SUBMISSION

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To: ACVM.Consultation@mpi.govt.nz

Submission on: **ACVM Requirements and Guidance Agricultural Chemical Registration Submission**

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1. Introduction

1.1. Animal and Plant Health Association New Zealand (APHANZ) welcomes the opportunity to comment on the ACVM Requirements and Guidance documents for the Registration of Agricultural Chemicals outlined within three separate consultation documents[1]

1.1.1. Registration Information for Agricultural Chemicals – (**proposed standard**)
1.1.2. Guidance Document: Agricultural Chemical Registration (**GDACR**)
1.1.3. Guidance Document; Chemistry and Manufacturing Information for Agricultural Chemicals (**GDCMI**)

that replace the **current guidance** document (ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand). The current guidance outlines the registration process for agricultural chemicals only under the Agricultural Compounds and Veterinary Medicines Act 1997 (the Act).

1.2. Comment on specific technical areas within the guidance document (*GDCMI)* will be delayed until the submission deadline of 5th January 2024. However, the document will be mentioned in this submission for completeness and where this guidance interacts with the documents that are the subject to this submission. (Note the blank section left for the submission in section 4 of this submission).

1.3. APHANZ members are focused on the clarity of the wording and intent of the requirements for registration, seeking to understand if there is any fundamental difference between what is proposed and what is currently accepted to register an agricultural chemical, and how the requirements / guidance relate to international standards/guidelines.

1.4 Generally members understood the logic for the change (one guidance document into one standard and two guidance documents) but were concerned about access to the information for new or intending applicants as there is no overview of the process.
The MPI webpage a few years back reflected the documents associated with agricultural chemicals in a logical format so all parts could be seen and logically interlinked. However, the current MPI website makes documents difficult to locate and most documents are accessed through google. This method brings up out of date documents and is a source of frustration.
Recommendation: It would be appreciated if the previous web format of the ACVM webpages were reinstated for transparency purposes, or the documents themselves provide a logical reference or an overview oof the documents associated with agricultural chemicals (registration, compliance etc) provided.

1.6 An overarching concern of members is that there is no link to international standards/ guidelines or like-regulators (i.e. FAO, Australian APVMA and OECD) except for active ingredients (Section 6.1.4 of the GDCMI) in the proposed standard. This is despite reference to international standards in the original guidance document to OECD templates and the like. This is concerning for a number of reasons:

- the lack of alignment with international standards may diminish the recognition of the NZ regulatory system.
- those registrants seeking registration elsewhere cannot rely on the New Zealand registration application requirements aligning with other regulators.

Recommendation: Reinstate reference to OECD and FAO standards/guidance by incorporation or acknowledgement in the standard or guidance documents.

[1] https://www.mpi.govt.nz/dmsdocument/59404-Guidance-Document-Agricultural-Chemical-Registration
https://www.mpi.govt.nz/dmsdocument/59401-ACVM-Requirement-Registration-Information-Requirements-for-Agricultural-Chemicals
https://www.mpi.govt.nz/dmsdocument/59461-Chemistry-and-Manufacturing-Information-for-Agricultural-Chemicals-Guidance-

2. ACVM Requirement: Registration information Requirements for Agricultural Chemicals (proposed standard)

1.4. It is noted that the proposed standard identifies that the key application requirements *must be* conducted if an applicant is seeking registration or variation of a registration of an agricultural chemical, as the status afforded tertiary law.

1.5. Revocation

Under revocation, the proposed standard is to replace the current guidance document. However, the elements that are decided as guidance (GDACR and GDCMI) are not referenced as replacing the current guidance document.
Recommendation: It would be helpful for the reader if there is a reference to the replacement documents either in the proposed standard or guidance (GDACR).

1.6. Background

The previous document ACVM Registration Information Requirements for Agricultural chemicals in NZ – 2011 listed the *risks to domestic food residue standard*s. This is omitted, although Section 4 (b) of the Act specifies *that there should be not breaches of domestic food residue standards.*
Recommendation: Please clarify this omission or reinstate.

1.7. Section 1.1 Application (Part 1 Requirements)

The registration requirement is designated under section 9 of the Act, which includes all agricultural compounds. The requirement specifically excludes provisional registration (under section 26 of the Act) but is silent on the reassessment of registered agricultural chemicals (under section 29 of the Act); the agriculture chemicals exempt from registration (under section 21 of the Act) and that for exceptional circumstances (under section 8c). For completeness and consistency sections 29 and 21 should be noted as specifically excluded/included where such sections relate to agricultural chemicals. Noting that the GDACR (11.4) references reassessment and section 8c of the Act (for exceptional circumstances)

The Application section does not mention the process for deregistration of an agricultural chemical (voluntarily relinquishing registration of an agricultural chemical or situations when re-registration is required). This is not covered in the GDAC.

Recommendation: For completeness and to remove ambiguity, include the reassessment of registered agricultural chemicals, exclusions when agricultural chemicals do not need to be registered and any exceptional circumstances where registration is not required. In addition, provide the deregistration process as it relates to agricultural chemicals. All within the proposed standard.

2.6 There is reference to standards and guidance documents within the proposed standard, which is helpful. However, some of the standards (i.e., ACVM Research Standard) are out of date and do not accurately reflect the requirements for research.
Recommendation: We would appreciate it if the ACVM team would look at the ACVM standard where the standard is out of date.

2.7 Section 1.2 Definitions

The terms *confidential information* and *reference product* are defined but not mentioned in the document, although such terms are referenced in the GDACR. Is there a section missing related to these two terms?

There is also nothing in the proposed standard that indicates that information provided by the applicant will be protected. Data protection is important to our members.

Recommendation:

1. *As there is nothing specific in the Act, we would ask that all information is treated as confidential and that this is specified in the standard as guidance in handling applications.*
2. *Remove definition of terms that are not used in the proposed standard.*

2.8 2.8.1 Section 2.1 (f) . this sentence reads all 'data assessment reports in accordance with clause *2.7 and papers' etc*. Is this referencing a data dossier or should there be a semicolon (i.e., '*clause 2.7; and papers*') to list another requirement. It is uncertain what is intended.

2.8.2 Section 2.1 (2) references documentation listed under 1(e) -(h) must be provided *relative* to the proposed change. Please clarify what is meant by the term 'relative.' We wish to have some clarity as to what applicants are required to provide. i.e., if the claim is substantial specific evidence to support that claim.

Recommendation:
Please clarify what is required in section 2.1 (f) and section 2.1(2)

2.9 Section 2.5 Application overview

2.9.1 Section 2.5(1) references the "person applying for registration' and then references the same as 'it' *must consider additional hazards'*.

Does 'it' refer to the applicant writing the application? Would a more appropriate address be the ' *person applying for registration'* rather than 'it.'

2.9.2 *Additional hazards, risks, or benefits,* not addressed through the standard expectations are not defined (i.e., what is a hazard, a benefit) in the context of the scenarios listed. Risks may be defined in the document *Risk Management overview*, but benefits and hazards are not.

2.9.3 In the guidance box (second bullet point) places the onus on the applicant to address all additional risks (unknown or unspecified). This 'comment' in a standard is unhelpful. All efforts to describe and mitigate known risks, should be in the guidance document. Transferring the onus onto the applicant to satisfy the risks the regulator is not aware of is legally unenforceable when the regulator has not specified the risk.

Recommendation :

1. *Clarify the terminology* used (hazards, benefits) through definition.
2. Remove the second sentence in the paragraph of the guidance box (2.5). "*However, the guidance cannot address all risks, especially for innovative products, and it is the applicant's responsibility to address additional risks comprehensively in the data volumes."*

2.10 Section 2.6 General requirements for data volumes

2.10.1 We assume that there has been a typing mistake with two section (1)'s.

2.10.2 We would note that this section could be simplified by removing the repeated words "*A person applying for registration or registrant "and creating bullet points.*

2.10.3 In section (2) or we would note that studies provided are noted as *being robust, reliable, and relevant.* There is no reference to international standards of such documents, as that provided by the OECD for specifically mentions OECD templates. such information, although the current guidance (Section 5.7).

Neither the guidance nor the proposed standard references any international standards.

Recommendation: Reference international standards FAO or OECD as guidance in the proposed standard.

3. Guidance Document: Agricultural Chemical Registration (GDACR)

3.1 There are some elements (in the current guidance) that have not been incorporated in the proposed standard or guidance. This may be intended or unintended and this section intends to examine if this is the correct interpretation. For example:

- Domestic food residues are mentioned in the proposed standard as additional hazards (S.2.5((2)(f)) that may be required. However, in the guidance document (section 8 of GDACR) the residues in crops must (rather than should) be supplied for products on or around food. In the current guidance domestic food residues must be supplied. Shouldn't domestic food residues be included in a standard if the term 'must' be used? Or is this an interpretation of the Act?

- Section 2.6 Provision of data and supporting Information. The proposed guidance does not reference an international standard or international guidance. Such information was proposed in the earlier version of GDCMI (refers FAO, Australian APVMA and OECD) and is in the referenced in the current guidance as OECD templates.

3.2 The registration process does not reference other relevant Acts (Waste Minimisation Scheme (WMS)/Health and Safety at Work Act HSWA) for agricultural chemicals. It is assumed that applicants will meet all other regulatory requirements, but this is not stated .

3.3 Receipt of Registration Applications
It is presumed that applications may be submitted electronically, via an online process and acceptance of the application is when the application is received by the regulator. Some regulators apply time waivers or assume the application is not officially received until a reviewer is available to review the document. To meet statutory time frames, guidance should include the official acceptance of an application.
Recommend: provide guidance of the timing of when an application is officially received and what the timing expectations are, specifically for electronic or on-line applications.

4. Guidance- Chemistry and Manufacturing Information for Agricultural Chemicals (GCMIC)- as provided 5th January 2024.

4.1 Introduction

Multi-national companies are only able to bring novel new product to small markets such as New Zealand by leveraging the synergies of a global regulatory system and using the same study across many geographies. If there was a requirement to initiate (or re-run) studies specifically for New Zealand, then this would likely impact the business case negatively and prevent many products from being launched in New Zealand due to the already narrow economic margins.

Alignment with international standards is therefore a critical aspect of any requirement for the manufacture of agricultural chemicals and it is the intent of this submission to provide alignment to international standards where applicable (section 4.1.1), provide feedback. .

The current wording of the guidelines assumes that the product has already been registered in other countries and is being manufactured commercially before registering the product in New Zealand, which may not often be the case and re-running these studies on commercial scale batches specifically for New Zealand would be difficult to justify. Commercial scale batches are typically not available and quality specifications are often yet to be defined at the time the product chemistry studies are conducted.

4.2 Generalised overview of changes

We think that ACVM should align more closely with APVMA around their requirements – they do to a degree but there remain areas in which closer alignment would be justified i.e. specifications, etc) and which are itemised in 4.3 of this document. New Zealand is a small market and the more uniqueness there is in the data requirements for NZ, the less appealing it becomes to introduce products here, or to continue with them when changes are made at the global level. For some products, when a global change occurs such as to the packaging or the formulation, the cost of generating data required specifically for NZ may ultimately mean that the more sensible thing to do from a financial perspective is to discontinue supply in NZ.

ACVM manage risks to NZ's trade in primary produce, public health, animal welfare and agricultural security. It is important to recognize that it is in the best interests of NZ in all these areas to have a wide range of products available for end users. The reason behind requiring data to support products is to ultimately manage these risk areas, however having overly unique data requirements poses risks to these same areas through the disincentivising effect it can have on the continued supply of, and introduction of new, products.

Incorporation of self-assessable changes for packaging plus the additional proposal to add "Self-assessable changes" to the guidance document is viewed positively by members. Aphanz would ask that ACVM considers other options (within self-assessable changes) which may meet similar criteria. We believe this would streamline the process for changes which are administrative and improve the ability of ACVM to align NZ practices with APVMA guidance. It is recommended that where the proposed changes are administrative in nature, they would be managed through a C9 administrative update and included in the next PDS update.

We propose that the following situations may be examples of self-assessable changes:

- Change of packaging (as per point 7.7.1)
- Changing the name of a site
- Changing an address of the site when there is no change in the physical location
- Addition of sites for re-labelling or packing of a product
- Addition of alternate methods to the QC or product specifications where publicly available, such as CIPAC
- Addition of alternate tradenames where the CAS number of the main constituent is the same/identical
- Changes to the typical batch size
- Proposals Finished product excipient changes which will not impact finished product release and expiry specifications, such as grade/standard, minor formulation changes (e.g., <5%) and minor seasonal adjustments should be self-assessable.
- NZ manufacturing facilities which are audited by ACVM, minor changes to the manufacturing process that do not adversely affect product quality or efficacy, such as changes to in process testing and limits should be self-assessable provided finished product specifications are still met.
- variations related to minor changes to an approved physicochemical test procedure, where the updated procedure is demonstrated to be at least equivalent to the former test procedure, appropriate validation studies have been performed and the results show that the updated test procedure is at least equivalent to the former

4.3 Detailed feedback to document

Section	Current wording	Ref.	*Recommended wording*	Reasoning
Definition	**definition of a 'formulation'** refers to a 'list of all the ingredients and concentrations.		Proposed to update the definition to that of 'formulation composition'.	The definition of 'Formulation' is a synonym for 'formulated product' which is already defined.
	definition of 'QC specifications'		'…of each batch or a representative sample for a continuous process after manufacture is complete'.	To include continual manufacturing process.
6.1.1 (2)	***An intermediate supplier***		transfer 6.1.1 (2) to additional guidance.	An intermediate supplier does not conform to a list of manufacturers of the active ingredient and should be listed as that exempt as a manufacturer.
6.1.3	***a. Physical state**** ***b. limits**** ***c. isomers****		Clarify the reference to '*'	The '*'do not have a corresponding referenced footnote or could refer to 6.1.3 (2)
6.1.4	***Specifications for active ingredients*** *MPI harmonises with the following agencies for specifications for an active ingredient (in this order): NZ EPA, APVMA, FAO. State whose specifications have been referenced.*	***NZ EPA/ APV MA/F AO***	clarification sought for specifications not referenced by ***NZ EPA/APVMA/FAO***	There is inconsistency in the EPA controls applied to products that share the same active ingredient. Gaining insights into the rationale behind these distinctions, especially in cases where more than one active source is used, would assist applicants in establishing internal specifications for sourcing purposes. Where specifications are not referenced by ***NZ EPA/APVMA/FAO***, what is the process for registrants to follow?
6.1.5	Active ingredient impurities	APV MA	Propose the new heading is: Active ingredient Analysis	Based on workshop recommendation

6.1.7	*"If a manufacturing concentrate is used, provide the following information: a) minimum concentration of the active ingredient in the manufacturing concentrate, b) minimum purity of the active ingredient if relevant, c) final concentration of active ingredient present".*		(c) final concentration of active ingredient after correction of active ingredient (a) for purity (b). i.e. c = a x b	This wording is confusing and the difference between (a), (b) and (c) is not easily apparent. It is believed that the intent is that (a) is the concentration of technical material added, while (c) is the final concentration after adjustment of purity. The definition of (c) should be updated to 'final concentration of active ingredient after correction of active ingredient (a) for purity (b). i.e. c = a x b

	States "You should identify and report on impurities under the following conditions: *a) Toxicologically significant impurities which are present at any level should be identified, characterised, and quantified.* *b) Impurities where the toxicology is unknown which are present at any level should be identified, characterised, and quantified.* *Any other impurities greater than or equal to 1 g/kg (0.1%) regardless of toxicity*		You should identify and report on impurities under the following conditions: a) Any impurities present at level greater than or equal to 1 g/kg (0.1%) b) Toxicologically significant impurities which are present at any level should be identified, characterised, and quantified."	The original wording is not consistent with generally accepted and globally harmonized approach to impurities present in active ingredients, which is to report and characterize all significant impurities - meaning all present at or above 0.1% - and all toxicologically significant impurities present at any level.

6.1.8 (1) and 7.3.2 (c)	*Provide at least three production scale batch analyses from each site. At least one of these batches must be produced in the last 2 years* (at time of submission)	FAO	Proposed rewording to: *Provide at least a five pilot batch analyses from a site. At least one of these batches must be produced in the last 5 years (at time of submission).*	International practice is for the provision of a 5-batch report (these are typically pilot batches as defined in section 3 definitions) and not a production scale batch. Currently, ACVM does not request the provision of a production scale batch. The provision of three production batches is of particular concern for novel active ingredients, especially if the product is not approved. In principle, the 5-batch (pilot) report is sufficient to address risks (consistent AI purity and impurity profile) if the 5 batches (pilot) show results are consistent and within expected ranges. For novel compounds, only a 5-batch (pilot) report may be available at the time the registrant approaches ACVM for the registration of the product. The provision of condition 7.4.1 (d) seems appropriate to ensure one production batch is provided before sales commence. Requesting a production scale batch to be produced in the last 2 years (prior to submission) would also force manufactures of agricultural chemicals to perform additional studies at later stages and specifically for such a small market like NZ, instead of using standard 5-batch analyses that have been generated for the purpose of all registrations globally.
6.1.8 (4)	*As ACVM is unable to verify APVMA information, reference to active ingredient manufacturing sites via an APVMA approval number and consequently provision of the approval notice (in lieu of data) is no longer available."*		APVMA provide the details (including approval number, site name and address, min purity and the impurity profile) to applicants in the new templates for 'Notice of Approval of an Active Constituent'	**- Supporting information (batch analyses), Additional Guidance** "While ACVM can no longer access details of an APVMA approval number directly to connect the source address based on public information, APVMA provide the details (including approval number, site name and address, min purity and the impurity profile) to applicants in the new templates for 'Notice of Approval of an Active Constituent'. Provision should be made in the guidelines to provide for this.

6.1.10	*You should provide validation data for the method(s) used to assay the active ingredient(s) and toxicologically significant impurities. If the method is a CIPAC method only selectivity and accuracy data are required.*		Given the practical constraints, registrants should provide the method, and not the validation data.	Analytical method validation reports are considered intellectual property, making it unlikely for manufacturers to share this data directly with the applicant. The alternative, having manufacturers submit this information in confidence to ACVM, presents a dilemma as Independent Data Assessors would be unable to review these reports.
6.2.3	*The following data on the physical and chemical properties of the product should be provided:* *e) viscosity and surface tension (liquids)* *g) oxidising properties* *h) corrosive hazard*		Guidelines for the required of the tests would assist registrants meeting the specifics.	Could ACVM offer further clarification on whether these tests are also applicable to products containing existing active ingredients. Guidelines for the tests are not provided . Conducting such tests, particularly for a New Zealand-based manufacturer performing them in-house, poses potential challenges in terms of resources. Understanding the exact requirements and guidelines would assist in efficiently meeting ACVM requirements.
6.2.3 a)	*Appearance, colour, odour, physical state*		*Appearance, colour, ~~odour~~, physical state*	Odour as a parameter, is no longer a FAO requirement. Given the subjective nature of describing odours, and the possibility for risk to worker health and safety (if they are required to routinely inhale substances), we propose that this be deleted. Retaining this would appear inconsistent with the broader goals of New Zealand's Health and Safety at Work Act.
6.2.4	Synergists, safeners and other critical excipients		Clarification and definition of critical excipients	What exactly is a critical excipient? Each formulation type is designed to perform in different situations (SC, EC, WG, etc). Are there any co-formulant type/function that ACVM considers "critical"?
Point 6.2.5 (1)	*states that "If the excipient is a mixture, its full formulation information, including chemical names, CAS numbers, and percentage of each component in the mixture should be provided. The individual components of the mixture can be listed in the data volume or supplied*		Addition of an additional option. In some cases, safety data sheets (SDS) may be submitted in lieu of the manufacturer's CoA".	We believe ACVM's requirement to provide details of every component is unreasonable and does not significantly contribute to the risk assessment process. The Safety Data Sheets (SDS) already disclose all relevant hazardous components, which should be sufficient for conducting a thorough and accurate assessment.

	separately and 'mixture' stated in the formulation table instead of a CAS number."			The APVMA guideline states that "in some cases, safety data sheets (SDS) may be submitted in lieu of the manufacturer's CoA". It is acknowledged that further compositional information may be required for excipients where the SDS does not contain sufficient detail however this should not be the default. It is true that some substances at extremely low concentrations may drive the overall toxicological and/or ecotoxicological hazards of a formulation, however, these risk areas are managed within the HSNO Act and are accounted for by: • Toxicological and ecotoxicological studies conducted with the actual formulation (i.e. including all impurities present). • Any other tox and ecotoxic hazard class, such as carcinogenicity, developmental toxicity, neurotoxicity, etc., for which there is no study with the formulated product is always evaluated based on mixture rules. This can be done based on hazards identified on ingredients' SDS documents and does not even require their components to be explicitly identified, just the hazards. We would ask ACVM to reconsider its stance on this matter and believe that aligning more closely with the practices of the APVMA would streamline the regulatory process.
6.2.6	*An alternative formulation can be registered if the proposed differences between formulations do not alter the following properties of the registered trade name product:* *a) identity and concentration(s) of the active ingredient(s)*		We would advise to add a fourth criteria for alternative formulation under the same Trade name: d) The hazardous classification and controls must be identical for both alternative formulations.	

	b) formulation type *c) physical and chemical characteristics of the formulated product to the extent that the risk profile under the ACVM Act changes.*			
6.2.7 (d)	*Product specifications should include:* *d) EPA may apply specifications to the formulated product under S77A of the HSNO Act, these are required to be part of the formulated product specifications*			EPA specifications (as mentioned) can be challenging to meet as they are not transparent and are often linked to the common impurities of multiple actives in the product. ACVM should allow these to be addressed by other means. For example, analysing these for each active and ensuring that the overall limit is not exceeded
6.2.7 [e]	***Specification for co-formulants***		Clarification required for co-formulations	It is not clear as to what is required here. Is ACVM proposing to set specifications for synergists, safeners and critical excipients? The specifications are set for the product, which may contain synergists, safeners and what ACVM calls 'critical' excipients. It is unclear as to how specifications would be set for a co-formulant.
6.2.7	***Product Specifications***			In principle, this is no different from what ACVM currently calls release specifications. During the formulation development stage, adherence to FAO requirements is crucial, involving comprehensive testing at multiple stages. Once the manufacturing process is well-established, ACVM could consider accepting a limited number of routine tests for commonly used liquid formulations such as OD, CS, EC, EW, SC SE, SL. These routine tests, including appearance, active content, specific gravity, and pH, could be deemed as a practical and blanket quality control requirement for these formulation types.

				Further, for well-established manufacturing plants and processes, if appearance, active content, specific gravity, and pH fall within allowable limits, it can be inferred that other parameters are also within the acceptable range. This pragmatic perspective aims to simplify the application process, alleviating the need for each applicant to argue for exemptions or substitutions in the testing regimen for every formulation.
6.2.8 (1)	***QC specifications***		***(6.2.8 (1) QC specifications*** Suggest ACVM to delete section 6.2.8 (1) in full as 6.2.7 covers product specification	
	Additional Guidance			Instead of adding complexity and uncertainty to the assessment process, ACVM could align with FAO specification and enforce via condition of registration (as per status quo) that product must comply with the product specification throughout shelf life. The QC management and what is tested for QC purposes should be on the registrant, as this is their obligation to ensure wider compliance with the product specifications (as per FAO). Please note the parameters prescribed under FAO guidance for the different formulation types, as well as relevant acceptable ranges, aim to ensure product remains fit for purpose throughout the products shelf life, this includes aspects related to the product phys-chem properties as well as product efficacy and residues in relevant commodities. As such, the FAO approach, and the enforcement of a condition of registration stressing that it is the registrant responsibility to ensure the product complies with FAO guidance, should suffice to ensure any risks under the ACVM Act are appropriately covered. The NZ EPA typically sets limits for impurities associated to the AI.

				Impurities associated to the AI are not managed in the scope of the formulated product, but during the formulation of the AI. The amounts of impurities associated to the AI (and that may have limits imposed by the EPA) are proportionally transferred to the product in the mixing/blending stages of the formulation. If the EPA imposes a control relevant to the formulation, these can be certainly added to the wider product specifications. It is unclear how Data Assessors would handle QC related data. ACVM has not provided clear guidance as to what exactly should be addressed and considered acceptable as part of QC. This is where FAO specs become relevant, as they provide clear compliance expectations for different formulation types. Under FAO guidance, the applicant knows what to test for, and both the Data Assessors and ACVM have a robust and predictable set of parameters to assess against
6.2.9 packaging	Packaging specifications for formulated product		The guidance currently says that if multiple packaging types might be used, that stability data should be generated for each. Overseas regulators allow packaging extrapolation to be undertaken whereby material with higher barrier properties can be used without additional testing. Requiring generation of additional data to change to superior packaging represents an unnecessary regulatory barrier in our view, and an allowance should be made here for registrants to generate data based on the “least good” packaging option they wish to allow for a given registration.	It is an improvement that new pack sizes within a range can go to market without a variation application. Ideally, ACVM should completely scrap the requirement for declaration of packaging types and instead use condition of registration saying that it is the registrant’s responsibility to ensure the package is fit for purpose and will ensure the product will comply with the product specifications throughout its shelf life. Under transport regulations, the package must match minimum certifications requirements for the transport of products managed under the scope of the ACVM Act (e.g. UN requirement). These transport requirements, in addition to the relevant/compliant storage stability study, are sufficient to ensure that the packaging is appropriate.

				The shape/colour/cap specification of the product packaging is not required. The only descriptor that should be captured is the packaging type (additional packaging info should be captured in the product declaration statement)
6.2.10 Product specs vs QC	*Provide a minimum of one batch analysis to confirm compliance with Product specifications (and any additional QC specifications, not included in Product specifications) from a production scale batch no more than 3 years old (at time of submission). For each additional site of manufacture a batch analysis meeting QC specification may be sufficient."*		**Proposed wording** "For new products that have not been commercialised, results from a minimum of one batch of the product (laboratory, pilot, or production scale) should be provided to demonstrate that the product is formulated within product specifications. For products that are already commercialised, in addition to the requirements above, provide a minimum of one batch analysis to confirm compliance with QC specifications from a production scale batch no more than 5 years old (at time of submission)."	Product specifications relate to the product and the management of risks related to the use/handling of the product. Regardless of where the product is produced, it is expected to comply with the (FAO) product specifications. QC use parameters implemented at the manufacturing site to check consistency in the manufacturing process. Product specifications are intended to show the properties of a formulation when made to the nominal composition and are not intended to be representative of a particular manufacturing site so should not be restricted to 3 years. As mentioned in the previous point, the product chemistry studies are completed prior to launch, therefore adding a restriction to the age of the batch would create a further barrier to bringing products developed more than 3 years ago to New Zealand as it would be difficult to justify repeating the chemistry studies. The age restriction for batch data could only apply to QC testing of commercial batches. We do not agree that a commercial batch should be required for determining the product specifications or that testing of QC parameters (where different to product specifications) be included in the initial registration as these two specifications serve different purposes. In addition, many companies do not, as a rule provide commercial batches where the product is not approved/registered. It is not clear if the commercial batch requirement I required where there is a change in the excipient.

6.3.3 -	***Manufacturing process*** *"(6) The typical batch size should be supplied as part of the original registration or variation information to support the batch analysis data to confirm a production scale batch."*		**Additional wording.** **Any changes to the typical batch size should be communicated to ACVM.**	Whether the typical batch size is 5,000 or 50,000 litres does not significantly impact the risk assessment or the regulatory process. The batch size does not alter the composition, quality, or safety of the product. Therefore, the constant updating of this information creates an administrative burden without providing substantial benefits. We suggest that the typical batch size could be provided during the initial submission and any significant changes to the batch size could be communicated as needed. This approach would streamline the process while still providing relevant information for the initial risk assessment.
6.4.1 (8)	*All Product specifications (FAO) (and any additional QC specifications, not included in Product specifications) should be tested before and after storage. Full details of the analytical methods used for each of the parameters should be provided. If different methods are used to those used for Product/QC specifications, validation should be provided (see 6.1.10)."*		**Proposed wording:** *All Product specifications (FAO) ~~(and any additional QC specifications, not included in Product specifications)~~ should be tested before and after storage. Full details of the analytical methods used for each of the parameters should be provided. If different methods are used to those used for Product~~/QC~~ specifications, validation should be provided (see 6.1.10)."*	As mentioned in previous points, commercial scale batches are typically not available and quality specifications are often yet to be defined at the time the product chemistry studies are conducted. The current wording of the guidelines assumes that the product has already been registered in other countries and is being manufactured commercially before registering the product in New Zealand, which may not be the case. Re-running these studies on commercial scale batches specifically for New Zealand would be difficult to justify.
6.4.1 ***(9)***	*The batch tested should be a production batch or a at least 5 L / 5 kg size batch of the same composition and otherwise representative of a production batch in terms of process (i.e., a laboratory or pilot scale batch which simulates equipment, procedures and controls). A technical argument*		**Proposed wording:** *The batch tested should be ~~a production batch or a~~ at least 5 L / 5 kg size batch of the same composition and otherwise representative of a production batch in terms of process (i.e., a laboratory or pilot scale batch which simulates equipment, procedures, and controls). ~~A technical argument discussing the similarity of the equipment, procedures and controls is expected if a production batch is not used.~~*	

	discussing the similarity of the equipment, procedures and controls is expected if a production batch is not used.			
6.4.1 (5)	*"(5) Stability studies should be conducted on the trade name product in the marketed packaging in the smallest proposed marketed pack size. Smaller packaging of the same construction and material than that proposed to be sold may be used."* ***"Additional Guidance** If very large pack sizes are proposed, address the potential for instability in these through data or justification e.g., phase separation/sedimentation."*		**Clarification of pack sizes sought**	It is not clear what the definition of 'very large pack sizes' is. To clarify, does this refers to 100 gram and larger or one kg pack sizes.
6.5.1(2)	Validation data *A method validation, method transfer or partial revalidation, should be provided from each site*.		If the method is implemented, as per method protocol, the method is valid.	The current approach suggests the manufacturing site is validated, not the method. The method validation is designed to validate the method, regardless of where the method is implemented.
6.5.4 (g)	*"The LOQ of an analytical method is the lowest amount of an analyte that can be quantitatively determined with defined precision under the stated experimental conditions. LOQ may be determined by measuring a reference standard solution that was estimated during a preliminary study. The solution is normally injected and analysed with between 6 and 10 replicates. You*		Proposed rewording: "The average response and the standard deviation (SD) of the n results should be calculated and the SD should be less than 20%. If the SD exceeds 20%, a new standard solution of higher concentration should be prepared, and the above procedure repeated". The LOQ can also be defined as the lowest analyte concentration that can be quantitatively detected with a stated accuracy and precision provision should also be made that if acceptable precision and accuracy can be shown then this can be accepted.	This appears to have been taken directly from the APVMA guidelines however it does not include the full details. In alignment with the APVMA guidelines this should be expanded, as per the proposed wording.

	should calculate the average response (X) and the standard deviation (SD). The LOQ is X + (10 × SD).”			
6.3.3	Flow chart			Specific details such as rpm and time requirements are proprietary information belonging to the applicant. We are willing to share essential process information and controls, but we believe that disclosing these minute details is not necessary.
6.4.1	Stability study		Clarification is required as to the storage stability studies required	In the case of alternative ingredients being suggested, is a storage stability study necessary for every combination of proposed alternatives? If that is the case, it would entail additional work, demanding more resources. The use of different alternative ingredients has not demonstrated any discernible impact on storage stability
6.4.1	Additional Guidance If multiple packaging types are proposed, data should be generated for each.		When referring to different packaging types, it is presumed that ACVM is specifying variations in packaging materials, rather than differences in shape or size.	Clarification is sought regarding the deemed equivalent or more superior packaging, to avoid necessitating a new storage stability study
6.4.3	If the active content differs by >5% of the initial reading, or there is a change of concern in any parameter, a real time study may be required with testing at regular intervals (typically at least 6-monthly). A suitable fixed temporary shelf-life or expiry date may also be imposed and/or other controls or expectations which will		**Additional wording** Alternatively, to a real time study, a kinetics rate study of the degradation process along with the identification of degradants may be provided.	The proposal would necessitate a current two-year registration waiting period. An additional option (adopting the EU approach of differing by >5%), could involve presenting a kinetics rate study of the degradation process along with the identification of degradants instead. This may streamline and expedite the registration process.
6.5.1	*a) Selectivity or specificity* *Specificity/selectivity of a method is the extent to which*		*Proposed wording:* *The selectivity of the analytical method must be demonstrated by providing data to show the absence of interference peaks with regard to degradation*	The proposed selectivity of chromatographic methods seems to only allow peak homogeneity / peak purity test rather than the option to provide data to show absence of interfering peaks via an

	the method can determine analyte(s) in a mixture without interference from other components in the mixture.		*products, synthetic impurities, and the matrix (excipients present in the formulated product at their expected levels*	interference screen. We would advise to include the APVMA statement in the ACVM guidelines (noted in the proposed wording).
	e) Accuracy (recovery) Report as percent recovery of known amount of analyte added or as the difference between the mean and the accepted true value together with the			ACVM proposed requirement for 9 recovery preparations with 3 replicates at 3 concentrations seems excessive and difficult to do in practice. This exceeds SANCO (minimum 2) and APVMA (minimum 3). We would suggest amending this to be in line with SANCO or APVMA guidelines.
(7)	For chromatographic methods, the validation report should include all raw data used to generate the final results (i.e., peak areas) and some example chromatograms (including solvent blank, matrix blank if used for specificity, standard and sample). Chromatograms showing separation of impurities should be provided.		**Proposed wording change in red.** For chromatographic methods, the validation report should include a summation of raw data used to generate the final results (i.e., peak areas) and some example chromatograms (including solvent blank, matrix blank if used for specificity, standard and sample) may be requested. Chromatograms showing separation of impurities should be provided.	The proposed requirement mandates the inclusion of all raw data, including areas used in result generation, and sample chromatograms. While we understand the importance of ensuring the validity of conclusions, the addition of tables containing raw data is a time-consuming task. Could we propose a revision to the statement, suggesting that it be modified to read "a request for raw data may be made"? This would allow a registrant to provide spreadsheets in response to specific requests, potentially streamlining the reporting process.
7.0 (5)	Data assessments are required. ***(7.0) (5)*** says some variations may require a data DAR.		Clarification sought	With so many spaces for interpretation under this proposal, the Data Assessor would likely not to know what to say regarding the variation without guidance as to which cases would trigger a data reassessment.
7.1	**Changes to approved formulation details** *(1) a) Technical rationale for the change*		*(1) a) Technical rationale for the change if applicable*	Changes to the formulation details are usually related to supply chain (i.e. new raw material source) which does not require a technical rationale.
7.4.1 -	**Adding or replacing a formulated product manufacturer** *"(1) b) Declaration or Information to demonstrate*		Proposed change: c~~) Product and QC specifications"~~	Requirement (c) for product and QC specifications is already covered in point (b). Therefore, it is proposed to remove this point.

	the proposed manufacturing site(s) will manufacture the product equivalent to that currently approved. i.e., the raw ingredients, formulation composition, manufacturing process (6.3.3), quality control, specifications, and packaging. *c) Product and QC specifications"*			
7.4.5 -	**Change in name of formulated product manufacturer(s)** *"(2) In addition to the information outlined in 7(6) provide".*		*Proposal to delete the following.* *"(2) ~~In addition to the information outlined in 7(6)~~ provide".*	Changes to formulated product specification or test methods are not included with a name change. Therefore, there is no need to meet 7(6) requirements.
7.7.1	**Change in composition of primary packaging.** *"(1) b) Technical rationale explaining the reason for the change(s) and the expected impact(s) the change(s) will have on the product properties including the quality and stability profile of the product (e.g., photosensitivity, temperature, oxygen or moisture sensitivity, and any other relevant parameters)."*		***Proposed wording*** *1) b) Technical rationale (if applicable) explaining the reason for the change(s) and the expected impact(s) the change(s) will have on the product properties including the quality and stability profile of the product (e.g., photosensitivity, temperature, oxygen or moisture sensitivity, and any other relevant parameters)."* 2) Changes to the packaging details are usually related to supply chain and do not have a technical rationale.	We commend ACVM for including the option for self-assessable changes for packaging. For clarification we suggest that a separate section entitled "Self-assessable changes" is added to the guidance document and ask that ACVM considers other options which may meet similar criteria. We believe this would improve clarity of the types of changes and the process for managing them while also aligning practices with the APVMA guidance. It is recommended that as the proposed changes are administrative in nature, they would be managed through a C9 administrative update and included in the next PDS update. We propose that the following situations may be examples of self-assessable changes: • Change of packaging (as per point 7.7.1) • Changing the name of a site

				• Changing an address of the site when there is no change in the physical location. • Addition of sites for re-labelling or packing of a product • Addition of alternate methods to the QC or product specifications where publicly available, such as CIPAC • Addition of alternate tradenames where the CAS number of the main constituent is the same identical. • Changes to the typical batch size
7.7.2	Changes to Product packaging		Proposed to revise and remove repetition from 6.2.9	This section is repeated in section 6.2.9 and should be revised to simply reference the UN packaging system requirements. It is widely acceptable that packages of superior quality will not impact the product. A sentence could be added that should packaging be downgraded then a variation is required and outline the acceptable packaging quality hierarchy (e.g. LDPE –> HDPE). The registrant should ensure that product packaging goes upwards in quality, and therefore no action is required.
Appendix 1	CAPSULE SUSPENSION (CS) Expected Test Parameters Free (non-encapsulated) content (if required)		Clarification as to when such tests are required. Referenced in 6.2.7 (8), but there is no indication if all or some of the tests are required for that formulation or a combination of the formulation.	Could ACVM provide additional details on when these tests are required, if necessary? Could you please clarify the conditions specified for this test?
	Appropriate validated method Release rate of active ingredient (if required)			
	CAPSULE SUSPENSION (CS) Expected Test Parameters Freeze/thaw stability			

5. About Animal and Plant Health NZ

We are the peak industry association representing more than 85 multinational and New Zealand based companies that manufacture, distribute, and sell crop protection and animal health products that keep our animals healthy and crops thriving. Our mission is to protect and enhance the health of crops, animals, and the environment, through innovation and the responsible use of quality products and services.

Our objectives are to:

- Strive for effective and sustainable animal health and crop protection technology through industry leadership and advocacy.
- Achieve a balanced and science-based regulatory environment that gives members freedom to operate and grow in New Zealand.
- Enable farmers and growers to supply high quality food and fibre into domestic and global markets.
- Create an environment that encourages competition through innovation.
- Promote stewardship and responsible use of products.
- Support the health and wellbeing of pets, livestock, and people.