To: ACVM team: ACVM.Consultation@mpi.govt.nz
Submission: "Update of Veterinary Medicine Adverse Event Guidance Documents & Reporting Form".
Date: 25 May 2021
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Submitted Information
The information supplied is what is available by 25 May 2021. Further information may be provided in future to inform ACVM.

1. Introduction

1.1 Agcarm welcomes the opportunity to provide feedback in response to the draft consultation documents titled "Update of Veterinary Medicine Adverse Event Guidance Documents & Reporting Form".

1.2 This submission represents the views of the animal health industry members of Agcarm which encompasses the majority of animal health products registered in NZ.

1.3 Agcarm notes that adverse event reporting is a key component of global pharmacovigilance and as such it is an important part of a wider system that helps ensure the safety and efficacy of animal medicines. Our main concern is that the guidelines help enable more effective pharmacovigilance and as such are consistent with global systems, while acknowledging that ACVM has other trade risks that need managing.

1.4 Members have expressed concern about the potential for increased workload to manage requests for information not directly related to AER. We consider that the scope of reporting should be consistent with requirements described by VICH or otherwise detailed in EU regulations. This ensures registrants can maintain a robust, efficient, and compliant global pharmacovigilance system worldwide.

2. Key points and recommendations

Agcarm:

2.1 Supports ACVM updating the Veterinary Medicine Adverse Event Guidance Documents & Reporting Form.
2.2 Recommends refinements to the definition of an adverse event as noted in Section 5 below.

2.3 Supports the need for a system to manage ACVM risks but strongly recommends that this be a separate system that is not linked to Adverse Events Reporting and is focused on managing residual risks.

2.4 Supports lack of efficacy as being included in the definition of an adverse event while also supporting the development of further guidelines on when lack of efficacy should be considered an adverse event.

2.5 Recommends extending the timeframe for providing feedback to voluntary reporters to 20 working days.

2.6 Recommends residues be excluded from the serious adverse event criteria.

2.7 Recommends removal of the section on Change of Product registrant under Statutory obligations.

2.8 Recommends an industry workshop on the new system before it comes into effect, so it is well understood by all stakeholders.

3. Data Privacy

3.1 In an early draft of these guidelines Agcarm had concerns with the proposal for sharing of adverse event reporter information with ACVM. Sharing of this data would not be consistent with global guidelines (VICH 42) and could become an impediment to end-users being willing to report events.

3.2 Agcarm notes that following further ACVM consultation with industry the draft guidelines now allow registrants the discretion to decide on whether to share the contact details of reporters of adverse events. Our members are generally satisfied with the provision of not routinely providing contact details, although our preference would be for reporter's personal data to be excluded from an adverse events report as the norm, and for this data to be available to ACVM only on request, with the approval of the reporter. We note that reporting adverse events is voluntary for veterinarians and customers and it would be preferable to seek permission from the reporter to provide their details if this were justified rather than provide these to MPI routinely, to ensure good and trusted customer relations. This would also enable us to provide more clarity as to why reporter contact details are needed when requesting permission.

3.3 We note that specific details such as location are not routinely entered into case submissions (e.g. in narratives) as many adverse events (globally marketed products) are also submitted to other jurisdictions where inclusion of this data is not approved. We are also unclear on what the purpose would be for collecting location data and what level of data would be required i.e. by province, post code or address, the latter of which again raises an issue with privacy. Our preference would be not to routinely provide location data unless there is a clear need for this.

4. Risk Mitigation Notification

4.1 The updated guidelines include a proposal to introduce a new notification "Risk Management Notification" - a mechanism by which MPI can manage risks posed by use of veterinary medicines, not previously covered by the pharmacovigilance programme. It is proposed this new requirement will cover situations involving the use of a veterinary medicine that has the potential to result in unacceptable outcomes for any of the ACVM Act risk areas including:

- potential residue issues, including any overdose/inappropriate dosing event that is likely to result in a residue violation if the label WHP was observed when sending the stock to slaughter.
- possible interactions with other products or compounds
- veterinary discretionary off-label use of products known to increase potential for unacceptable ACVM Act risk area outcomes.
- illegal off-label use (that is, contrary to label directions without veterinary advice)
- Events that should be considered to be serious and notified with urgency include any that:
- may result in a residue issue with risk to food safety. This includes any overdose/inappropriate dosing event that is likely to result in a residue violation where the label WHP was observed when sending the stock to slaughter.
- have resulted in interference with disease diagnosis or control.

4.2 Agcarm is supportive of there being a system for managing ACVM risk areas but does not support the proposed approach of adding this onto the adverse event reporting system which is focused on pharmacovigilance. We note that the adverse event definition from VICH (VICH GL 24) does not include non-adverse events in reporting programs and the purposes of the two systems are distinctly different. We are concerned that combining them together will create confusion with reporters and end-users.

4.3 We note that the scope of the Risk Management Notification includes many risks that would also be adverse events e.g., food safety risks and possible interactions which could result in confusion. Should they be reported under both systems or just one? If so, which one? Our key concern here is that current systems for pharmacovigilance are not undermined.

4.4 Another point of difference is that adverse events are generally reported to a registrant who then manages the investigation and reports to ACVM but for Risk Management Notifications the farmer or veterinarian will engage directly with ACVM in managing the event. This is another potential source of confusion if the systems are to be combined.

4.5 It would appear that reporters for a Risk Management Notification would be required to provide their contact details to ACVM. This lack of data privacy could deter reporters of ACVM risks coming forward and may have an impact on the current systems where an overdose/inappropriate dosing event happens, and farmers approach their veterinarians for advice and often registrants become involved in providing supporting information to veterinarians. Combining the two systems could raise data privacy concerns that erode both the willingness of users to report AERs and to seek guidance and advice about residue issues from registrants.

4.6 We note that “Veterinary discretionary off-label use of products known to increase potential for unacceptable ACVM Act risk area outcomes” is very wide-ranging and ambiguous. It could be interpreted to include all veterinary discretionary off-label use. More guidance is needed on what kinds of off-label use veterinarians need to report.

4.7 While Agcarm is supportive of establishing a system for management of ACVM risks our view is it should be a separate system that is not part of adverse events reporting. We note our members view the adverse event reporting guideline as a compliance document, which is used to ensure they comply with the conditions of registration for products in New

Zealand. We consider that the guideline should describe reportable information that is necessary to fulfil legal requirements. Additional information outside of this scope should be contained in a separate document.

4.8 We suggest that a separate ACVM system should focus on managing residual ACVM risks that are not covered by AER, which are likely to be mainly residue risks for export markets that exceed requirements for food safety in NZ.

5. Definition of an adverse event

5.1 We note the proposed definition of an adverse event is worded differently in the guidelines for registrants and the guidelines for veterinarians and animal owners. We think that the definition should be the same for both.

5.2 The definition in the guidelines for veterinarians and animal owners includes *"Events that do not create an obvious adverse outcome but potentially might…"* Our view is this is too vague and all-inclusive to be practical and should be reworded.

5.3 We note that "alleged interactions with other products or compounds" is not clear in the wording if this alleged interaction has resulted in an adverse event. Similarly, "use of human drugs in animals (reported as concurrently used with the registered product)" is also not clear in wording if the concurrent use has resulted in an adverse event. Does MPI wish to request any concurrent use/alleged interaction regardless of whether an AE has occurred or not?

5.4 Our members had various views on the point at which lack of efficacy should be considered an adverse event. We note that lack of efficacy fits the VICH definition of an adverse event and that companies have global reporting obligations for this based on individual company policies and procedures that extended beyond the ACVM requirements.

5.5 Some were of the view that any reported lack of efficacy needs to be investigated and reported on and that this takes away any subjectivity in determining an adverse event. Others expressed concern about the potential for adverse events reporting to become unnecessarily burdensome and overloaded if all cases of lack of efficacy are reported and have suggested a need for further guidelines on when lack of efficacy is classed as an adverse event, particularly when dealing with large groups of animals. This issue was discussed at AVMAC and it has been proposed that ACVM will provide guidance on when lack of efficacy of teat sealants should be considered an adverse event.

5.6 We note the serious adverse event definition "results in residue risk to food safety. This includes violative residue detections or inhibitory substance (IS) grades". In VICH this is not described in the serious classification and in previous guidelines it was under the adverse event definition rather than serious adverse event. This change would result in separation of serious classifications between geographies, in particular with EU and US. To resolve this, we propose that residues be excluded from the serious adverse event

criteria. Timelines for routine reporting vs alert/immediate notification can still be observed regardless.

6. Causality assessment

6.1 We note the proposed requirement to list all other equally plausible causes when a causality assessment of B (possible) is nominated. This could be exhaustive, and we propose it be limited to 1-3 causes. Equal plausibility cannot be provided in each scenario of a B causality assessment where multiple products are used. A registrant can only provide assessment for its own registered products.

7. Interactions

7.1 Registrants are responsible for assessing adverse events in relation to their own registered products as per registration conditions. There should be no expectation that the registrant would have the appropriate expertise to assess or evaluate the impact of human medicines or other registrant products on animals in single AE reports where no data is held internally regarding efficacy, safety, and residue profiles for these products. It is considered correct to include human or other registrant products as concurrent products for full case information.

7.2 We note that if a registrant became aware of an interaction with human medicine or other VMPs then it would be considered significant new information that would be reported to ACVM under registration condition 65.

8. Feedback to voluntary reporters

8.1 We note that adequate response oversight and internal discussion take time. This timeline should be the same as the routine AE reporting timeline to keep the count simple and possible to achieve (20 working days).

9. Change in Product registrant (Statutory obligations – heading 4 page 5)

9.1 We note that finalisation of open adverse events is not always possible at the time of change in Marketing Authorisation Holder. This whole section can be removed as closure of cases is negotiated directly within pharmacovigilance contracts between the involved parties.

10. Further briefing/workshop on the new AE system

10.1 Our members have requested the opportunity for further discussion with ACVM on the new AE system before it is in place, so it is well understood. To this end, we would like to suggest an industry workshop on the new system be convened before it comes into effect.

11. About Agcarm

11.1 Agcarm is the industry association for manufacturers and suppliers of animal health and crop protection products. For further information and a full list of members, see www.agcarm.co.nz.

11.2 Agcarm member products protect public health, improve animal welfare, and help environmental management. They:

- Play a pivotal role in growing high yield, sustainable food, and fibre products.
- Help supply healthy, nutritional, and affordable food.
- Keep New Zealand's agriculture, horticulture, and forestry sectors internationally competitive.

11.3 Our members are committed to safety, innovation, and product stewardship.