)). Such signals are considered to be hypotheses and do not necessarily imply causal relationships between the exposure and the health effect or outcome. Signal detection does not replace hands-on clinical review of case reports and veterinary medical judgment. Also the limitations and biases associated with reported data may limit utility, will require cautious interpretation. Nevertheless, EPA believes that the methods described above and use of the newly-developed standardized incident reporting template- will considerably improve the ability of the Agency to evaluate the data it receives and ensure the continued safety of these products.

IMPLEMENTATION

EPA is now inviting all pet spot-on registrants to adopt use of the standardized enhanced incident and sales reporting templates for annual enhanced reporting. Submission of annual enhanced reporting allows for a comprehensive analysis of data that complements the existing quarterly submission of 6(a)(2) incident data, a requirement of FIFRA. EPA believes that submission of the enhanced reporting on an annual basis is adequate because it will allow the Agency to assess trends in incidents over a comparable period of time that is independent of seasonal shifts in usage. Seasonal shifts on the use patterns of spot-on products will continue to be monitored through continued quarterly 6(a)(2) reporting.

Moving forward, registrants may request a further change to the conditions of registration to remove the two-year expiration when templates are successfully used. Use of the templates will become a condition of registration. This procedural change will support the objectives of pet spot-on mitigation by ensuring that consistent, high quality, and useful data are received in a timely fashion, while reducing regulatory burden. EPA will continue to actively manage these registrations by reviewing labels for mitigation whenever registrant-requested amendments are submitted and periodically through Registration Review. EPA may still initiate action at any time to address concerns if unreasonable adverse effects are identified. Such actions can range from mandatory label changes to cancellation of the registration.

Registrants can request to change the condition of quarterly submission of enhanced incident reporting to an annual submission, and/or request removal of the two-year registration expiration date, by submitting the following to the appropriate Product Manager for the product:

1. Submit a current (*e.g.*, quarterly) report using the EPA enhanced reporting templates for incident and sales data in electronic format (*e.g.*, CD), and
2. Submit a cover letter formally requesting that EPA amend the conditions of registration
    a. From quarterly submission of enhanced reporting to annual submission of enhanced reporting using the templates, and/or
    b. To remove the two-year expiration date.

    The cover letter should state the following:
    a. All registration numbers included in the data submission.
    b. That EPA templates have been used for the current submission of enhanced reporting.
    c. That EPA templates will be used from this point forward for subsequent submissions of enhanced reporting.
    d. That no other changes to the registration are requested.

Registrants who have already submitted a request according to this process to switch from quarterly to annual reporting, and who now wish to request removal of the two-year expiration date, should submit a new cover letter to this effect.

Once a request has been received, EPA will verify that the submission has been made using the provided templates, and that the templates have been utilized as intended. If removal of the two-year expiration date is requested, EPA will review the registration materials (*e.g.*, product label and CSF) and will notify the registrant of any changes that need to be made to reflect current mitigation. Upon verification of successful template use and resolution of any other issues, EPA can amend the conditions of registration to reflect annual submission of enhanced reporting using the templates and/or remove the expiration date.