April 2020

News & Views

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In this issue...

Covid-19

Business as usual

The ACVM team is still open for business. ACVM staff commenced working from home on 23 March 2020, prior to the Level 4 Alert and Lockdown. We are well placed to work remotely – our business and IT systems enable it, and we are focussed on continuing to deliver our important regulatory functions during this period. For any concerns, issues or queries, please contact: approvals@mpi.govt.nz

Air freight

We have received many requests for assistance and guidance on the importation of ACVMs by air freight. Air freight services facilitated by government began Monday, 30 March 2020. Details for exporters and importers are here: https://covid19.nzte.govt.nz/page/air-freight-option-for-immediate-export

Calendar

17 April:	*Public consultation begins for 2nd quarter MRL round*
1 June:	*Extended deadline for submissions on AMR reassessment (see page 6)*
16 June:	*Public consultation ends for 2nd quarter MRL round*
22 July:	*Winter Workshop (cancellation likely)*

New Zealand Food Safety
Haumaru Kai Aotearoa

Ministry for Primary Industries
Manatū Ahu Matua

Management of Adverse Event Investigations on Farm by Registrants

Attendance of serious adverse events by veterinarians has been identified by the New Zealand Veterinary Association (NZVA) as an essential service at Covid-19 Alert Levels 3 and 4.

MPI agrees that events characterised by moderate to severe pain and distress in affected animals, due to inefficacy or an adverse safety outcome, must be appropriately investigated by the attending veterinarian with the primary focus being alleviation of the pain and distress. It is considered likely that, as a result of the veterinarian's investigations, information will be obtained to indicate whether the event may qualify as a product alert.

Product alerts

A product alert is a serious adverse event resulting in moderate to severe pain and distress in affected animals that requires immediate notification to MPI because there may be more serious adverse events if the use of the product is not stopped or restricted.

Should the possibility of a product alert case be suspected, further investigation will be required and this may include additional on-site visits.

However, as Level 4 measures require the limitation of travel as much as possible, MPI does not consider it appropriate for a company veterinarian to visit instead of, or as well as, the attending veterinarian.

This being the case, MPI accepts that the investigation of adverse events will need to be conducted predominantly via remote communication channels and the options usually available to product stewards to appropriately investigate the event may not be immediately available. The expectation remains, however, that events be investigated and communicated to MPI as comprehensively as possible, which may require increased co-ordination with the attending veterinarian to gather the required information on the company's behalf.

MPI will provide further advice as the alert status changes.

COVID-19

We're all in this together.

Stay safe.

Don't burst your bubble.

FYI

Regulatory oversight of inhibitors

MPI recently completed consultation on the regulatory oversight of inhibitors. The consultation document can be found at https://www.mpi.govt.nz/news-and-resources/consultations/?opened=1 by filtering on closed consultations. MPI Policy will review the submissions over the next few weeks.

Labelling agricultural chemicals

The revision of the Guidance Document: Labelling Agricultural Chemicals is nearing completion. The draft has now had changes made in response to consultation in September last year and is undergoing a final check both internally and with AVMAC (our advisory council). Although this has now been extended to April 16, we still hope to publish the final document in May.

Advertising guidance

The ACVM team continues to work on revision of the advertising guidance document. We have been working closely with key stakeholders on its revision. With the COVID-19 situation, there will be some delay in progressing this, but we hope this will be kept to the minimum.

Veterinary medicine application forms

A new application form specifically for requesting variations to veterinary medicines will be available very soon. It will replace the various forms for manufacturing changes. We are also updating the "Application to Manufacture" form. Watch this space.

Magnesium in Dairy Cows

Magnesium supplementation in dairy cows
Magnesium supplements fed to dairy cows may comply with the description of oral nutritional compounds in the Schedule 2 entry 25 of the Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011. Such products are exempt from the requirement for registration under the ACVM Act 1997 as long as all relevant regulations and conditions are complied with.

Magnesium supplementation and Salmonellosis in dairy cows
There have been reports from New Zealand and Australia of Salmonella infections occurring in dairy cows that were receiving magnesium supplements at the time. Magnesium delivered as prills, pellets, powder and via the drinking water was described in these literature reports.

MPI has to date received adverse event reports in association with prill and granulated magnesium oxide products only. These reports have described abortion, scours, loss of production and deaths in otherwise healthy pregnant or lactating dairy cattle with Salmonellosis identified as the inciting pathogen. Cessation of the current form of magnesium supplementation and vaccination against Salmonella typically resulted in the prevention of new cases within days.

Although sufficient information exists to suggest that there may be a causal relationship between the use of magnesium supplementation (particularly magnesium oxide in prill or granulated form) and development of clinical Salmonellosis, the exact physiological mechanism remains unclear. Please note, however, that magnesium oxide prills and granules are in widespread use in New Zealand with only a relatively few adverse events occurring. It is considered therefore that whatever the physiological mechanism may be, it is likely to be multi-factorial and not necessarily predictable.

Risk communication strategies
Based on the available information, all magnesium prill or granulated supplements are to include the following or similar statement: "The feeding of this product to dairy cows may increase their risk of clinical Salmonellosis. It is recommended that veterinary advice is obtained to ascertain potential risks associated with the use of this product in your environment before product is used". The inclusion of a similar statement on the labels of other magnesium supplements is not mandatory at this time but should be considered.

MPI is also working with industry groups like Dairy NZ to ensure their stakeholders are aware of the issue and have enough information to make an informed choice about magnesium oxide supplementation. Once this process is completed the information will be published on the MPI website.

meetings update

AVMAC and AMR CG
Due to the COVID-19 response our AVMAC and Antimicrobial Resistance (AMR) CG meetings to be held in March were cancelled. At this stage, we hope the planned meetings in July will still occur.

International meetings
A number of meetings for international bodies, such as Codex, have been postponed. Some Codex meetings have been rescheduled for later this year or early next year. As the situation is constantly evolving, it is unclear whether rescheduled international meetings will occur. Even if the situation returns to normal there are still likely to be issues caused by a compressed schedule of meetings to fit in with other work priorities along with the availability of flights. We will keep you informed of developments as they become available.

ACVM Policy Interpretation Updates

Intra-Ruminal Bolus Characteristics

Agricultural compounds that are intended to provide a source of nutrients to achieve a nutritional benefit are exempt from the requirement for registration as per Schedule 2, Part B, entry 25 of the Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011. However, **products that are formulated as intra-ruminal boluses are specifically excluded from this entry.**

As a group these products contain a high concentration of nutrients and a risk profile including unacceptably excessive pay out. Regulatory oversight is therefore necessary to confirm that sufficient product quality measures are in place to minimise this risk before the product is sold in New Zealand. Although not all boluses include nutrients or levels of nutrients that are associated with toxic outcomes in the treated animal, they still require registration as products are included or excluded in Schedule 2 entries based on general characteristics rather than particular characteristics of an individual product's risk profile.

The existing definition of an intra-ruminal device in the Regulations is "a device designed to be administered orally to a ruminant animal to provide prolonged and sustained release of nutrients or therapeutic or pharmacological substances or preparations". It is important to recognise that although intra-ruminal boluses may be presented as a nutritional compound included in a separate device that limits pay out, products that have characteristics that achieve the same outcome without a separate device component are still captured in the definition of an intra-ruminal bolus. The following policy definition of the characteristics of an oral nutritional intra-ruminal device is therefore provided for clarity:

An oral nutritional intra-ruminal device is any agricultural compound that has the following characteristics:

1. A product with a formulation that includes nutrients and which, following administration, will deliver those nutrients to the treated animal over a prolonged period (days to months) rather than immediately (within hours); and
2. The prolonged delivery of nutrients may be achieved as a result of the intrinsic nature of the ingredients themselves or via a specific method of manufacture or mechanism. This can include, but is not limited to, the physical form of the active resulting in retention in the ruminal tissues (e.g. copper wire), the addition of an insoluble heavy material (e.g. iron ballast), the addition of a poorly soluble ingredient, a method of manufacture that increases resistance to dissolution, or the inclusion of a physical object that modifies nutrient release (e.g. plastic vessel and aperture with spring mechanism).

Mineralised Drench Claims

The addition of minerals to anthelmintic drenches to provide a supplemental source of those nutrients is established practice in New Zealand. Informal policy was established nearly 20 years ago that this practice could be accepted but to preserve the intended primary purpose of such products as anthelmintics, no label claims could be made in association with the nutrients.

It remains important from a good pharmacological practice perspective that mineralised anthelmintics are used only when the anthelmintic action is the primary reason for use. MPI has no intention to approve an anthelmintic that is also intended to deliver therapeutic levels of nutrients. In consequence, to ensure that the user is provided with sufficient information to appreciate that the nutrients included in drenches are intended to provide a supplemental source of those nutrients only, we will require product labels in future to have a suitable use claim relating to the purpose of the nutrients.

For currently registered products a use claim will need to be proposed for approval and, as long as the claim is nutritional in nature, no supporting information will be required. This can be achieved via a C9 application that must be submitted and approved prior to the next planned label reprint or within 24 months, whichever occurs first.

For new product registrations, cross-reference to a currently registered mineralised drench in the absence of additional data is appropriate to support a general supplemental claim for the included nutrients when the dose rate of each nutrient is consistent with that of the referenced product. If the dose rate is higher than a currently approved mineralised anthelmintic, data (which could include literature references) will be required to confirm that it is still consistent with a purely nutritional benefit and will not pose a potential safety risk.

Reassessments

Antimicrobial resistance reassessment

Tranche 1
In November last year, registrant companies that own trade name products containing macrolides, later-generation cephalosporins, and penicillins, collectively known as the Tranche 1 antibiotics, were asked to submit applications to reassess those products by 31 March 2020.

This reassessment is the first of five tranches of work under MPI's antimicrobial resistance (AMR) work plan, and will review the registrations to ensure the use information and labels are consistent with both good agricultural practice and the prudent use of antibiotics. At the same time, the residue profiles of those products approved for use in food-producing animals will be reviewed to make sure there are appropriate maximum residue levels (MRLs) assigned to all food from treated food-producing animals to ensure good agricultural practice is being followed.

Extended deadline
Since establishing that March deadline, we have seen the emergence of COVID-19 and a complete change in the way we live and work. To help reduce the pressure on companies at what is already a difficult time, the ACVM team has extended the deadline for reassessment applications to 1 June 2020. For those applicants who have already submitted applications or have them ready, we will be staggering the reassessment appraisals by active ingredient rather than accepting and assessing the 100+ individual product applications at once as originally planned. This will hopefully reduce the workloads on both sides throughout the reassessment process without significantly delaying its outcomes.

Tranche 2
The Tranche 2 review, establishing AMR importance classification to registered veterinary aminoglycosides, fluoroquinolones, early-generation cephalosporins, and lincosamides, and the proposed regulatory changes for products containing them, is underway. Like the Tranche 1 review, a final discussion paper covering the Tranche 2 review outcomes and rationale will be made publicly available when it is complete.

Review paper on website
The Tranche 1 review paper can be found on the MPI website on the Controlling and preventing antimicrobial resistance (AMR) landing page under the "Antibiotic Review and Reassessment Programme" heading. All future review papers will also be uploaded there.

VTA Brodifacoum proposed reassessment

The settings for the new vertebrate toxic agent (VTA) registration conditions were drafted and sent out for consultation to interested parties.

We received submissions from a number of individuals/groups.These are being correlated and salient points will be published in a summary document.

Based on the submission responses, the following changes may be incorporated into the proposal:

- The VTA 'User' classifications will be simplified to those who have a user certificate (professionals) and those who do not (home users). The controls for these groups will remain as proposed.
- The phrase relating to volunteers being under the direct control of a suitably qualified person (impacting "predator free 2050") will be removed. An alternative mechanism for this group will be investigated.

We will obtain consensus among the industry as to:

- implementation of the controls by industry management or by ACVM conditions of registration (involving a reassessment), and
- implementation of an education / certification course suitable for both professionals and volunteers.

ACVM Regulatory Programmes – Compliance Activities

The new Regulatory Programmes Compliance Adviser's first few months have been busy processing complaints regarding potentially non-compliant ACVM products. Between January and March the Regulatory Programmes team received:

- 29 complaints regarding unregistered ACVM products (The majority of these complaints related to exempt products that were non-compliant with the conditions of exemption or products being sold that should be registered.)
- 10 complaints regarding ACVM registered products (The most frequent complaint related to decanting and selling of registered products into unapproved packaging and pack sizes.)

We remind everyone that an ACVM registered product cannot be broken down, decanted and sold in unauthorised packaging and pack sizes. Any entity performing repacking/relabelling into smaller pack sizes must be approved on the product's registration, have the necessary certification (e.g. GMP for veterinary medicines and vertebrate toxic agents), and only registered pack sizes with the correct labelling can be sold. Veterinarians are authorised to decant product for animals under their own care, but this product must not be advertised or sold.

We also received 12 notifications relating to non-conforming batches of ACVM registered product released or yet to be released to the market.

One non-compliance event has been referred to MPI Compliance for further investigation.

We have observed that there are still some ACVM registered antibiotics being advertised by some registrants and sellers in the distribution chain.

ACVM registered antibiotics with condition 58, must not be advertised. Please ensure you remove any that are still being advertised from your website. Further communications regarding this matter will be distributed to relevant parties, along with a list of products that have registration condition 58.

2019 events

Of the 152 non-compliance events reported in 2019 (excluding batch specific variations and rapid alerts), 76% are considered appropriately actioned and are now closed.

Watch this space....

- We are in the process of creating an online reporting tool to make it easier to report products that may not be compliant.
- We are also working on a form to make it simpler for registrants to report a non-conformance regarding their own product.

AgChem team field trips

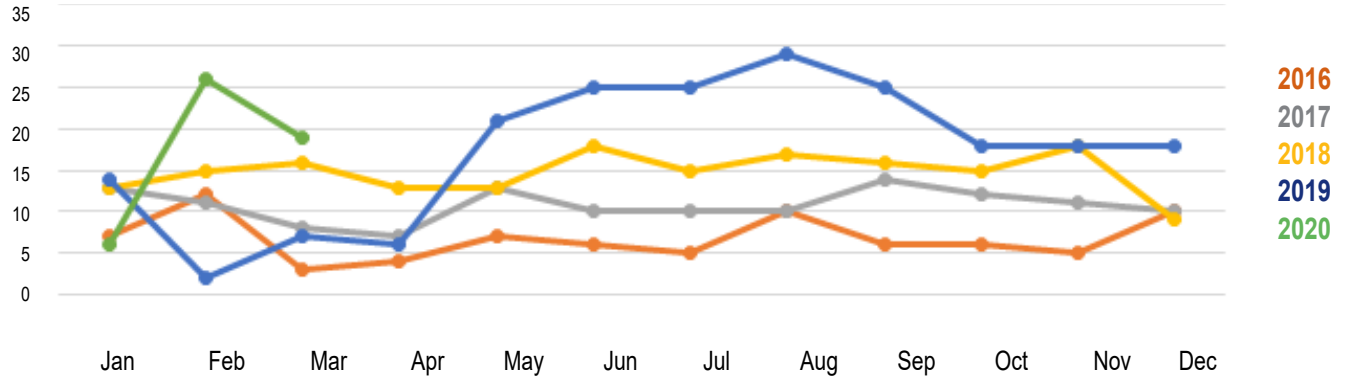
The AgChem team participated in two field trips during the past three months. The first was to the Grochem manufacturing facility in Wellington. There the team learned about manufacturing of agricultural chemicals, supply chain practicalities and quality control. The second trip was facilitated by BASF and involved visiting several stakeholders in Hawke's Bay. There the team visited grape trials, saw a sprayer demonstration, visited New Zealand Apples & Pears, and T&G's packhouse in Hastings.

These learning opportunities are part of the AgChem team's effort to stay on top of manufacturing, agronomic and commercial/export practices across the range of crops that the team regulates. Talking to our stakeholders, and seeing the work they do in person is very helpful in giving us an on the ground perspective we can apply in our role as the regulator. The team is extremely grateful to the various organisations that graciously took time out of their schedules to host us.

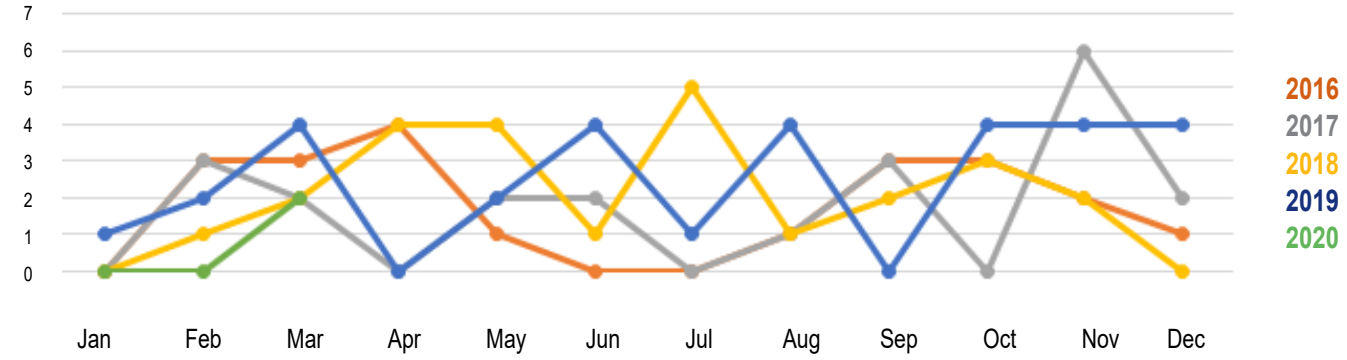
Performance Metrics

In the year to date, 44 compliance related activities have been logged, an increase from previous years. This reflects the additional resource and focus in the ACVM team on compliance.

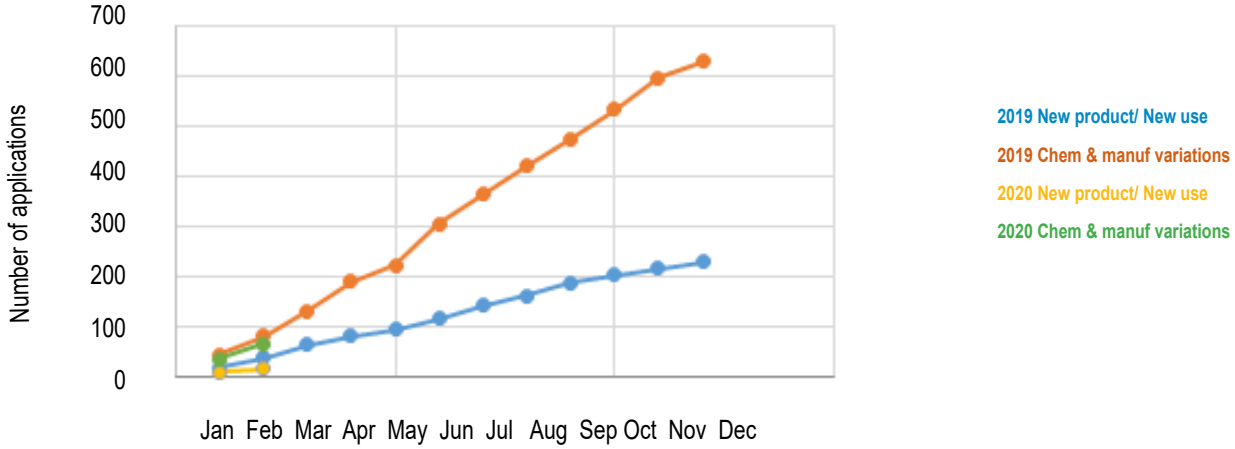
Total Compliance Related Activities
including reported non-compliance events, batch specific variations, regulatory alerts and non-conformance reports



Good Manufacturing Practice (GMP) Site Audits Performed

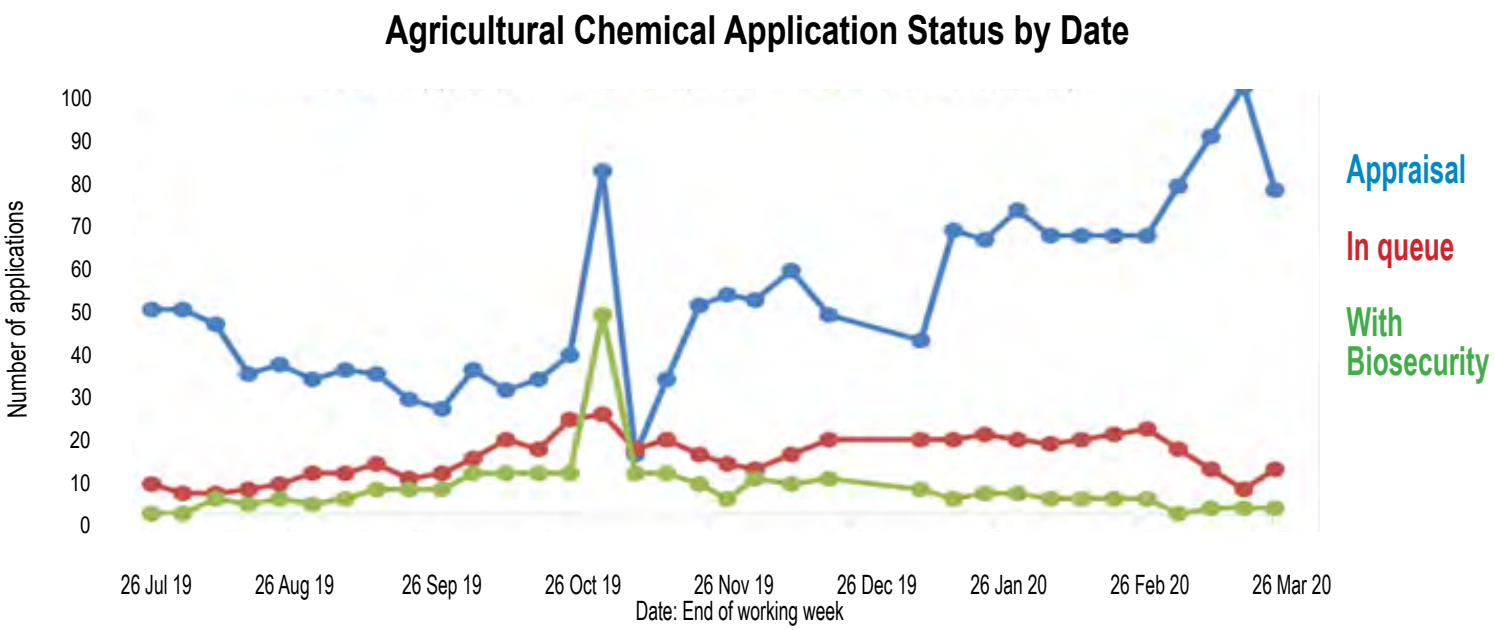


2019 - 2020 ACVM Technical Application Approvals (Cumulative Volumes)



Performance Metrics

The AgChem team continues to keep their application queue to a manageable level with 65 applications in appraisal and 9 in the queue. One is with Plant Imports for Biosecurity assessment.



There is still a significant backlog of Vet Med applications, which has been gradually increasing since the end of November. This is mainly due to being short-staffed in recent months (a vacancy in the vet med team since September 2019, and staff being on leave), and application volumes.