Triage and risk analysis:
Post-market surveillance of pesticides
and veterinary medicines in Australia

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Overview

1. Role of the APVMA
2. Risk Analysis & Regulatory Science
3. Chemical Review Program
4. Adverse Experience Reporting
5. Compliance
6. Case Studies
7. Conclusions
### 1. Role of the APVMA

#### Pre-approval/registration
- Approve active constituents
- Register products
- Approve product labels
- Issue permits

#### Post-approval/registration
- Review existing chemicals
- Adverse experience reporting
- Compliance activities

> Legislation - can only approve/register if no impact on human health, the environment and trade, AND a product must be effective

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### National Registration Scheme

<table>
<thead>
<tr>
<th>APVMA</th>
<th>Australian States &amp; Territories</th>
<th>Product registrants &amp; users</th>
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<tbody>
<tr>
<td>Regulates up to the point of retail sale</td>
<td>Control of use</td>
<td>Stewardship</td>
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2. Risk Analysis and Regulatory Science

Making a defensible regulatory decision based on the best available scientific evidence at that point in time

Weight-of-evidence (amount & quality of data)

Uncertainty
- more data
- conservative assumptions
- do not approve/register
3. Chemical Review Program

- Program for re-evaluating existing (approved) pesticides and veterinary medicines based on human health and/or environmental concerns
- Nomination – credible, new (scientific) evidence
- Prioritisation – severity and probability
- Data call-in – published and unpublished data
- Risk analysis – technical, expert input, peer review
- Consultation – industry, users, community
- Regulatory decision – affirm, change or suspend/cancel
‘Classic’ post-market pharmacovigilance program

What is an adverse experience?
An unintended or unexpected effect of a product when used according to label instructions. This includes impacts on human beings, animals and crops, damage to the environment or lack of efficacy.

Reporting - anyone can report an AER (online reporting facility)

Evaluation – each AER is classified as probable, possible, probable or possible off-label, unlikely or unknown

Outcomes – additional data collection (trend analysis), label changes, chemical review, compliance action
5. Compliance

AERP Chemical Review Compliance

Validation of regulatory decisions

Product labels – do they contain the correct information (directions for use, safety directions etc)

Formulations – do the products contain what they are registered to contain (active and non-active constituents, impurities limits)

Proactive or reactive compliance activities
6. Case studies – Fipronil & Naphthalene

Fipronil
- Agricultural & veterinary insecticide (flea treatment)
- 73 AERs from 1998-2006 (30 off-label, 12 insufficient information, remainder were skin reactions in people)
- Expert input from dermatologist
- Registrant also reported high incidence of skin reactions
- Nominated for chemical review – review ongoing
- Regulatory action – changes to product labels

Loose naphthalene flakes
- Nomination for review – concerns from USyd academics regarding risk to babies & infants
- Referral to DoHA
- Packaging unable to be modified to mitigate risk
- Products withdrawn from market
7. Conclusions

Key triage elements
(things that help the APVMA make regulatory decisions)

- Awareness of higher order principles (legal & administrative frameworks)
- Work instructions (consistent approach to decision making)
- Risk analysis (international harmonisation, use best practice approaches)
- Always validate information/data
- Make use of internal and external expertise
- Communication – use networks
- Expect the unexpected – innovate when needed