SPOT-ON ENHANCED REPORTING PILOT

CONCLUDING WEBINAR & IMPLEMENTATION

U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (RD) and Health Effects Division (HED)
May 10, 2018

OVERVIEW

- Background
  - Concern over Spot-On Incidents
  - Mitigations
- Review of Enhanced Data 2010-2015
- Pilot Information
- Review of Pilot Submission Data
- Implementation of template use
- Q & A

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).

- EPA responded with mitigation measures:
  - Label mitigation
  - Limitation of CSFs to one formulation
  - 2 year time-limited registrations
  - Enhanced quarterly incident reporting with corresponding sales data

See https://www.epa.gov/pets/epa-evaluation-pet-spot-products-analysis-and-plans-reducing-harmful-effects for additional information

REVIEW OF ENHANCED DATA 2010-2015

- Registrants have made appreciable efforts to comply with enhanced incident reporting requirements.
- The enhanced reporting was compiled by HED into electronic format for analysis.
- Several important inconsistencies in the data submissions were noted.
- These inconsistencies need to be resolved to support meaningful analysis of the data submissions.

REVIEW OF ENHANCED DATA 2010-2015
DATA INCONSISTENCIES

- Lack of standard data fields and terminology
- Data Formats
  - Inconsistent among the companies and within the same company over time
    - PDF, Excel, Word documents, paper submissions…
  - Incomplete and missing data
- Sales Data
  - Inconsistent formats
  - Some companies included global incidents while others only US incidents
  - No sales data for some quarters or years
  - Reported total sales data included multiple products

PILOT

- To address the data submission and analysis difficulties, EPA created two reporting templates:
  1. Spot-on **incident data** reporting template
     - Standardizes variables/field names and definitions providing a consistent data format to allow for meaningful statistical analyses
  2. Spot-on **sales data** reporting template
     - Ensures EPA has necessary information on # doses sold for each product (sales data in consistent format)

PILOT
OBJECTIVES

- Test standard templates that will facilitate submission of enhanced incident reporting and sales data in a format that can be analyzed in a meaningful way
- Obtain feedback from Pilot participants and other interested stakeholders on the feasibility and usability of the templates to inform analysis
- Modify the templates based on feedback

PILOT

- 5 volunteer companies:
  - Agreed to submit incident and sales data for one year (January-December 2016) using EPA draft templates in excel format
  - Provided feedback on usability and feasibility of the templates via teleconference, webinar, and email correspondence.

HED REVIEW OF PILOT SUBMISSION DATA

- **HED Data Compilation and Review**
  - Reviewed data, undertook data cleaning, combined data from different Pilot participants into one master (SAS) file, and linked with sales data
  - Undertook further data review to look for outliers/unusual values, misinterpreted inputs/instructions, inconsistencies, etc.
  - Provided pilot participant-specific data reviews and Excel data files to each company (separately) at the end of October
  - Performed review/analysis to assess feasibility of HED analysis framework
    - Focused on data quality and ability to perform analysis using statistical software
      - ☑ HED confirmed data structure can be analyzed
      - ☑ HED can develop code to automate analysis
      - ☑ HED can perform statistical analysis outlined in framework

HED REVIEW OF PILOT SUBMISSION DATA

Data Snapshot

5	Companies volunteered to participate
CY 2016	Reporting Period
32	Number of registered products
44	Number of unique data elements • Product, severity, breed, symptoms, exposure timing…
100%	Percent of records with case narratives

Data Quality

- Minor data issues were identified in Pilot (e.g., coding inconsistencies, formatting, etc.)
- EPA has revised template to address, so some of these minor issues should be resolved
- EPA statistical programming confirms that data is structured and can be readily analyzed

HED REVIEW OF PILOT SUBMISSION DATA

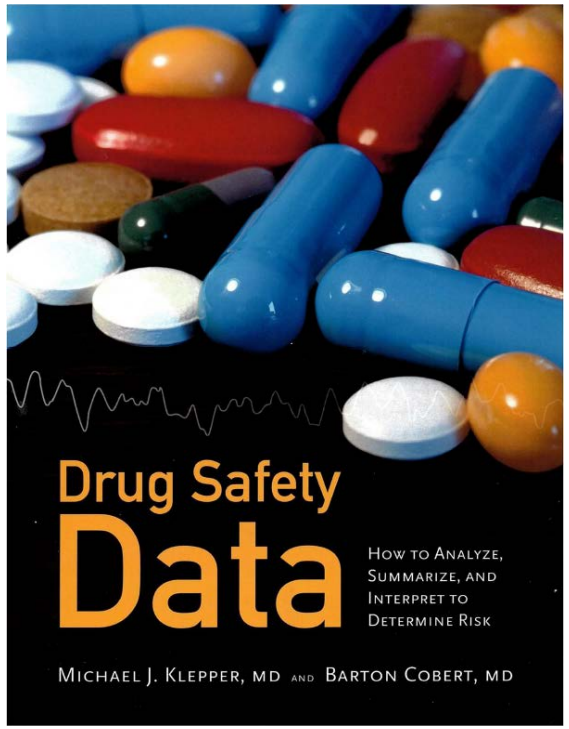
- **HED Findings**
  - Registrants made good faith effort to participate in the Pilot and work towards improving data submissions for better product stewardship
  - Overall, the 5 participating spot-on registrants succeeded in following both the EPA sales and incident templates for their data submissions.
  - Notably, the pilot submissions demonstrated that providing largely useable and useful data in machine readable format for data analysis is possible
  - Important information included in the databases (body weight of animal, severity outcomes, symptoms, timing of symptoms, and sale volume/quarter, etc).

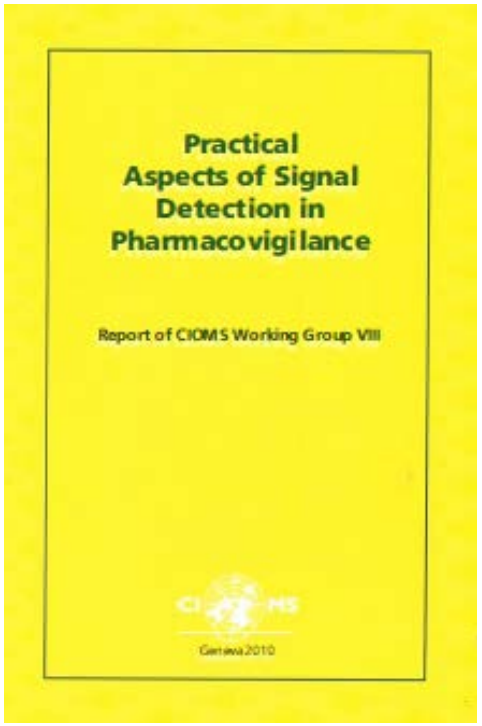
HED ANALYSIS FRAMEWORK

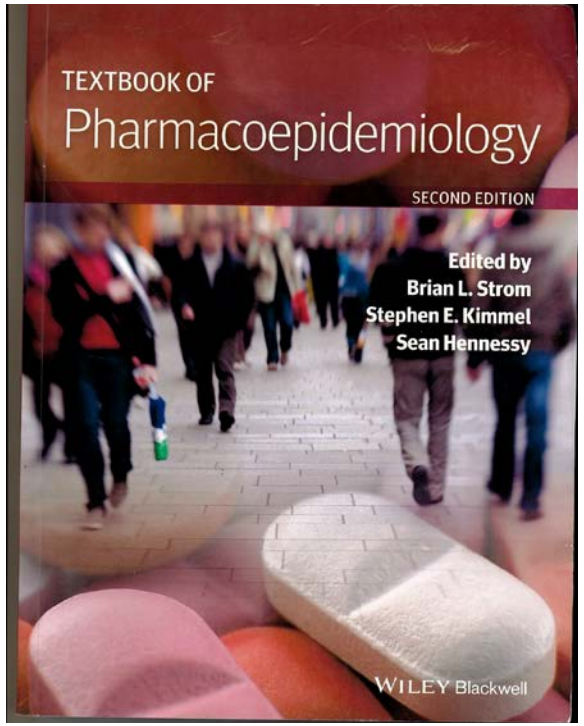
Specificity

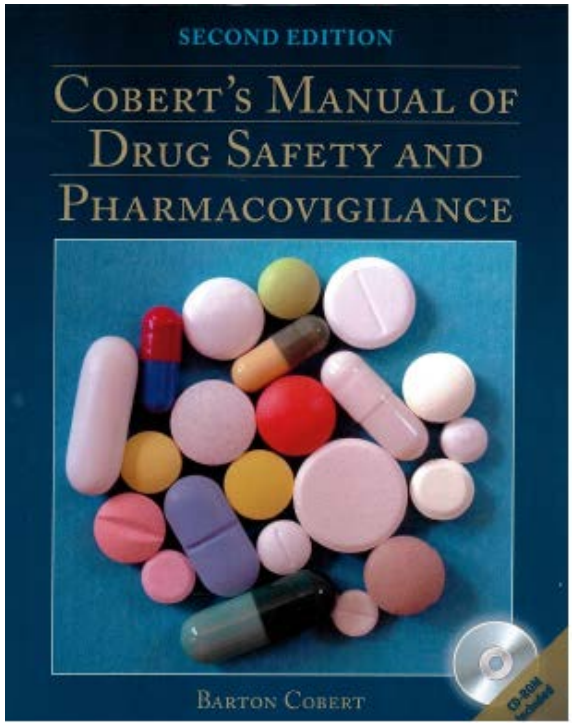
Level	Description	Aim
Level 0	Aggregate Query of EPA Incident Data System	Characterize IDS reporting trends by year, severity, and registered product
Level 1	Product Comparison of Severity of Outcomes	Examine if specific products are disproportionately associated with severe clinical outcomes
Level 2	Product Comparison of Severity of Outcomes + Sales Data	Examine if specific products are disproportionately associated with severe clinical outcomes, adjusting for sales data
Level 3	Signal-Based Case-by-Case Review & Causality Analysis	Perform in-depth analysis of structured symptoms data, followed by case narrative review by veterinary professionals

HED ANALYSIS FRAMEWORK









HED ANALYSIS FRAMEWORK

- **Limitations**
  - Detected signals are hypotheses only, and do not necessarily imply causal relationships
  - Does not replace hands-on clinical review of case reports – medical judgement
  - Limitations and biases associated with reported data require cautious interpretation
- **Confidentiality**
  - Analysis must be done such that a registrant will not be able to use results to derive the sales volume of any other specific registrants

IMPLEMENTATION
USE OF STANDARDIZED TEMPLATES

Registrants can request to change the condition of quarterly submission of enhanced incident reporting to an annual submission by submitting the following to the appropriate Product Manager for the product:

1. Submit a current quarterly report using the EPA enhanced reporting and sales templates in electronic format (CD), and
2. Submit a cover letter formally requesting that EPA amend the conditions of registration from quarterly submission of enhanced reporting to annual submission of enhanced reporting using the new templates.

IMPLEMENTATION
CONTINUED

The cover letter should include the following:

a. All registration numbers included in the data submission
b. EPA templates have been used for the current quarterly submission of enhanced reporting.
c. EPA templates will be used from this point forward for subsequent annual submissions of enhanced reporting.
d. No other changes to the registration are requested.

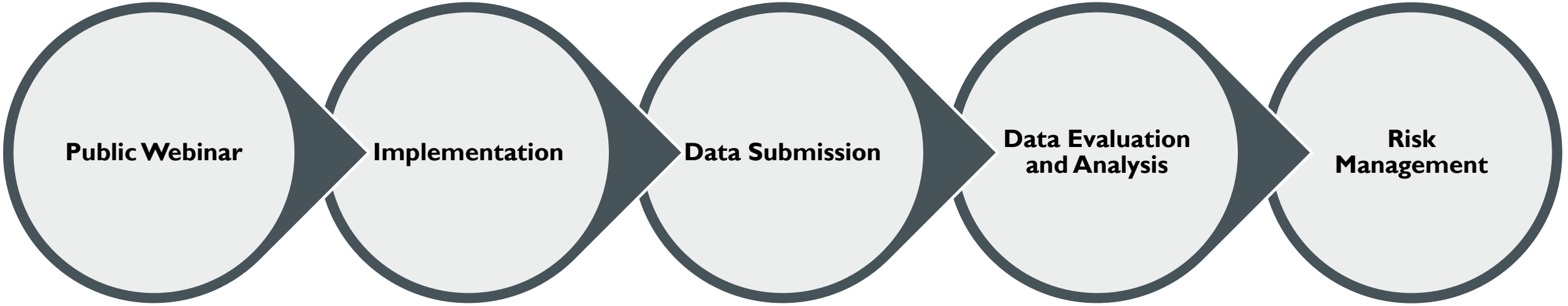
IMPLEMENTATION
CONTINUED

- Once a request has been received:
  - HED will verify that the submission has been made using the provided templates, and that the templates have been utilized as intended.
  - Upon verification, RD will amend the registration to reflect annual submission of enhanced reporting using the standardized templates. The registration will retain the current expiration date.

IMPLEMENTATION

- Tracking: If registrants have not submitted a request for annual submission of enhanced reporting using the templates within one year's time, then EPA will contact the registrants to determine intentions.

IMPLEMENTATION FRAMEWORK



- Schedule technical webinar(s) to address questions on template use

- Receive and QA/QC template submissions
- Amend registrations from quarterly to annual reporting, as appropriate

- Perform data analysis and assessment

- Work with registrants on product safety and registration, as needed

QUESTIONS & COMMENTS

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