New Zealand Food Safety
Ministry for Primary Industries
Manatū Ahu Matua

ACVM February Workshop

Wednesday 20 February, 9.00am - 4.00pm

Jet Park Hotel & Conference Centre

63 Westney Road, Mangere, Auckland

(Please note there may be some minor changes to the agenda on the day)

AGENDA

8.30am - 9.00am	**Tea and coffee available**	
9.00am - 9.10am	**ACVM Welcome and Opening**	
9.10am – 9.30am 9.30am – 9.40am 9.40am – 10.00am 10:00am – 10.15am	**ACVM Updates** 1. ACVM Manager update (staff, work programme, performance measures) 2. Approvals Operations update 3. General updates (joint reviews, AMR, data protection, exemption regulations) 4. Reassessments	
10.15am - 10.45am	**Morning tea**	
10.45am – 11.00am 11.00am – 11.30pm 11.30am – 12.00pm	**5. Cost Recovery** Cost recovery update **6. Manufacturing** Brexit update ACVM expectations of Registrants regarding manufacturers Manufacturer descriptors in PDS **7. Common problems with applications** Deficiencies commonly seen Q&As	
12.00pm - 1.15pm	**Lunch**	
1.15pm – 2.45pm	**Environmental Protection Authority** 8. Application processing/timeframes 9. Reassessment programme 10. Q & A session	
2.45pm – 3.15pm	**Afternoon Tea**	
3:15pm - 4:00pm	**Break-out session** **1. Veterinary medicines** ▪ Vet Med Chemistry & Manufacturing guideline ▪ Equivalence guideline ▪ Q & As	**Break-out session** **2. Agricultural chemicals** ▪ NZ Wine growers application rates ▪ Review of old actives (herbicides) for Animal Transfer ▪ Efficacy requirements ▪ Labelling of ag chems ▪ Q & As

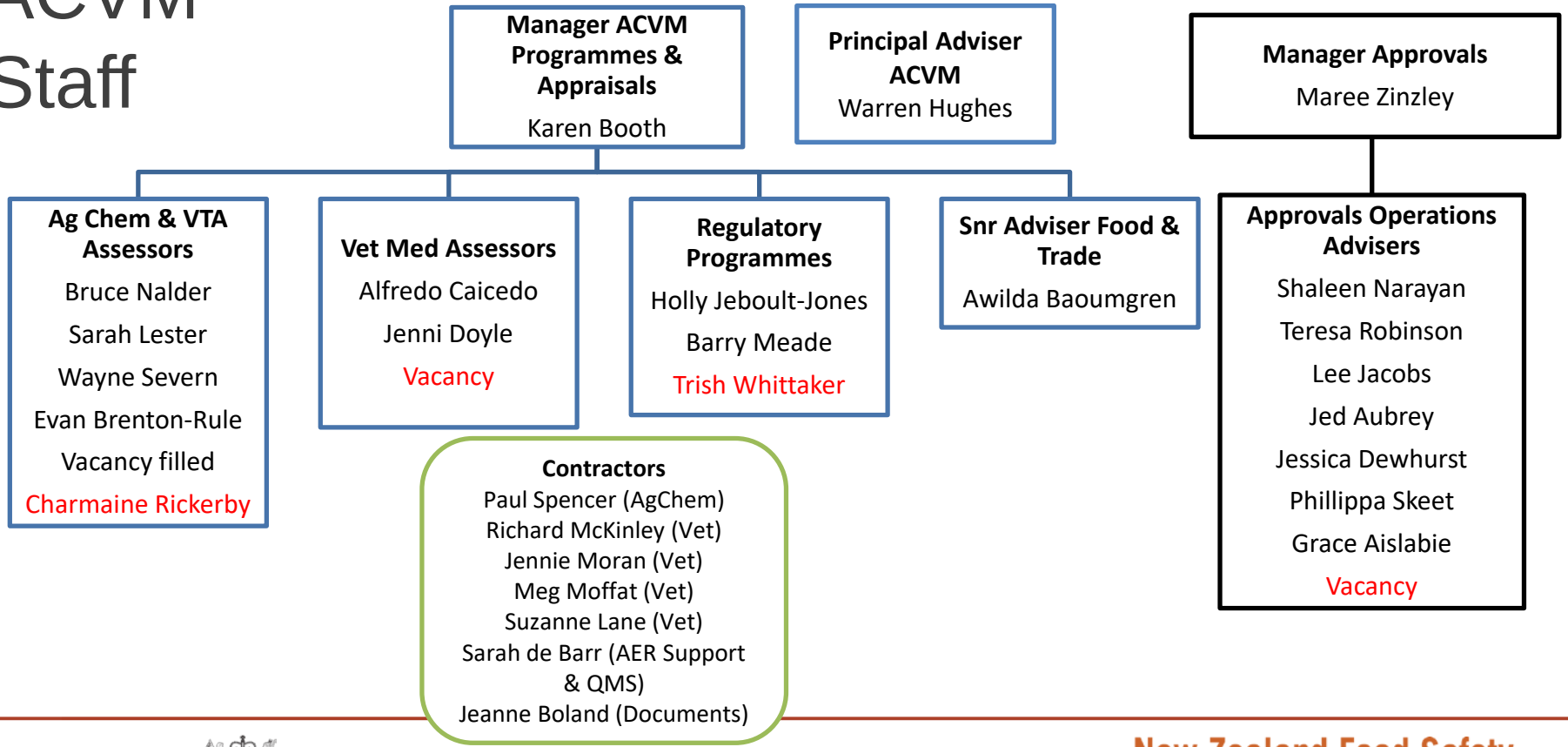
4.00pm	**Close**

New Zealand Food Safety
Haumaru Kai Aotearoa

ACVM Group Update

ACVM Workshop
20 February 2019
Karen Booth

ACVM Staff


Manager ACVM Programmes & Appraisals
Karen Booth
Principal Adviser ACVM
Warren Hughes
Manager Approvals
Maree Zinzley
Ag Chem & VTA Assessors
Bruce Nalder
Sarah Lester
Wayne Severn
Evan Brenton-Rule
Vacancy filled
Charmaine Rickerby
Vet Med Assessors
Alfredo Caicedo
Jenni Doyle
Vacancy
Regulatory Programmes
Holly Jeboult-Jones
Barry Meade
Trish Whittaker
Snr Adviser Food & Trade
Awilda Baoumgren
Approvals Operations Advisers
Shaleen Narayan
Teresa Robinson
Lee Jacobs
Jed Aubrey
Jessica Dewhurst
Phillippa Skeet
Grace Aislabie
Vacancy
Contractors
Paul Spencer (AgChem)
Richard McKinley (Vet)
Jennie Moran (Vet)
Meg Moffat (Vet)
Suzanne Lane (Vet)
Sarah de Barr (AER Support & QMS)
Jeanne Boland (Documents)

2018 Achievements

1. MPI one process for ACVM and Biosecurity approval applications completed
2. RTT OPs Guideline and application forms published
3. Amitraz Reassessment completed
4. Veterinary Medicine Equivalence Guideline published July ‘18
5. Two MRL rounds completed
6. Two registrant workshops February and July
7. Two ACVM 101 workshops

2019 In Progress

- VTA review (brodifacoum)
- AMR activities
- Reassessment (see Reassessment presentation)
- Ag Chem Chemistry & Manufacturing Guideline - in draft
- Vet Med Chemistry & Manufacturing Guideline (non-biologicals) – second round of public consultation est. March/April ’19
- Business analyst working on requirements for on-line system and pharmacovigilance tool

System Audits

Proposed for 2019:

- RVM seller compliance with operating plans (compliance and information gathering)
- Manufacture and sale of fertilisers (compliance with exemption regulations and information gathering)

In progress (2018-19):

- General Oral Nutritional Compounds (focusing on pet food and Calf Milk Replacements: labelling compliance, advertising compliance, and fit for purpose).
- Current Hemp Industry Practices In Relation to Hemp as Oral Nutritional Compounds Including Animal Feed Commodities and Hemp-Based ONC Products.
- Research, Training and Testing Operating Plans. A number of RTT OP holders have been selected (both agricultural chemical and veterinary medicine), and audits have begun. The audit is intended to check fitness for purpose of RTT OPs.

ACVM in Numbers – *Registrations*

ACVM receives ~ 2,600 registration applications/year

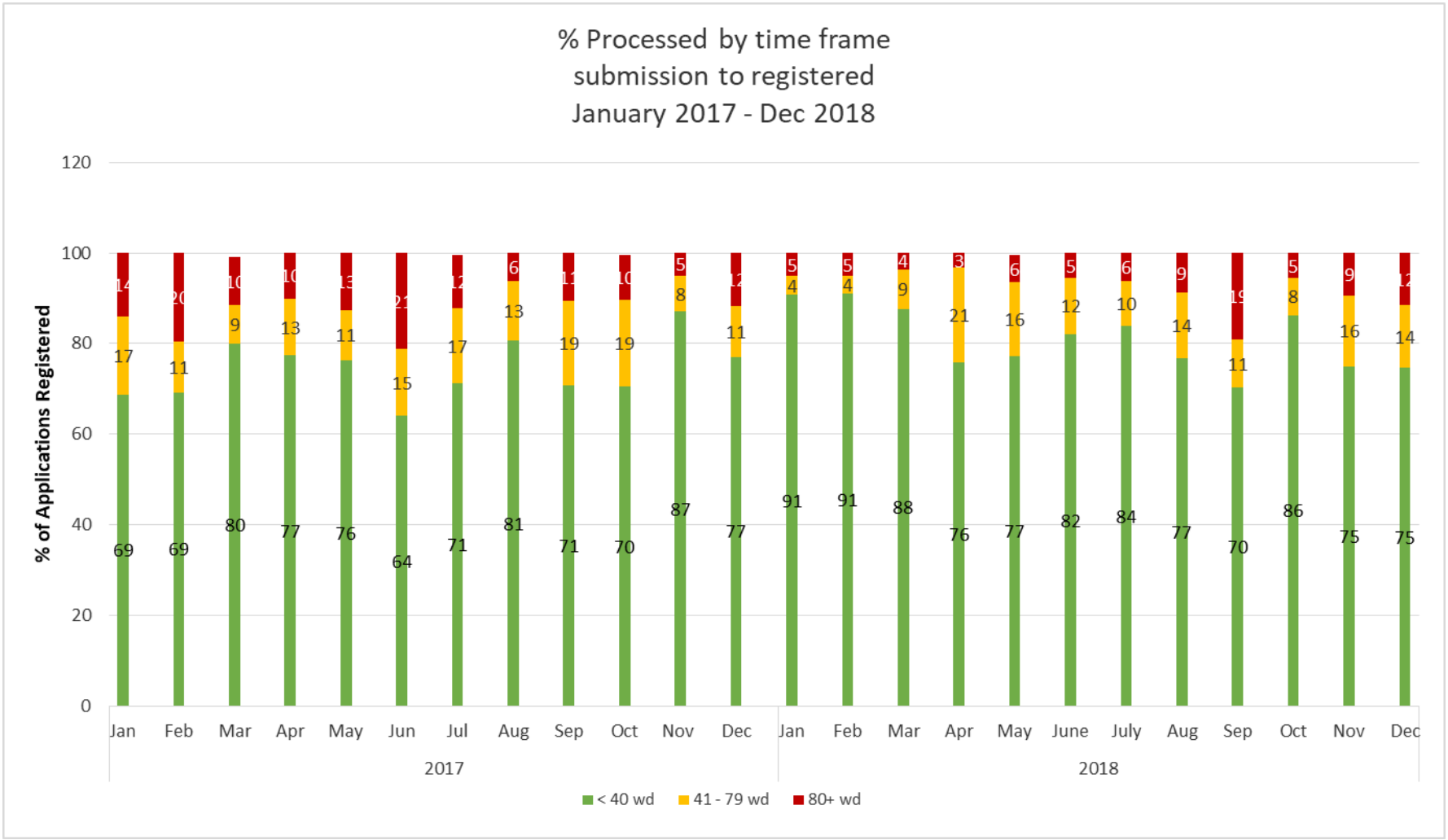
Application Type	Number (Jan – Dec 2018)
New products	167
New uses	40
Chemistry & Manufacturing changes	654
Administrative	1247
Research Approvals	26

ACVM in Numbers – *Other Authorisations*

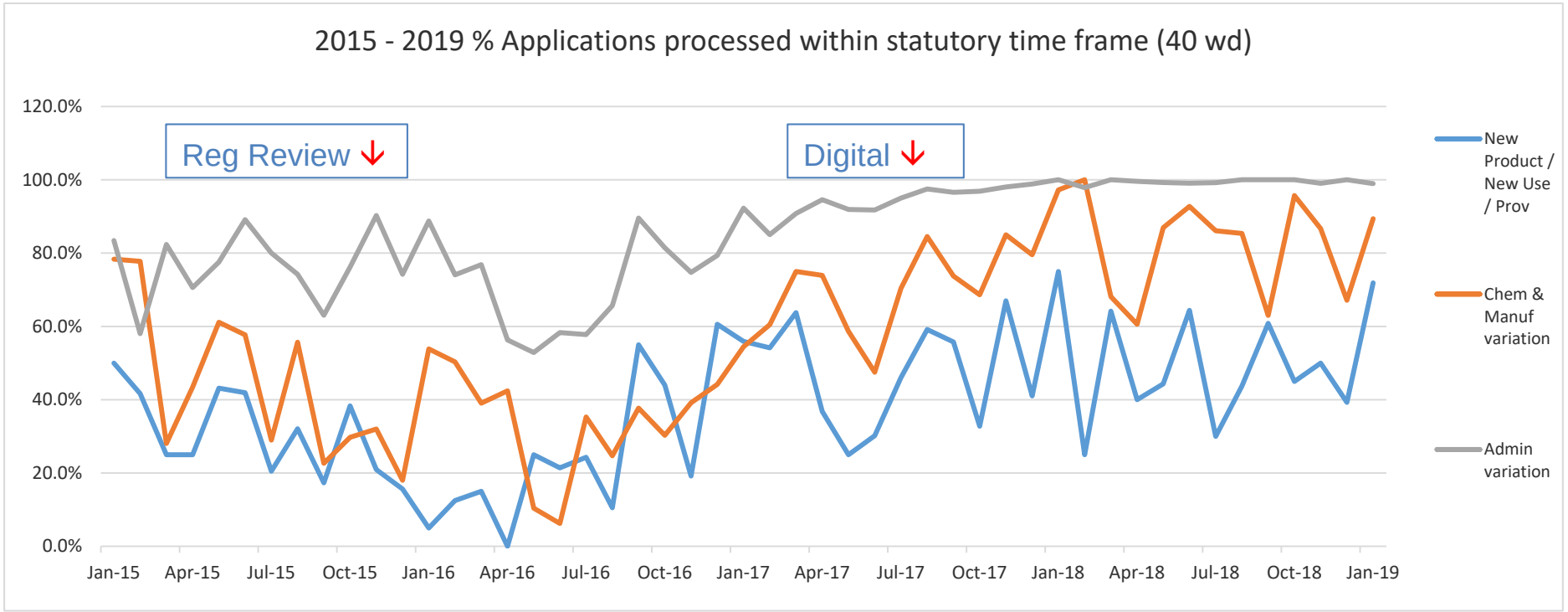
	2016	2017	2018
Special Circumstances	138	138	141
Maintenance Compounds (non-dairy)	558	789	703
GMP Audits (site days)	21 (45)	21 (50)	25 (38)
PS & RTT OPs	15	12	7
RVM Sellers OPs	5	33	18
Data Assessments	28	11	33
Deviations	40	22	21

ACVM in Numbers – *Post Authorisation*

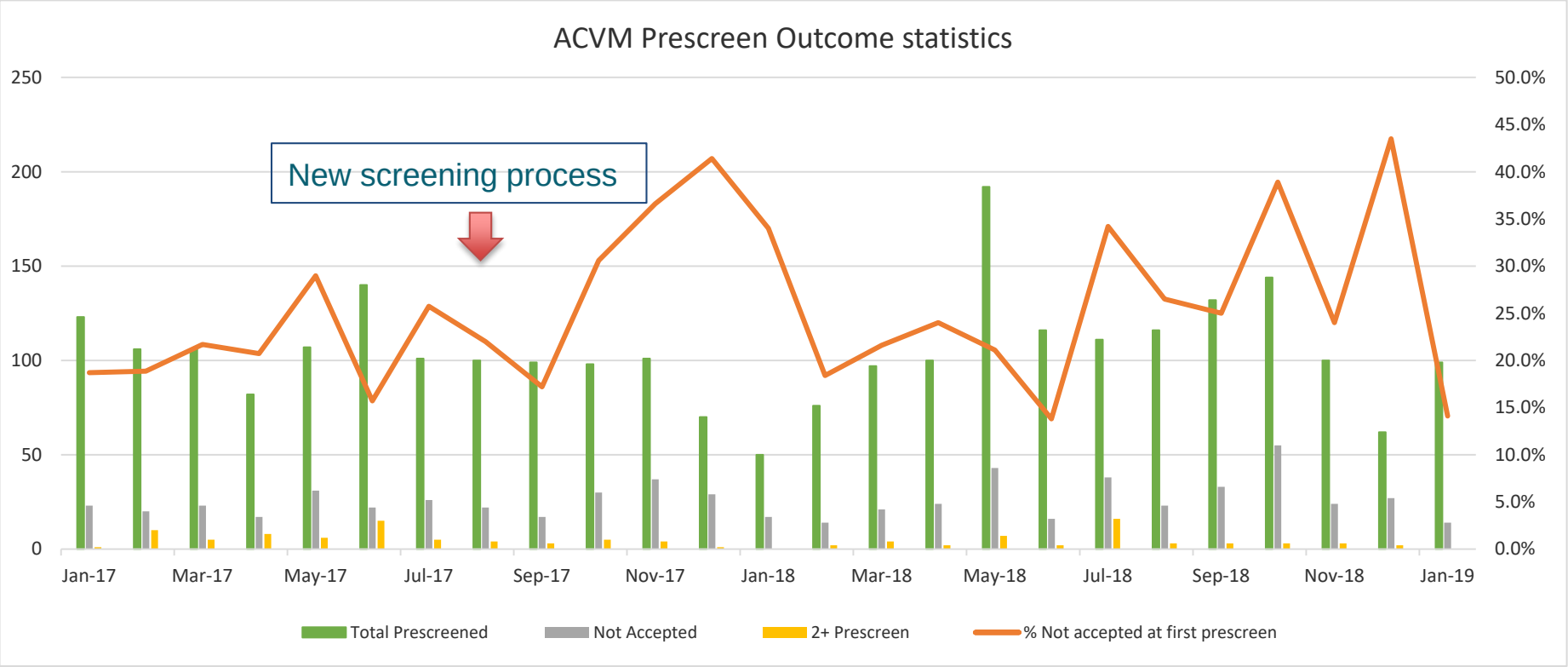
	2016	2017	2018
Compliance Matters	50	91	115
- Recalls	5	8	12
Batch Variations	20	21	43
Rapid Alerts	33	15	19
AERs	1222	1192	1362
Ministerials	43	41	45
Residue Investigations	19	17	26


% Processed by time frame
submission to registered
January 2017 - Dec 2018
% of Applications Registered
120
100
80
60
40
20
0
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec
2017
Jan Feb Mar Apr May June July Aug Sep Oct Nov Dec
2018
< 40 wd
41 - 79 wd
80+ wd

Performance for processing within 40 working days



Pre-screen statistics



How to contact ACVM

- First point of call – contact your Operations Adviser for any general application queries, meeting requests etc.

- For applications that have passed pre-screen and are in appraisal – contact the Technical Assessor

- For general queries approvals@mpi.govt.nz
- For compliance issues ACVM-recallsandcompliance@mpi.govt.nz
- For RVM Seller Ops ACVM.RVMSellers@mpi.govt.nz

- For Adverse Events ACVM-AdverseEvents@mpi.govt.nz

ACVM 101 Workshops

- Ran in October (Wellington) and November (Auckland) 2018
- Received high level of interest and good attendance
- Workshop handbook available on website
- Workshops for 2019
  - data assessors
  - ACVM 101?
  - other?

ACVM Website

ACVM Home page

MPI Home page


Thank you
Any questions?

New Zealand Food Safety

Haumaru Kai Aotearoa

Approvals Operations Update

ACVM Workshop

20 February 2019

Teresa Robinson

Ministry for Primary Industries

Manatū Ahu Matua

Agenda

Approvals Team update

Application Feedback

- Electronic submissions
- Application forms
- Confidential PDS
- Labels

Approvals Team Update

Maree Zinzley

Manager Approvals Operations

Shaleen Narayan
Senior Adviser

Works across all legislations

Adviser – Position Vacant

Jillian Edwards

Adviser

Started February 2019, ACVM Act

Phillippa Skeet
Adviser

Started January 2019, ACVM Act

Jessica Dewhurst
Adviser

Part-time, works under the ACVM Act and approvals inbox

Teresa Robinson
Adviser

ACVM Act

Jed Aubrey
Adviser

Works across ACVM Act and Animal Products Act

Lee Jacobs
Adviser

Works across ACVM Act, Animal Products Act & reporting

Grace Aislabie
Adviser (Enquires)

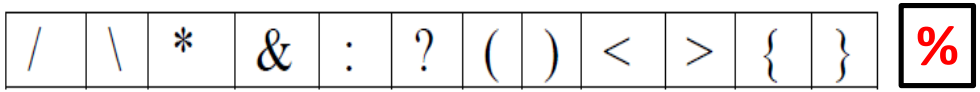
Started January 2019, approvals inbox

Application Feedback – Electronic Submissions

- Overall improvement on application submissions
- We want electronic documents – do not require documents to be printed off, signed and then scanned back to us.
- Please do not send us ‘protected’ PDF documents
  - We need to be able to electronically approve PDF documents
- ShareFile
  - Emails with attachments over 25Mb are blocked
  - Email your advisor for a sharefile link

Application Feedback – Electronic Submissions

- File names
  - Unable to upload documents with ‘special’ characters in file name:



  - Dates are always required for PDS and Label file names e.g. 20170919 P1234 PDS
  - All variation files need dates (or some individual descriptor) in file name e.g. 20190212 A1234 ACVM1V form
  - If submitting updated or amended documents, please also update file name with new date of submission or similar
  - All covered by our guideline for E-files

Application Feedback – Application forms

- Submitting a variation application, remember to:
  - Indicate ALL variation types by highlighting in bold
  - Provide ALL the relevant forms

- Variation to registration of an ACVM trade name product ACVM 1V (March 2018)

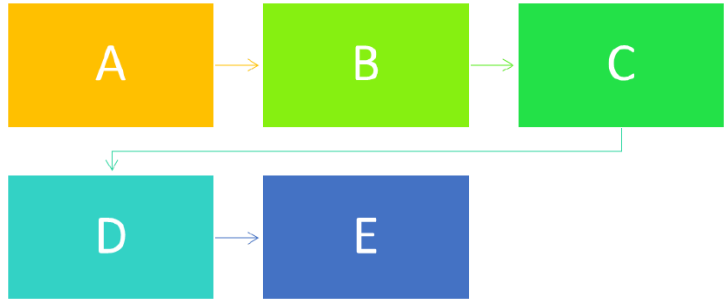
Application Feedback – Application forms

6. **Variation Application Type** (Indicate type by highlighting in BOLD.)	**Form to use**
C1 Change in formulation	ACVM 6
C2 Change in active ingredient manufacturer	ACVM 7
C2 Change in formulation manufacturer	ACVM 8
C2 Change in manufacturing process, including changes in AI or formulated product specifications	ACVM 9
C3 Change in packaging	ACVM 10
C3 Change in shelf life	ACVM 11
C4 Extension of use to include additional target host or species C5 Extension of use to include control of additional pests, weeds, species, diseases or conditions	ACVM 12
C6 Change in dose regime or application rate or timing C7 Change in method of administration/application	ACVM 13
C8 Change in withholding period	ACVM 14
C9 Administrative change, such as phone number, postal/email address.	Provide details in section 7 below. No additional form required.

Application Feedback - PDS

- Manufacturing process
  - Either in Section B5 of PDS
  - Or last page of the PDS
  - **not** as a separate document.

B5 Manufacturing Process	
State typical batch size or range	5,000L
Provide a flowchart (either within this box or as an electronic attachment to this document) representative of the manufacturing process from beginning of the process until release.	



Application Feedback - PDS

- Submission of Confidential PDS
  - Registrants responsibility to organise third party to send confidential part of the PDS especially if the products due to expire
  - Registrant completes Part A and Part C (date and sign)
  - Third party (or third parties) completes Part C
  - Mark PDS as confidential and say who the confidential information belongs to on the PDS itself
  - This avoids confusion, especially where there may be more than one confidential third party involved.

Submission of Confidential PDS - Registrant

Part A: General Information

A1 Trade Name of the Agricultural Chemical See guideline for wording of trade name and list of prohibited substances.	
Trade Name	**Reg Number** (if assigned)
Herbicide B	P9999

A2 Registrant Information See guideline.		
Registrant's Full Legal Name		
Registrant		
Overseas applicants, provide Companies Act reference number		
Street/Physical Address (for service)	**Postal Address** (for communication)	
123 Lambton Quay Wellington	PO Box 123 Lambton Quay Wellington	
Contact Name	**Tel**	04 1234 123
	Mobile	021 1234567
R. Registrant	**Email**	R.registrant@company.co.nz

Read "Identification Table" on page 1 of guideline before completing this footer. (Ignore ACVM Use table.)

Herbicide B

Reg No	Trade Name	Authorised Person's Signature	Date
P9999	Herbicide B	*R. Registrant*	15/02/2109

ACVM Use	
Page 1 of 10	ACVM-AC-ETEM-05 March 2018

Part B. Product and Manufacturing Specifications--Commercially Sensitive Information

B1 Active Ingredient Manufacturer/Formulator See guideline.			
Active Ingredient	**Manufacturer's/ Formulator's Name**	**Site Address**	**Postal Address (if different)**
Refer to confidential PDS submitted by M. Manufacturer			

Part C: Statement and Notices

Applicant Statement			
I confirm that: ▪ I am authorised to make this application as the registrant OR a person with legal authority to act on behalf of the registrant noted in section A2; and ▪ the information supplied in and with this application is truthful and accurate to the best of my knowledge; and ▪ I understand that, if this product is registered, any change to the information provided in this application must go through MPI's 'variation to registration' process or I will be in breach of the product's registration conditions.			
Name	R. Registrant	**Tel**	021 1234567
Signature	*R. Registrant*	**Email**	R.registrant@company.co.nz
		Date	15/02/2109

Submission of Confidential PDS – Third party

Part A: General Information

A1 Trade Name of the Agricultural Chemical See guideline for wording of trade name and list of prohibited substances.	
Trade Name	**Reg Number** (if assigned)
Herbicide B	P9999

A2 Registrant Information See guideline.		
Registrant's Full Legal Name		
Registrant		
Overseas applicants, provide Companies Act reference number		
Street/Physical Address (for service)	**Postal Address** (for communication)	
123 Lambton Quay Wellington	PO Box 123 Lambton Quay Wellington	
Contact Name	**Tel**	04 1234 123
	Mobile	021 1234567
R. Registrant	**Email**	R.registrant@company.co.nz

Commercially sensitive to M. Manufacturer

Part B. Product and Manufacturing Specifications--
Commercially Sensitive Information

B1 Active Ingredient Manufacturer/Formulator See guideline.			
Active Ingredient	**Manufacturer's/ Formulator's Name**	**Site Address**	**Postal Address (if different)**
Ingredient A	A Manufacturing Ltd	123 Lambton Quay, Wellington, New Zealand	Same as site address
Ingredient B	B Manufacturing Ltd	456 Queen Street, Auckland, New Zealand	Same as site address

Submission of Confidential PDS – Third party

Herbicide B

Reg No	Trade Name	Authorised Person's Signature	Date
P9999	Herbicide B	*M. Manufacturer*	15/02/2109

ACVM Use	
Page 3 of 10	ACVM-AC-ETEM-05 March 2018

Part C: Statement and Notices

Applicant Statement

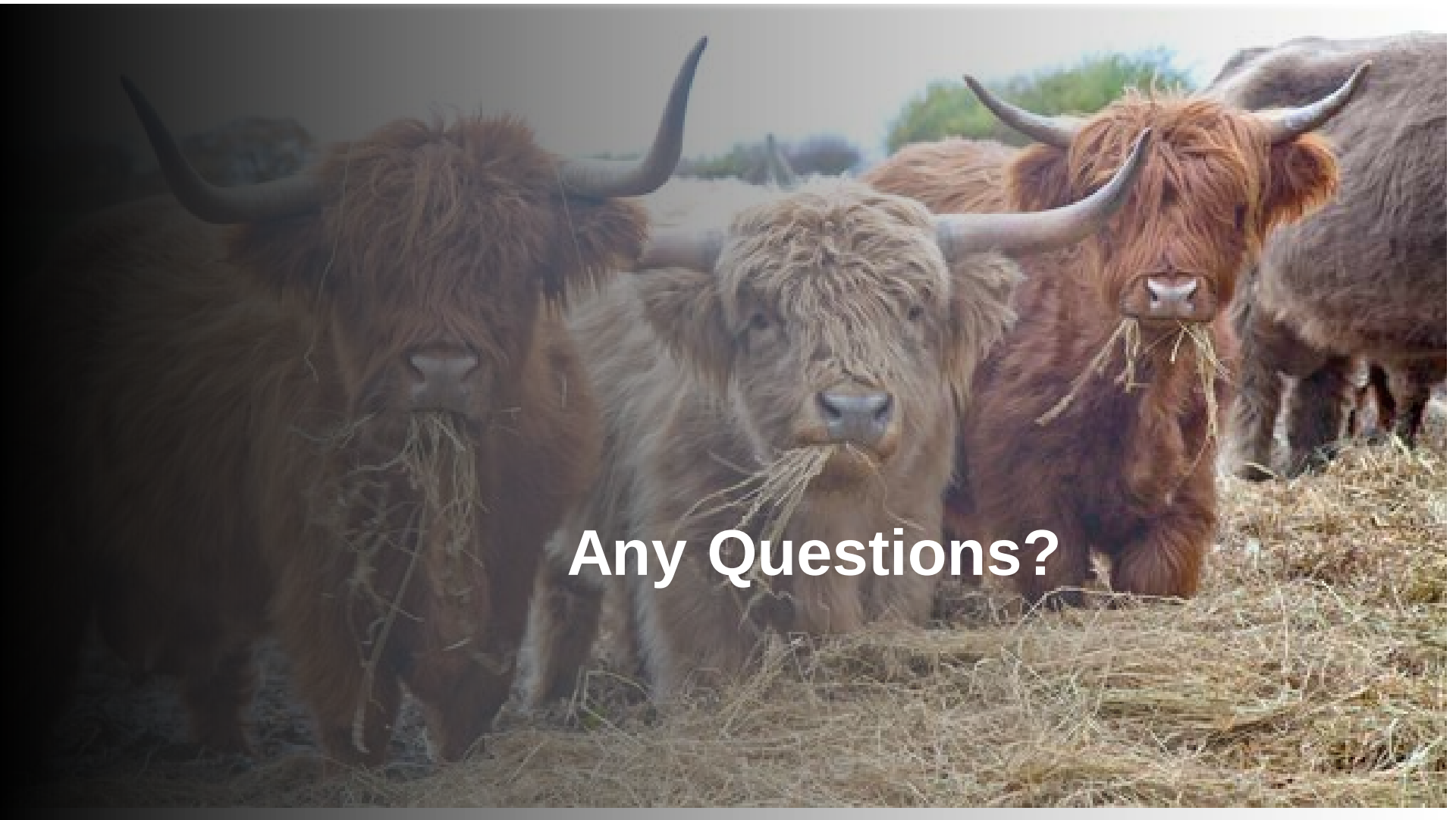
I confirm that:

- I am authorised to make this application as the registrant OR a person with legal authority to act on behalf of the registrant noted in section A2; and
- the information supplied in and with this application is truthful and accurate to the best of my knowledge; and
- I understand that, if this product is registered, any change to the information provided in this application must go through MPI's 'variation to registration' process or I will be in breach of the product's registration conditions.

Name	M. Manufacturer	**Tel**	021 1234567
Signature	*M. Manufacturer*	**Email**	M.Manufacturer@company.com
		Date	15/02/2109

Application Feedback - Labels

- We require the product label for **every** variation application and renewal application
- If label has no changes
  - State this on ACVM 1V form and include the last approved label WITHOUT MPI's stamp
- If label has changes
  - State this on ACVM 1V form and include a clean label AND full tracked changes label
  - Should be clear what has been moved, deleted or an addition


Any Questions?

New Zealand Food Safety
Haumaru Kai Aotearoa

Updates – Policy Matters

ACVM Workshop
20 February 2019
Warren Hughes

Ministry for Primary Industries
Manatū Ahu Matua

Joint Reviews

- In 2015 ACVM participated with Australia and Canada on a joint review for a veterinary medicine
    - ➢ 2016 approval issued
- A few registrants have since expressed interest in joint reviews
- ACVM encourages registrants to consider joint reviews, benefits included:
    - Reduced regulatory effort (time and costs)
    - Better understanding of other regulatory systems
    - Ability to harmonise end points including MRLs

Joint Reviews

- To encourage joint reviews, it is recognised we need to:
  - Better publicise the system
  - Produce guidance material on requirements
- Registrants need to play their part by thinking about opportunities for new products

Antimicrobial Resistance (AMR) Update

- A review of year 1 activities from the NZ Action Plan on AMR on our website
  - The follow up to the 2009 survey on bacteria sensitivity to antibiotics in animals is underway
  - Prudent use directive published
  - Reassessment of antimicrobials has commenced
  - Reviewing advertising of antibiotics
- The 2014-2016 Antibiotic Sales report was published in November 2018

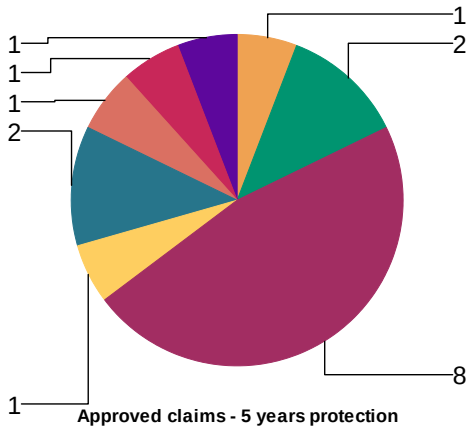
Confidential Information Protection

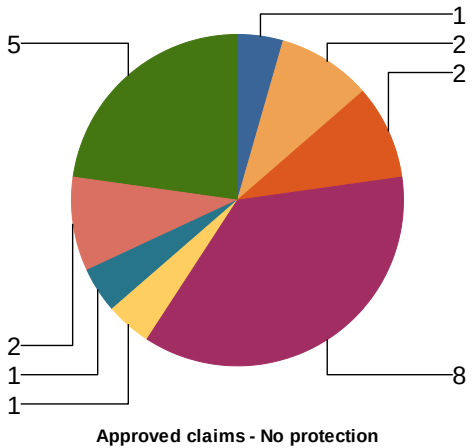
- The amendment to the Act is slightly over 2 years old
- What has been the impact?
- A light analysis in relation to C4 applications (additional target crop/species) was undertaken
    - ➢ Limited to C4 applications due to limitations in our database

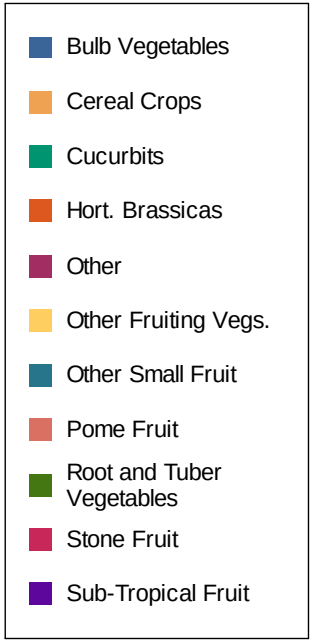
Confidential Information Protection

Registered Agricultural Chemicals

For C4 - Target host

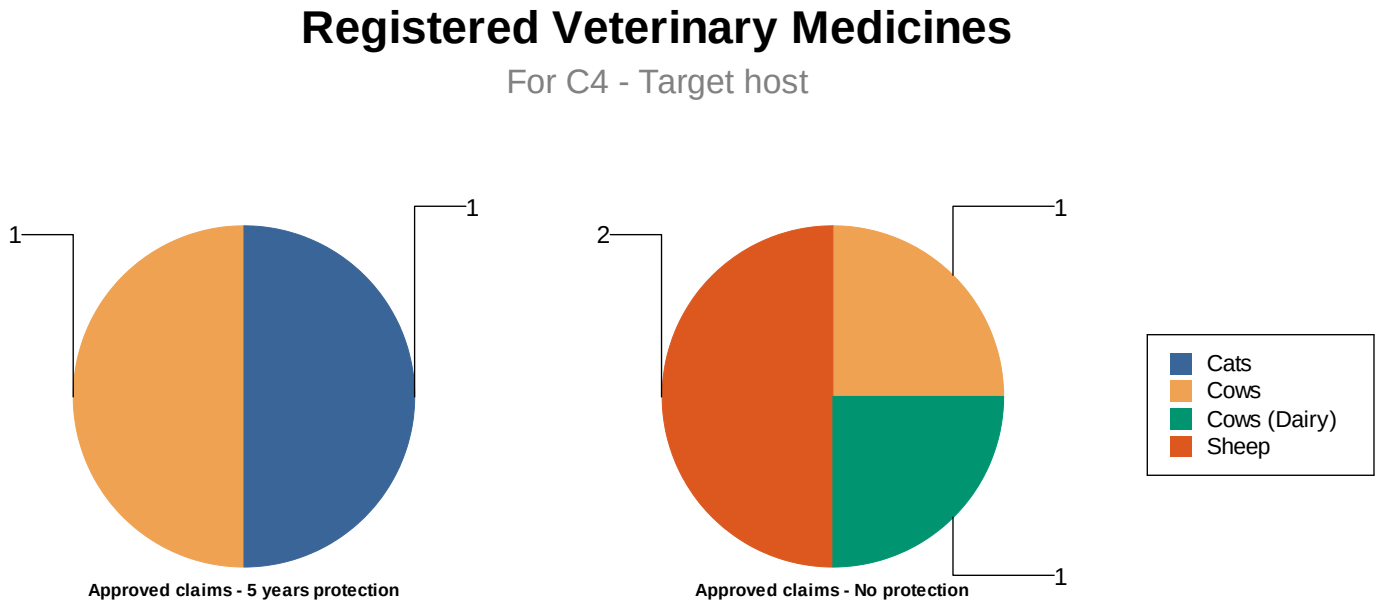






From 6 November 2016

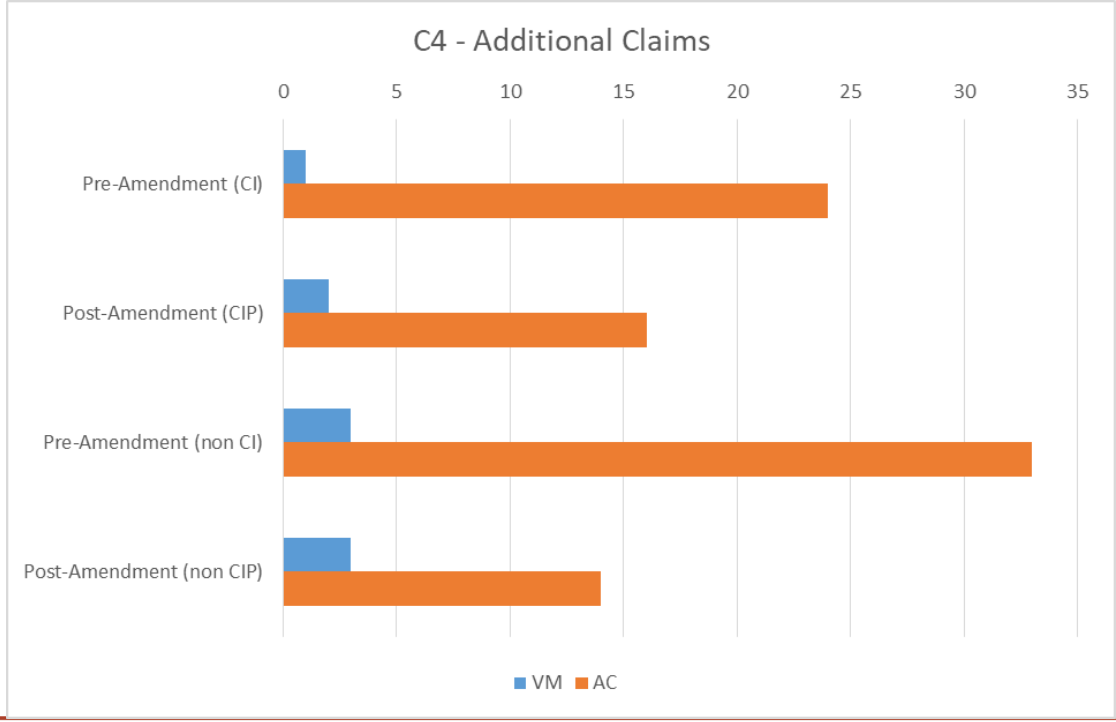
Confidential Information Protection



From 6 November 2016

Confidential Information Protection

C4 Additional claims approved 2 years prior to amendment to Act and 2 years post amendment to the Act



CI – Confidential Information, CIP – Confidential Information Protection, VM – Veterinary Medicine, AC – Agricultural Chemicals

Amendment to the ACVM (E&PS) Regs

- The Cabinet paper seeking Cabinet approval to amend the Regulations is nearly completed

- Should Cabinet agree to amend the Regs, then Parliamentary Council Office will draft the Regulations

- Timeline for completion is likely to be in the second half of this year


Thank you!

New Zealand Food Safety
Haumaru Kai Aotearoa

Update on Reassessments Under the ACVM Act

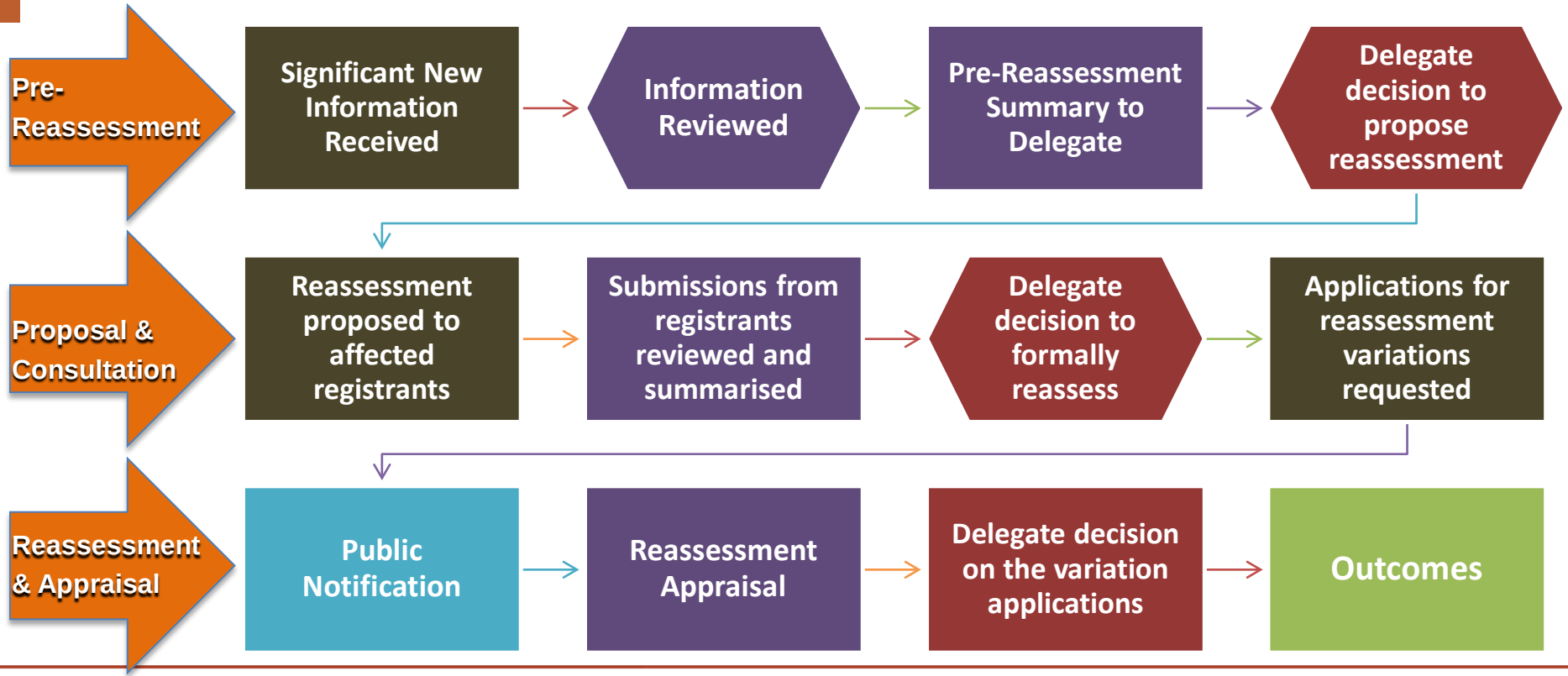
ACVM Workshop
20 February 2019
Awilda Baoumgren

Ministry for Primary Industries
Manatū Ahu Matua

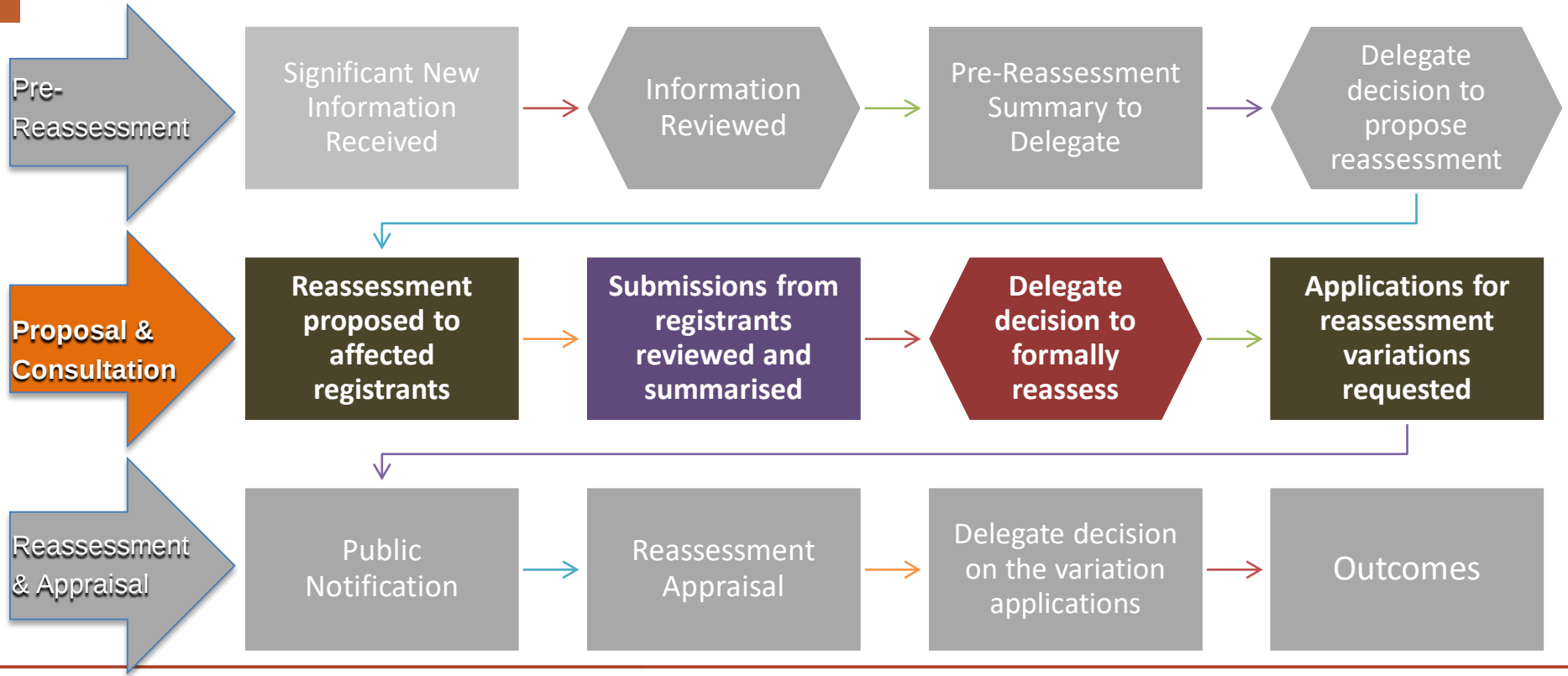
Reassessment under the ACVM Act

- Reassessment process summary
- An update on reassessments currently in progress
- Reviews and future reassessment proposals being considered

The Reassessment Process



The Reassessment Process



Reassessment Proposal

- Registrants of affected products are contacted with proposal to reassess
- Letter outlines “what,” “why,” and expected outcomes
- Request for registrant comment on the issue
    - ACVM risks from the registrant perspective
    - Other considerations associated with the issue not raised in the letter
    - Whether they support reassessment – and whether open to voluntary change if indicated

Reassessment Proposal Submissions

All submissions reviewed and summarised

- Adjustments to risk profile or issues to be managed
- Wider MPI discussion with other impacted teams – Market Access, Animal Welfare, Chemical and Microbiological Assurance, Animal Products, etc.
- Final recommendation to Delegate: Scope, interim controls, and advice as to whether the reassessment should progress

❖ Delegate decides whether to go to watching brief, request voluntary changes, or formal reassessment

Reassessment Proposal Outcomes: Watching Brief

The situation that triggered the consideration for reassessment monitored

- International status
- Domestic status (e.g. EPA, MoH)
- Trade and Market Access status
- Adverse Events in NZ and overseas

→ Proposal to reassess may later be reconsidered

Reassessment Proposal Outcomes: Voluntary Changes

New risk profile can be addressed by agreed changes

- Label information amended
- Minimal or no further consideration needed
- Registrant(s) already have information to support change

→ Registrant(s) can progress to variation with or without public notification

Reassessment Proposal Outcomes: Formal Reassessment

Variation with public notification required

- Additional data and information required to fully assess revised risk profile (historical and new information reviewed)
- Interim controls may be needed to manage risk
- Potential outcomes of the reassessment are significant or broad-reaching

→ Variation applications publicly notified and assessed as a group

Outcomes of Formal Reassessment

- Dependent on risks to be managed
    - Variation approval granted with grace period to action changes (labelling, reporting, additional information)
    - Variation approval granted with immediate changes actioned
    - Variation approval declined – could lead to suspension or de-registration
- Other outcomes to be actioned such as MRL promulgation may impact post-decision next steps (case by case)
- Additional reassessments may need to be considered for similar products

Reassessments Currently In Progress

Reassessments Currently In Progress: ACs

Pre-Harvest Use of Glyphosate in Cereal Crops

- Results from the Food Residue Surveillance Programme (FRSP) showed that the current MRL is consistently being exceeded in cereal grains, particularly wheat
- A review indicated that good agricultural practice was being followed, but label directions may need to be clarified further
- Pre-reassessment consultation concluded that all submitters agreed reassessment was appropriate.
- The decision to formally reassess has been made and registrants will be contacted in the next 3 months.

Reassessments Currently In Progress: VTAs

Brodifacoum-based Vertebrate Toxic Agents

- Recent issues and residue detections indicated that a review of the current controls on the anticoagulant VTAs was needed
- Initial review found that brodifacoum-based products needed the most immediate work, and was proposed for reassessment
- Decision was made to progress a formal reassessment due to the potential changes to product labelling and regulatory controls across all products
- Working with wider MPI to ensure all aspects of the risk profile are addressed in the scope dictating the eventual call for information and reassessment

Reassessments Currently In Progress: VMs

Antibiotic Reassessment: Penicillins, 3rd and 4th Generation Cephalosporins, Macrolides and Ketolides

- A review of all existing antibiotic registrations underway as part of the New Zealand AMR Action Plan.
- First group of active ingredients proposed for reassessment encompasses more than 110 products from 20 different registrants
- Work is now underway to review the AMR risk profile of all active ingredients in these antibiotic families to evaluate what changes will be required for affected products
- Registrants will be expected to provide variation applications by **1 July 2019** to action changes

Reassessments Currently In Progress: VMs

Decoquinate, Lasalocid, and Monensin in Ruminants

- New Zealand MRLs for these three compounds found to be significantly out of step with international MRLs in both scope (species) and value
- Pre-reassessment consultation completed, and decision has been made to reassess due to trade risks
- Currently working through data on file for all registered products and internationally available data to establish a baseline for revised MRLs
- Applications will be progressed for public notification and assessment when this work is complete

Future Reviews/Reassessment Proposals

- **Ag Chems**
    - Review of herbicide active ingredients with respect to animal transfer and animal WHPs
    - Varroaicide product realignment as treatments for food-producing animals (e.g. making them VMs not ACs)
- **VTAs**
    - Wider anticoagulant VTA review and reassessment following brodifacoum reassessment
    - Other VTA reviews/reassessments as indicated

Future Reviews/Reassessment Proposals

- **Vet Meds**
    - Review of mineralised food-producing animals products, particularly iodine- and selenium-based products
    - Review and alignment of registration controls for certain product groups (teat sanitiser labelling, clostridial vaccine RVM status, altrenogest WHPs)
    - Lignocaine MRLs and WHPs: 2015 EMA review
- **ALL**
    - Reassessments stemming from other projects (MRL review; EPA reassessments)


Thank you!

New Zealand Food Safety

Haumaru Kai Aotearoa

Cost Recovery Update

ACVM Workshop

20 February 2019

Karen Booth

What has happened?

From 14 November 2018 to 16 January 2019, MPI consulted on 11 proposals for changes to cost recovery in the food system, 4 of which were related to changes in the ACVM system.

MPI sent 28,000 emails to fee payers seeking feedback on the Discussion Document and met with nine industry organisations, including AgCARM and ARPPA.

22 submissions were received - 6 relating to one or more proposals for changes in the ACVM system.

Proposals Related to ACVM

Proposal 1: **Decrease** the base hourly rate for approvals. The hourly rate is used for the TNP registration process (from $155 per hour to $135 per hour)

11 in support; 1 against (opposed as wanted charges to be decreased further)

Proposals Related to ACVM

Proposal 2: **Decrease** fees for Trade Name Product (Pre-screening and Registration of TNP)

- For pre-screening, $67.50 plus $135/hr after the first half hour (currently $540 fixed fee)
- For registration of TNP, $405 (currently $540 fixed fee)

4 in support; 0 against

Proposals Related to ACVM

Proposal 8: **Simplify** the process for amending ACVM levy rates (no financial implications)

4 in support; 0 against; 1 unclear

Proposals Related to ACVM

Proposal 9: **Clarify** ACVM levy provisions

- Who pays the levy

  3 in support; 1 against (a general comment regarding Government fees and charges)

- Part Two: What the levy funds

  4 in support, 0 against

Next Steps

Cabinet will consider policy changes in March and, if approved, draft regulations will be considered through April and May

MPI expects it will be able to confirm any changes in late May

Any changes will take effect from 1 July 2019.

Update on Industry Report

MPI is developing annual performance reporting covering all cost-recovered activities. Report content includes work programme update, financial performance, and financial and non-financial key performance indicators.

MPI will be progressively releasing these performance reports by sector, with biosecurity (passenger) clearance, red meat, dairy and fishing first.

The ACVM sector report is expected to be released towards the end of 2019.


Thank you
Any questions?

New Zealand Food Safety

Haumaru Kai Aotearoa

Ministry for Primary Industries

Agricultural Compounds and Veterinary Medicines (ACVM) Group

ACVM Workshop – February 20 2019

Agenda:

1. Brexit Update (MRA)
2. Relationship/Communication Expectations (Registrants/Manufacturers/Agents)
3. Manufacturer specific sections in PDS

JANUARY 2019 UPDATE

Bilateral agreements signed

On 21 January 2019, New Zealand and the United Kingdom signed 2 bilateral agreements:

- Sanitary Measures Applicable to Trade in Live Animals and Animal Products (the Veterinary Agreement)
- Mutual Recognition in Relation to Conformity Assessment (the Mutual Recognition Agreement),

Signing of the agreements is significant as it ensures existing trade arrangements between New Zealand and the United Kingdom (UK) will continue after the UK exits from the EU. The agreements are intended to come into effect either as soon as the UK leaves the EU (in the event of a 'no deal' Brexit) or at the conclusion of any transition period that might be agreed between the UK and the EU.

The agreements align with those currently in use between New Zealand and the European Union (EU). They recognise the high quality of New Zealand's food production standards and will provide certainty for New Zealand companies that export animal products to the UK.

The Mutual Recognition Agreement allows products to be tested, inspected and certified in New Zealand before being exported to UK and vice-versa.

For New Zealand veterinary medicine manufacturers, signing of the agreements means Good Manufacturing Practice (GMP) certificates that accompany their exports to the UK will continue to be recognised and accepted by UK authorities. No extra steps, such as additional GMP inspections, will be required.

Two Bilateral Agreements

(Signed 21 January 2019)

1. Sanitary Measures Applicable to Trade in Live Animals and Animal Products (Veterinary Agreement)

2. Mutual Recognition in Relation to Conformity Assessment (Mutual Recognition Agreement)

New Bilateral NZ/UK Agreements

- Come into effect either as soon as UK leaves the EU (No-deal) or at the conclusion of any transition period.
- The agreements align with those currently in use between NZ and the EU.
- Allows product to be tested, inspected and certified in New Zealand before being exported and vice-versa and enables GMP Certificates issued by MPI to continue to be recognised by UK authorities.

Government advice available on Brexit

MPI and MFAT are:

- monitoring the progress of Brexit.
- working to minimise any disruption to New Zealand's primary sector exporters.

Get regular Government updates on Brexit and how it could affect New Zealand:

- https://www.mfat.govt.nz/en/countries-and-regions/europe/united-kingdom/brexit-the-uk-and-europe/
- https://www.nzte.govt.nz/export-assistance/regional-resources/europe/brexit

Registrants and outsourced activities (Contracted Activities)

Outsourced Activities

Any activity related to manufacturing that is outsourced to a third party, which is covered by the GMP Guide, should be appropriately defined, agreed and controlled in order to avoid misunderstanding that could result in a product (or work) of unsatisfactory quality.

Outsourced activities can include:

- Manufacturing related activities
- Down-packing/re-packing/Assembly
- Re-labelling/Overlabelling
- Testing activities
- Label printing
- Product Sterilisation
- Release for Supply
- Autoclave Qualifications and Requalifications
- Equipment Calibrations

Responsibilities under the ACVM Act

Registrant

- **Ultimately responsible** for product compliance with approved registration details

Other parties

- Manufacturers, Distributors, Vets, Wholesalers, Retailers
- Users: storage and use; + prescribing and advertising (vets)

❖ **All have obligations** under the ACVM Act and Regulations

Responsibilities under the ACVM Act

The registrant still bears overall responsibility even when contracting a manufacturing activity to a third party

- Must carefully chose third party and their activities
- Ensure each party's responsibilities are clearly defined
- **Ongoing hands-on oversight is required to ensure conformance**

Responsibilities under the ACVM Act: Registrant Oversight

Ongoing hands-on oversight means

- Ensuring the third party has all up to date approval information
- Qualification of the third party company
- Performance monitoring
- Establishment and maintenance of technical (quality) agreements

Registrant Oversight

Ensure the third party has all current approved product details/particulars

These include:

- Active (Technical) material supply
- Raw material, specifications & quality
- Manufacturing methods & equipment
- Packaging Materials/Labelling
- QC Testing methods

Registrant Oversight

Qualification of the third party company

- Process used to **provide an appropriate level of confidence** that the contracted party is able to supply materials of consistent quality, and components and services complying with requirements.

- Qualification should be done prior to outsourcing and until confidence established

Registrant Oversight

Qualification of the third party company

ACVM Expects the contracted third party has:

- The required facilities, equipment, and expertise to perform the contracted activities
- Applicable licensing or ACVM approval (e.g. current GMP certificate for relevant category and scope)
- **Approval by ACVM and is listed in the Product Data Sheet (PDS)**

Registrant Oversight

Performance monitoring

Important to monitor third party performance through various ways:

- Check of product received
- Annual product reviews
- Audits and inspections
- Clear and regular communication
- Review of contract(s), KPIs etc.

Registrant Oversight

Technical (Quality) Agreements

- Set out responsibilities for each party in relation to regulatory and quality (GMP) requirements
- Separate to, but sits alongside, commercial contract (and is referenced in the commercial contract)

➢ **Quality and commercial agreements must be consistent** - both applicable to the same activities.

Registrant Oversight: Quality Agreements

The purpose of a quality agreement is to ensure:

- Each party understands requirements and obligations
- There is full and ongoing compliance with the particulars in the product registration
- Responsibilities are defined
- Reporting channels and timelines for communications are established
- Final product is of a consistent quality and meets regulatory requirements

Registrant Oversight: Quality Agreements

Should also include responsibilities for:

- Records/documentation
- Validation
- Stability studies
- Change control
- Issues management, including processes for complaints and recalls
- Release for supply

And allow audits and inspections by contract giver

Registrant Oversight: Quality Agreements for Ag Chems and Exempt Products

- GMP not required, but QMS expected
- Technical/quality agreement is expected to be in place to ensure quality and conformance
- Minimum requirements for a documented system for Ag Compounds are stated in ACVM Regulations (7- 15)

Specialised Quality Agreements: Distribution and Marketing

Minimum requirements

- Relevant aspects of Registration Conditions (e.g. RVMs, AB sales reporting)
- Complaints, Product Recalls
- Storage conditions
- Advertising etc.

Specialised Quality Agreements: Warehousing and Dispatch

- If agreement is only for storage or dispatch, still need an agreement to ensure that the **storage temperature and security of product is maintained.**
- If the third party is taking sales orders directly, all relevant conditions of registration apply (e.g. **RVM Seller approval** may be required)
    - Registrant still expected to ensure appropriate stewardship and conformance to regulatory requirements

Specialised Quality Agreements: Release for Supply

- Step of manufacture that ensures the TNP conforms to approval before entering the distribution chain for sale in the NZ market.
- Involves a comprehensive review of batch and related records to ensure that:
    - The approved process has been followed
    - All starting materials (including packaging), intermediate and finished product comply with the approved specifications
    - Imported product still conforms with specifications after transit

Specialised Quality Agreements: Release for Supply

- The party undertaking release for supply is directly responsible for confirming the product is suitable for release to the New Zealand market
- Must be present in New Zealand, or have direct authority over New Zealand distribution and/or entities performing final checks or functions (labelling/relabelling)
- Release for supply entities do not currently require GMP approval

Multiple Contracted Parties

More than one party can perform different aspects of manufacturing, e.g.

- Manufacture at A, testing at B
- Manufacture and testing at A, labelling/packing at B
- Manufacture at A, labelling/packing at B, QC testing at C

Responsibilities and relationships between each party must be clearly specified

Why is this so important?

Establishing and maintaining third party contracts, lines of responsibility, and regular communication and monitoring is critical to good product stewardship and pharmacovigilance

Changes to product and/or registration without other party knowing;

Working to outdated information and product particulars; and/or

Lack of clarity around responsibility, especially where QC and post-manufacture checks are concerned

Can Lead To

Problems with:

Trade

Border Clearance

End User Clarity/Compliance

Adverse Events

Hort/Animal Product Residue Issues

Recalls

And:

Compliance Action

Product Suspension or Cancellation

Why is this so important?

Remember, the registrant is always responsible for product conformance so is liable for any product/regulatory issue.

Manufacturing Details Specified in the Product Data Sheet

Manufacturing

- Wide range of different products
- Wide range of manufacturing processes
- Many different companies involved
- Many different testing laboratories, test methods, and specifications involved

Different level of risk for each product

Manufacturing in the PDS: Part B

- B1: Active Ingredient Manufacturer(s)
- B2: Active Ingredient Minimum Purity and Impurities
- B3: Formulation Details
- B4: Manufacturer(s) of the Formulated Product, including the Release for Supply entity
- B5: Manufacturing Process
- B6: Specifications of the Formulated Product
- B7: Packaging Details
- B8: Distribution Process

Manufacturing in the PDS: Part B

- B1: Active Ingredient Manufacturer(s)
- B2: Active Ingredient Minimum Purity and Impurities
- B3: Formulation Details
- B7: Packaging Details

- Establishes and the formulation and all starting materials
- These details form the basis of the risk profile of the product (efficacy, safety, residues, stability)

Manufacturing in the PDS: Part B

- B4: Manufacturer(s) of the Formulated Product, including the Release for Supply entity
- B5: Manufacturing Process
- B6: Specifications of the Formulated Product

➢ Establishes and details the manufacturing and QC procedures managing the product quality and consistency

➢ Further characterises the product and its risk profile

Manufacturing in the PDS: Part B

- B7: Packaging Details
- B8: Distribution Process

- Characterises the packaging (including pack sizes) for the product, and any specialised distribution requirements
- Provides information on the post-manufacture handling and transport requirements to manage risk between manufacture and use

Chemistry, Manufacturing, and the Risk Profile

Why require so much chemistry and manufacturing information for each product?

- All products, even generic (B2) products, are unique due to differences in ingredients/components, manufacturing process, quality control (in-process and formulated product specifications), manufacturing equipment, and packaging materials
- These details characterise the product, and dictate how it will behave on storage and use

Chemistry, Manufacturing, and the Risk Profile

Therefore…

Accurate and details chemistry and manufacturing information is critical to stability, but also the entire efficacy, safety, residue, and stability risk profiles.

And registrants need to provide all the relevant information in detail because…

Assessors are not Mind Readers

Section B4 - Formulated Product Manufacturers

PDS – Vet Meds, Ag Chems and VTAs

To make it simple the current PDS Guideline states:

B4 Manufacturer(s) of the Formulated Product

‘Provide the name site address and function of all facilities involved in any step of manufacture. This includes but is not limited to the following: bulk product formulation, filling, packaging and labelling, contract sterilisation, external analytical laboratory testing, re-packing/re-labelling and release for supply.

1) Formulator (manufacturer)

2) Lab/testing? Not listed, so have to presume it is the formulator

3) Re-packers/Relabellers – What are they actually doing?

4) Release for Supply

B4 Manufacturer(s) of the Formulated Product
See guideline.

Company name	Street address of manufacturing site	Manufacturing step/Function
TNP Corporation Ltd	27 Syringe Way, Boulder, Colorado, USA	Manufacturer/formulator
Product Fine Ltd	12 Cardboard Lane, Sydney NSW, Australia	Manufacturer/formulator
Chemical Supply Ltd	21 Tennant Street, Timaru	Repacker/Relabeller
Other Chemical Supply Ltd	35 James Road, Wellington	Repacker/Relabeller
Product Supply Services Ltd	30 Crofton Way, Papatoetoe, Auckland	Repacker/Relabeller

Provide details of the main company responsible for 'release for supply' of this product.

Company Name	TNP Corporation Ltd
Site Address	27 Syringe Way Boulder, Colorado, USA

PDS – B4 – Formulated Product Manufacturers

- Formulator (manufacturer)
- Lab/testing?
- Re-packer/Relabeller - NONE
- Release for Supply – No NZ entity

B4 Manufacturer(s) of the Formulated Product
See guideline.

Company name	Street address of manufacturing site	Manufacturing step/Function
Chemical Supply Limited	12 Manufacturing Road, Shandong, 3439820, China	Formulation, packaging, labelling

Provide details of the main company responsible for 'release for supply' of this product.

Company Name	Chemical Supply Limited
Site Address	12 Manufacturing Road, Shandong, 3439820, China

PDS – B4 – Formulated Product Manufacturers

- Formulator (manufacturer)
- Lab/testing?
- Re-packer/Relabeller

- Release for Supply? Why is no one listed?

B4 Manufacturer(s) of the Formulated Product
See guideline.

Company name	Street address of manufacturing site	Manufacturing step/Function
Chemical Supply Limited	12 Manufacturing Road, Shandong, China	Formulator
Product Supply Services Ltd	30 Crofton Way, Papatoetoe, Auckland	Repacker/Relabeller

Provide details of the main company responsible for 'release for supply' of this product.

Company Name	
Site Address	
Postal Address (if different)	

What does a good PDS manufacturer list look like?

PDS – B4 – Formulated Product Manufacturers

- All functions listed and each manufacturer identified
- QC testing functions specified
- Release for Supply entity identified

B4 Manufacturer(s) of the Formulated Product
See guideline.

Company name	Street address of manufacturing site	Manufacturing step/Function
Product Fine Ltd	12 Cardboard Lane, Sydney NSW, Australia	Formulation of bulk product, filling, and packing
Chemical Supply Ltd	21 Tennant Street, Timaru	External quality control laboratory (Assay testing)
Other Chemical Supply Ltd	35 James Road, Wellington	External quality control laboratory (all other testing)
Product Supply Services Ltd	30 Crofton Way, Papatoetoe, Auckland	Repacker/Relabeller

Provide details of the main company responsible for 'release for supply' of this product.

Company Name	Product Fine Ltd
Site Address	12 Cardboard Lane, Sydney NSW, Australia
Postal Address (if different)	

PDS – B4 – Formulated Product Manufacturers

- Each manufacturer responsible for all steps
- Each listed as release for supply entities to clear their own products

Note: would be ideal if they specified they only cleared product from their site, but good that they're all listed!

B4 Manufacturer(s) of the Formulated Product
See guideline.

Company name	Street address of manufacturing site	Manufacturing step/Function
TNP Company Limited	112 Horticultural Road, VIC, Australia	All Steps
Product Fine Ltd	12 Cardboard Lane, Sydney NSW, Australia	All steps
Chemical Supply Ltd	30 Crofton Way, Papatoetoe, Auckland	All Steps

Provide details of the main company responsible for 'release for supply' of this product.

Company Name	TNP Company Limited
Site Address	112 Horticultural Road, VIC, Australia
Postal Address (if different)	
Company Name	Product Fine Ltd
Site Address	12 Cardboard Lane, Sydney NSW, Australia
Postal Address (if different)	
Company Name	Chemical Supply Ltd
Site Address	30 Crofton Way, Papatoetoe, Auckland
Postal Address (if different)	

Section B5 – Manufacturing Process

The Manufacturing Process

- The manufacturing process is **all steps** from dispensing through packaging to product labelling
- The manufacturing process information in the PDS should cover all steps and process controls:
    - The addition of all ingredients and intermediates
    - All critical control points, and where they occur in the process
    - All heating, cooling, and blending steps, including timing and duration
    - Details of bulk storage, filling, as post-manufacture storage
    - Details of product labelling including application of batch and expiry information

The Manufacturing Process: Common Errors

- No process listed at all
- Incomplete process – missing preliminary steps or production of intermediates; process stops at the end of the blending process (i.e. no filling, packaging, or labelling steps)
- Incomplete/absent critical control points – information not there at all; only includes some points, or some details (e.g. “heated”, but no temperature); does not include timing/duration descriptors (e.g. “30 minutes until dissolved” or “until solution is clear”);
- No information bulk storage – process clearly indicates bulk storage is done (large batch size) but details are excluded

Key points to remember

- Ensure that third party manufacturers, and the processes they undertake, are clearly identified
- Ensure that the relationship between the registrant and other parties is well defined to prevent confusion
- Make sure chemistry and manufacturing information is complete, detailed, and accurate for all products at all times
- The registrant is always ultimately responsible for products and their registrations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Common Application Errors (and how to avoid them)

ACVM Workshop
20 February 2019

Ministry for Primary Industries
Manatū Ahu Matua

Why is this important?

- Saves money – we charge for time taken
- Speeds up the application process
  - Delay while the application is with the applicant
  - Once we receive the additional information or clarification, it goes back into prescreen or if already under appraisal, then the assessor's queue.
  - New versions of information (eg amended label, PDS, data volume) must be rechecked.

General – Submitting your application

- Use the most recent forms and templates from the website each time.
- Sign and date with the correct date (including updates) – also footers.

Data assessment reports

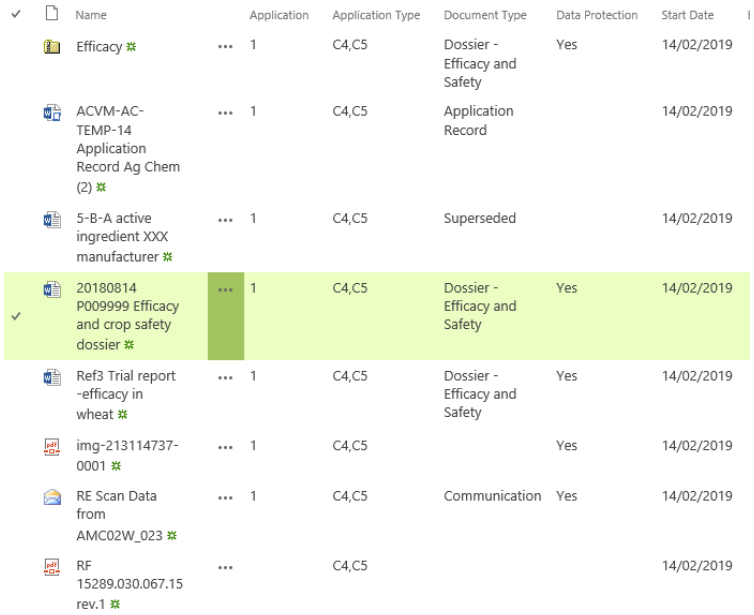
- Address all non-compliances in the Data Assessment Reports. If more data is required to address these, it should go back to the data assessor to be included in the DAR.

- The applicant must make all arguments. The data assessor cannot make arguments on your behalf.

- All data (including raw data), arguments and information which was supplied to the data assessor should also be provided with the application.

File names

- Individual files should be identifiable from their names – descriptive and unambiguous
- No numerical strings (eg scanned documents) or code names
- We can spend a lot of time looking for information if this is unclear
- See the file naming guide (E-files for ACVM applications guideline)



Name	Application	Application Type	Document Type	Data Protection	Start Date
Efficacy	1	C4,C5	Dossier - Efficacy and Safety	Yes	14/02/2019
ACVM-AC-TEMP-14 Application Record Ag Chem (2)	1	C4,C5	Application Record		14/02/2019
5-B-A active ingredient XXX manufacturer	1	C4,C5	Superseded		14/02/2019
20180814 P009999 Efficacy and crop safety dossier	1	C4,C5	Dossier - Efficacy and Safety	Yes	14/02/2019
Ref3 Trial report -efficacy in wheat	1	C4,C5	Dossier - Efficacy and Safety	Yes	14/02/2019
img-213114737-0001	1	C4,C5		Yes	14/02/2019
RE Scan Data from AMC02W_023	1	C4,C5	Communication	Yes	14/02/2019
RF 15289.030.067.15 rev.1		C4,C5			14/02/2019

Variations – Are all changes included?

Labels

- Highlighted and clean versions. **All** changes must be highlighted.
- If there are any differences other than the proposed variation, please explain.
- Ensure statutory statements are correct.
- Check ACVM website address and the MRL statement are updated:

See www.foodsafety.govt.nz for registration conditions.

It is an offence for users of this product to cause residues exceeding the relevant MRL in the Food Notice: Maximum Residue Levels for Agricultural Compounds.

PDS

- Differences from the previous version to be noted and explained.

Time Waivers

- Time waivers are requested by the applicant to “stop the clock” while responding to a question, or if the application can’t go to the delegate for another reason (eg HSNO approval).
- In future, we will let you know when a time waiver should come into effect unless you let us know to the contrary.
- The time waiver itself has no effect on how quickly an application is processed.
- If a requested time waiver is refused, the application should proceed to delegate decision and this will likely have a recommendation to decline.

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Agricultural Chemicals & VTAs

Ministry for Primary Industries
Manatū Ahu Matua

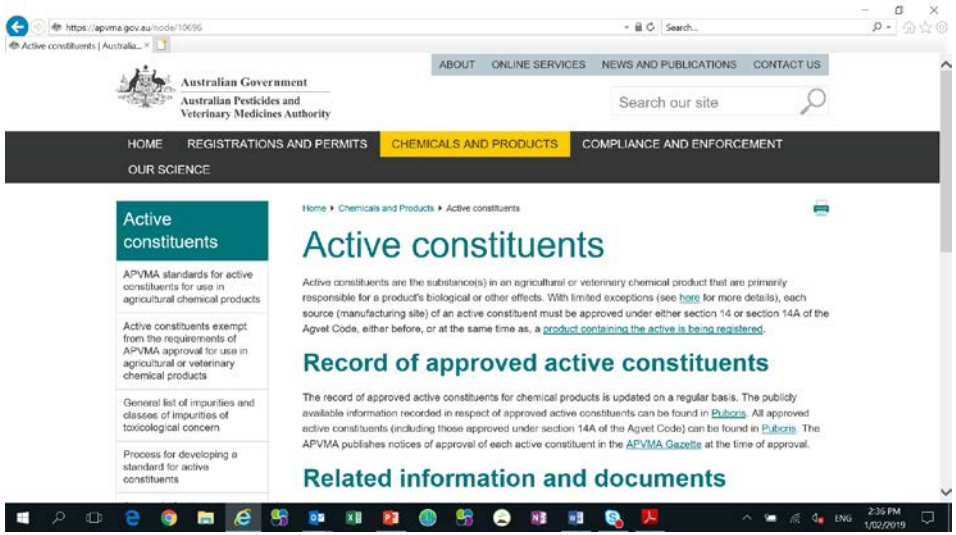
AC/VTAs - Chem & Manufacturing

Active ingredient

APVMA no longer publishes the TGAC list of approved manufacturing sites.

The APVMA approval must be provided with the application for every new site.

VTAs – batch analyses must be provided.



AC/VTAs - Chem & Manufacturing

Active ingredient

If adding a new active ingredient manufacturer, the analytical method must be identical to the current a.i. manufacturer. If not, the new analytical method must be supplied.

As the analytical method is not required to be stated on the PDS, this is often overlooked.

(Note method validation is not currently required for active ingredient technical material)

Part B. Product and Manufacturing Specifications--Commercially Sensitive Information

B1 Active Ingredient Manufacturer/Formulator

See guideline.

Active Ingredient	Manufacturer's/ Formulator's Name	Site Address	Postal Address (if different)

B2 Active Ingredient Minimum Purity and Impurities

See guideline.

Active Ingredient	Manufacturer/Formulator	% Minimum Purity	Impurity and %

AC/VTAs - Chem & Manufacturing

Active ingredient in formulated product

A specific analytical method name is required to be stated on the PDS (B6). This is to align with validation.

- If adding a new formulated product manufacturer, the analytical method must be identical. If not, the new analytical method and validation* must be supplied. (Both methods stated on PDS)

*When supplying a validation for an analytical method, check whether this is for use in the active material or the formulated product (sometimes both).

B6 Specifications of the Formulated Product		
Release Specifications See guideline.		
Parameter	**Range (include units if applicable)**	**Method**
Expiry Specifications See guideline.		
Parameter	**Range (include units if applicable)**	**Method**

AC/VTAs - Chem & Manufacturing

Release and expiry specifications

If not all parameters are included, then an argument should be made to explain why the parameters chosen are sufficient to ensure consistency and quality of every batch.

BAITS: INCLUDING BAIT CONCENTRATE (CB), BAIT (READY TO USE) (RB)

Recommended Test Parameters	Relevant CIPAC Method/Comments
Appearance (physical state, colour)	Observation of physical appearance are required, eg sedimentation
Active content	Appropriate validated method
Acidity/alkalinity or pH	MT 31, MT 75 or MT 191
Retention of palatability	Only required if significant physical changes were observed on storage
Packaging stability	Observation of packaging stability and integrity

DUSTABLE POWDER (DP)

Recommended Test Parameters	Relevant CIPAC Method/Comments
Appearance (physical state, colour)	
Active content	Appropriate validated method
Acidity/alkalinity or pH	MT 31, MT 75 or MT 191
Dry sieve test	MT 59.1
Packaging stability	Observation of packaging stability; there should be no caking in the pack on storage

EMULSIFIABLE CONCENTRATE (EC), EMULSION (OIL IN WATER) (EW) and EMULSION (WATER IN OIL) (EO)

Recommended Test Parameters	Relevant CIPAC Method/Comments
Appearance (physical state, colour)	
Active content	Appropriate validated method
Acidity/alkalinity or pH	MT 31, MT 75 or MT 191
Emulsion characteristics	MT 36.3 (0.1-5% dilution) or MT 183 (1% dilution) or MT 180
Packaging stability	Observation of packaging stability

SUSPO-EMULSION (SE)

Recommended Test Parameters	Relevant CIPAC Method/Comments
Appearance (physical state, colour)	
Active content	Appropriate validated method
Acidity/alkalinity or pH	MT 31, MT 75 or MT 191
Dispersion stability	MT 180

AC/VTA – Chem & manufacturing

Batch Analyses

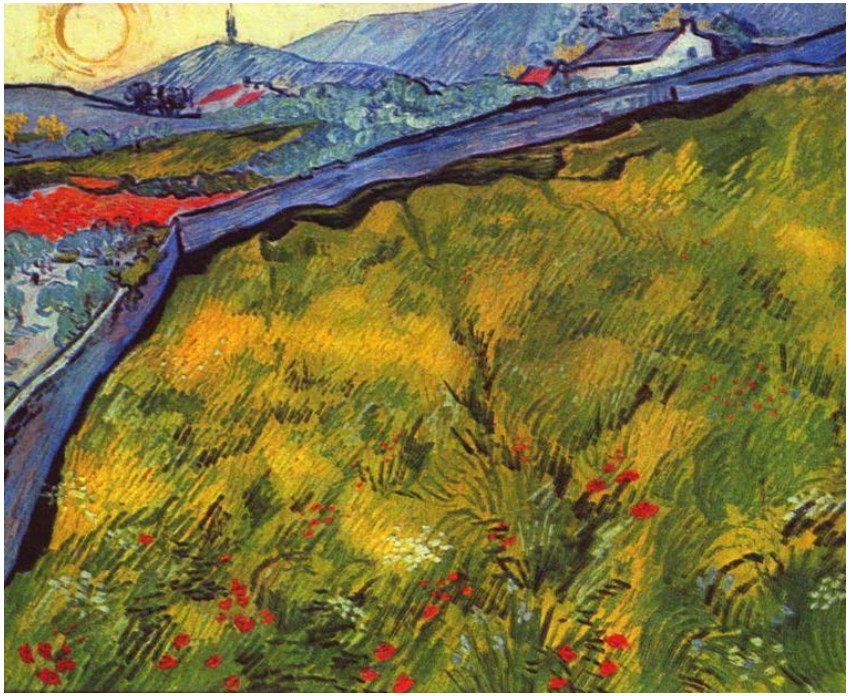
- Check any batch analyses that are submitted meet all the requirements in the relevant guidelines (date of manufacture, batch number, batch size, manufacturing site, analytical methods)
- All relevant parameters measured
- Results meet relevant specifications

Stability Testing

- VTAs – 3 batches real time

AC/VTAs - Other

- Make sure packages match up – for example that efficacy and residue trials use the same use pattern as proposed on the label.
- Explain any deviations or extrapolations
- An expert opinion may be used to support deviations



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Veterinary Medicines

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VM - Chem & Manufacturing

Active ingredient

Compendial standards (B2/B3):
USP/BP/EP

- Monograph required

Non-compendial = Manufacturer Specifications (MS). Avoid tech/food/chemical/etc grade.

- In-house analytical methods
- Chemical & physical characteristics

Batch analysis required

Disclose min purity & max impurities

VM - Chem & Manufacturing

Formulation details (B3):

- Full list of ingredients
- Select units g/L or g/kg
- Express overages (stability) for AI
- CAS numbers to match dossier
- SG for liquids

VM - Chem & Manufacturing

Manufacturers (B4):

- Ensure appropriate manufacturing functions
- Correct Approval:

  A= International GMP

  B= Other MPI recognised

  C= MPI GMP approved

VM - Chem & Manufacturing

Manufacturing process (B5):

- State typical batch size
- Provide flowchart (attachments are lost)

VM - Chem & Manufacturing

Release/Expiry Specifications(B6):

- Disclose methods for each parameter
- Include appropriate limits

VM - Chem & Manufacturing

Packaging details (B7):

- Full description of each packaging including:
  - Containers (material & thickness)
  - Stoppers
  - Closures
- Is recycled or not

VM - Chem & Manufacturing

Distribution process (B8):

- For RVMs requiring sellers/purchasers to have OP
- Special transport conditions (cold chain)


Questions?

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Veterinary Medicines Breakout Session

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Suggested Topics

- Veterinary Medicine Chemistry & Manufacturing Guideline
- Equivalence Guideline
- Q & As

Chemistry & Manufacturing (Chemical) Guideline

- Review of the second round of consultation now complete
- Comments received from 15 registrants and an ARPPA group submission
- Currently working to finalise:
    - Final draft of the Chemical C+M (Chemical) Guideline
    - Summary of changes document comparing to current standard
    - Revised PDS
- Final round of consultation to start in late Feb/Early March

Equivalence Guideline

- Applicable to **chemical** pharmaceutical products.
- Can not be used to obtain registration for immunobiologicals including vaccines.

Methods to demonstrate equivalence:

- Chemical equivalence (as per GL definition)
- Pharmaceutical equivalence (as per GL definition)
- Biological equivalence (as per GL definition)

Equivalence

A thorough understanding of your formulation and its performance is required before you can decide

1) Whether equivalence to a reference product can be demonstrated

2) Which product would be the most appropriate reference product to demonstrate equivalence.

- A reference product should be pharmaceutically equivalent - or in some cases a pharmaceutical alternative (see guideline definition)
- Should be innovator product for which MPI holds efficacy data
- Needs to be a product that is or has been registered in NZ

Equivalence Guideline

Pharmaceutical Equivalence

- Can be considered if bioavailability is minimally dependant on product formulation.
- Applicable to test and reference products that are defined as “Closely similar”
- All differences must be identified and demonstrated as being clinically insignificant

Equivalence Guideline

Biological equivalence

- *In vivo* studies
- Required when formulation, manufacturing process, physicochemical properties can impact bioavailability

Blood level study

Used when product systemically absorbed + AI concentration is related to drug action

Pharmacological end-point study

Used when cant measure rate/extent of AI absorption, or AI concentration in tissue is not related to drug action

Clinical end-point study

Compares therapeutic effect between test product and reference product

Intramammary Products

Biological Equivalence

- AI is locally acting, hence blood level and pharmacological BE studies are not applicable.
- Milk sampling difficult – testing same compartment into which AI was administered.

Therefore an appropriate clinical field trial is used to compare efficacy of a test and reference product i.e. non-inferiority study design.

Pharmaceutical Equivalence

EMEA GL 344/1999

- Might be considered for a very limited number of formulations
- Must be "**closely similar**"

Pour-Ons

Anthelmintics

- Most often require *in vivo* blood level studies
- Trial design must account for variability in absorption via dermal route - cross-over whenever possible
- Closely consider sample size (traditional numbers for BE too small)

Could establish pharmaceutical equivalence if

- Same AI, same solution type, same dose rate and volume.
- Excipients same (or equivalent) at the same concentration. If different, need to demonstrate that they will not alter the bioavailability of AI
- Physicochemical properties must be comparable i.e. viscosity, density etc

Spot on’s for companion animals

Systemic absorption

- Check it meets criteria of systemically absorbed topical solution 7.1(4)d in GL.
- If so, pharmaceutical equivalence is appropriate for demonstrating therapeutic equivalence.
- If not – BE study. Blood level most appropriate

Locally Acting

- Need to demonstrate efficacy to the standard i.e. >95% AM reduction
- 1 dose confirmation study may be accepted
- Each host and parasite species claimed must be included
- If systemically absorbed, then distributed back to skin – blood level study
- If a solution with identical formulation and PC properties, requirements for efficacy and safety can be waived

Oral suspensions

- AIs with poor aqueous solubility are often formulated as suspensions
- For oral suspensions, dissolution may limit absorption of AI, which is formulation dependant
- For systemically acting AIs, blood level BE studies are appropriate for confirming therapeutic equivalence


New Zealand Food Safety
Haumaru Kai Aotearoa
Any other questions?
Ministry for Primary Industries
Manatū Ahu Matua

New Zealand Food Safety
Haumaru Kai Aotearoa

Ag Chem / VTA breakout session

ACVM Workshop
20 February 2019

Ministry for Primary Industries
Manatū Ahu Matua

Suggested Topics

NZ Wine growers application rates

Efficacy requirements

Labelling of ag chems

Review of old actives (herbicides) for Animal Transfer

Q & As

NZ Winegrowers – Application rates

We understand that NZ Winegrowers has been requesting that registrants include a rate/100m row on their labels, as well as the rate/100L water that we recommend.

(See the Agricultural label rates position statement on our website)

Efficacy

Are NZ requirements set at the right level?

Labelling of Ag Chems

- Incorrect labelling
- All companies that import, manufacture or sell agricultural compounds must:
    - Know what the requirements for their products are.
    - Have adequate systems and checks in place to ensure that products sold in NZ meet the ACVM requirements, whether manufactured in NZ or internationally.

Herbicide Animal Transfer Review

- Recent applications have highlighted a historical lack of available animal residue data for certain herbicide products used on animal feeds including pasture
- A review is underway to evaluate what data is available (held by ACVM and internationally) to address the data gap
- Expected Outcomes
    - Animal commodity MRLs for herbicide agricultural compounds
    - Call for additional data where none is available
    - Setting/changing pre-grazing intervals and/or WHPs


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Environmental Protection Authority
Te Mana Rauhī Taiao

Reassessments 101

ACVM Workshop
20 February 2019

2

New Zealand’s chemical management approach

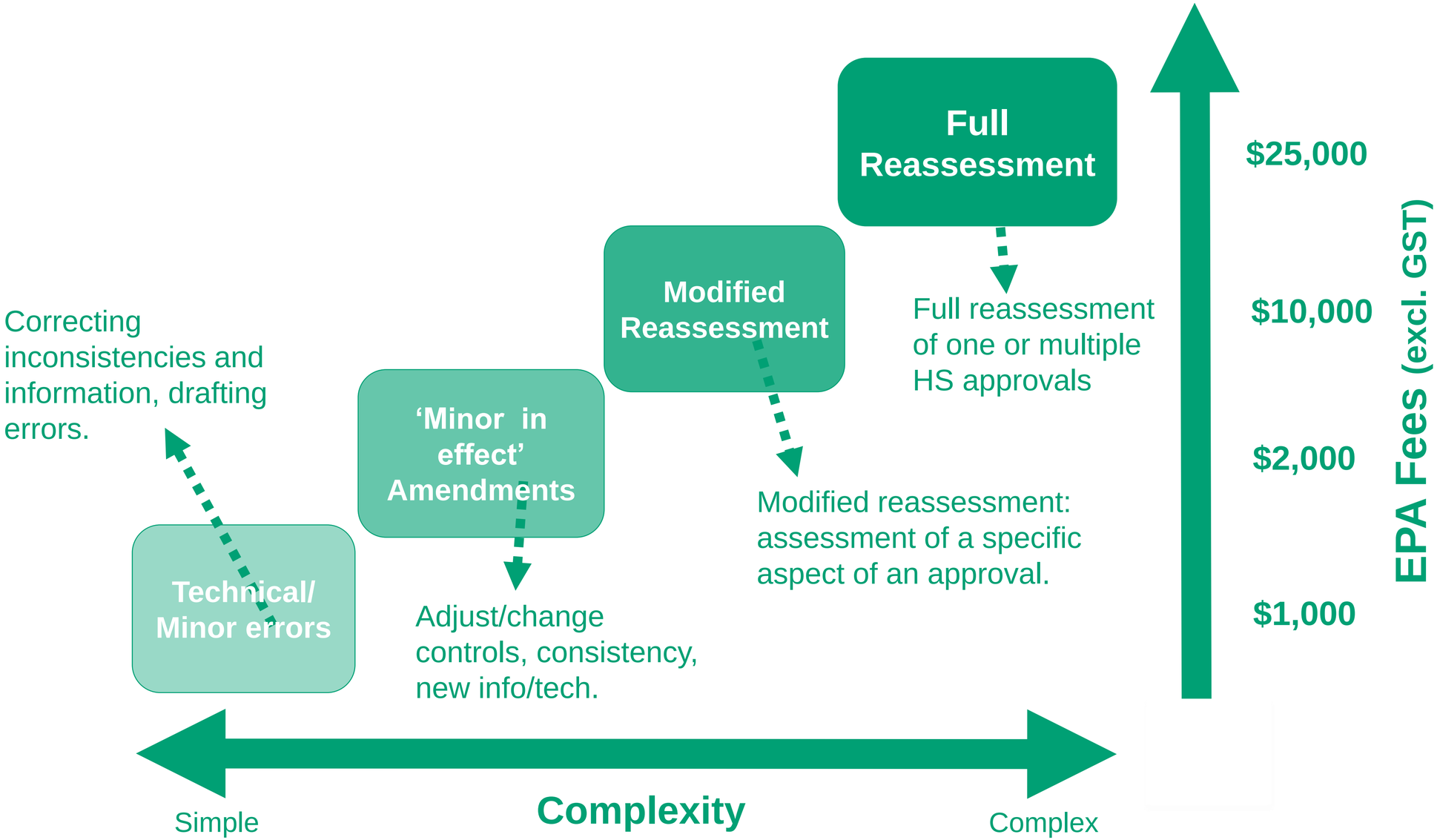
- EPA’s goal to protect the environment and the people who live and work in it for a better way of life.
- Responsibility for regulation of chemicals is shared between EPA and WorkSafe New Zealand.
- All hazardous substances require an approval under the Hazardous Substances and New Organisms (HSNO) Act. Approvals do not expire.
- EPA continues to assess and approve hazardous substance applications, providing transparency with information to the public.

3

All about reassessments

- Reassessments are the mechanism to change or decline existing approvals.
- Outcomes include: hazard classification changes, controls changes, restriction of certain uses, or decline the approval.
- Reassessments may cover a single formulated substance, a single chemical and all related formulations, or a wider group of substances.
- Applications are handled and processed by EPA Hazardous Substance Reassessments team.

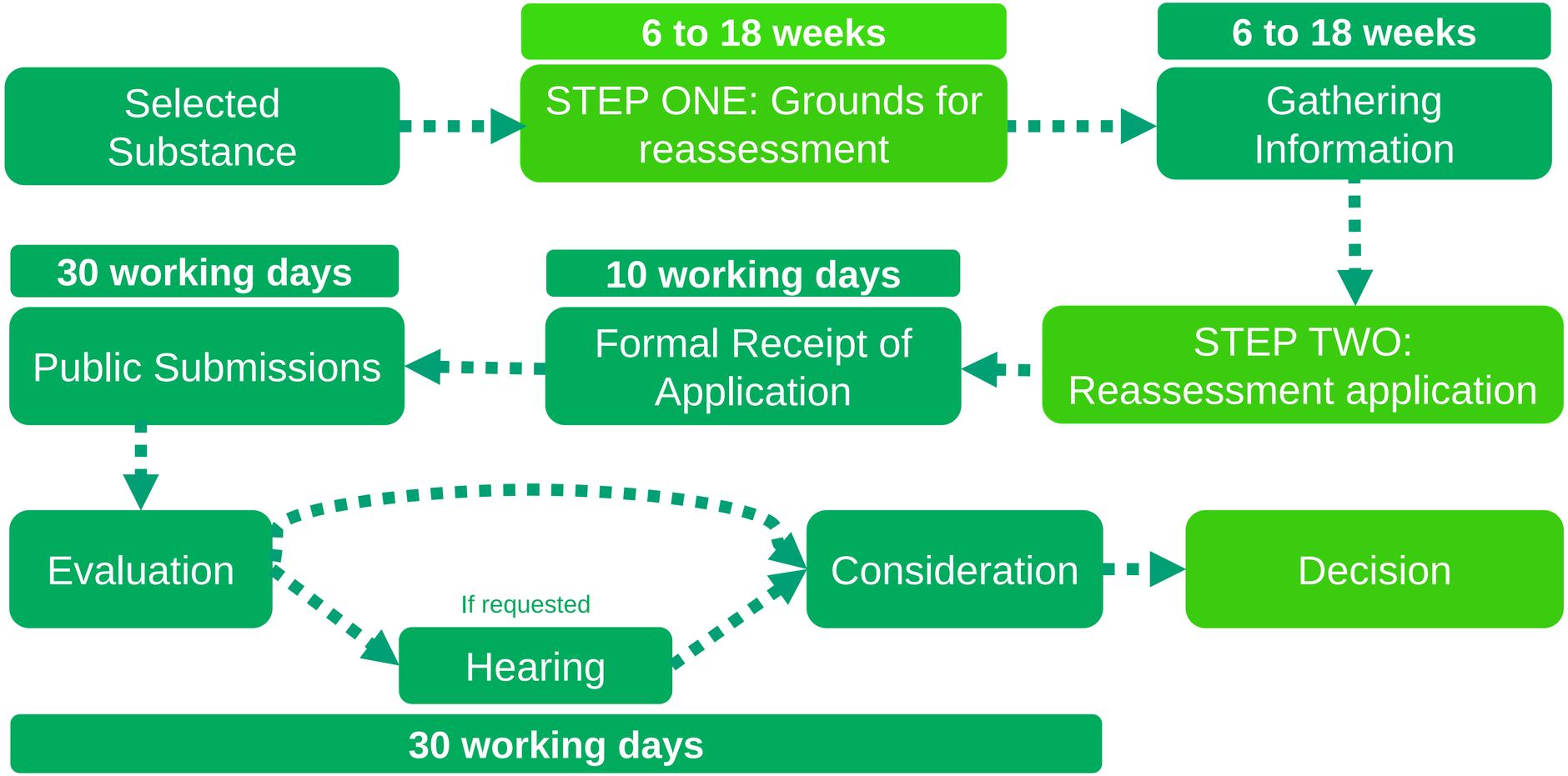
Reassessments and Amendments



Reassessment Process

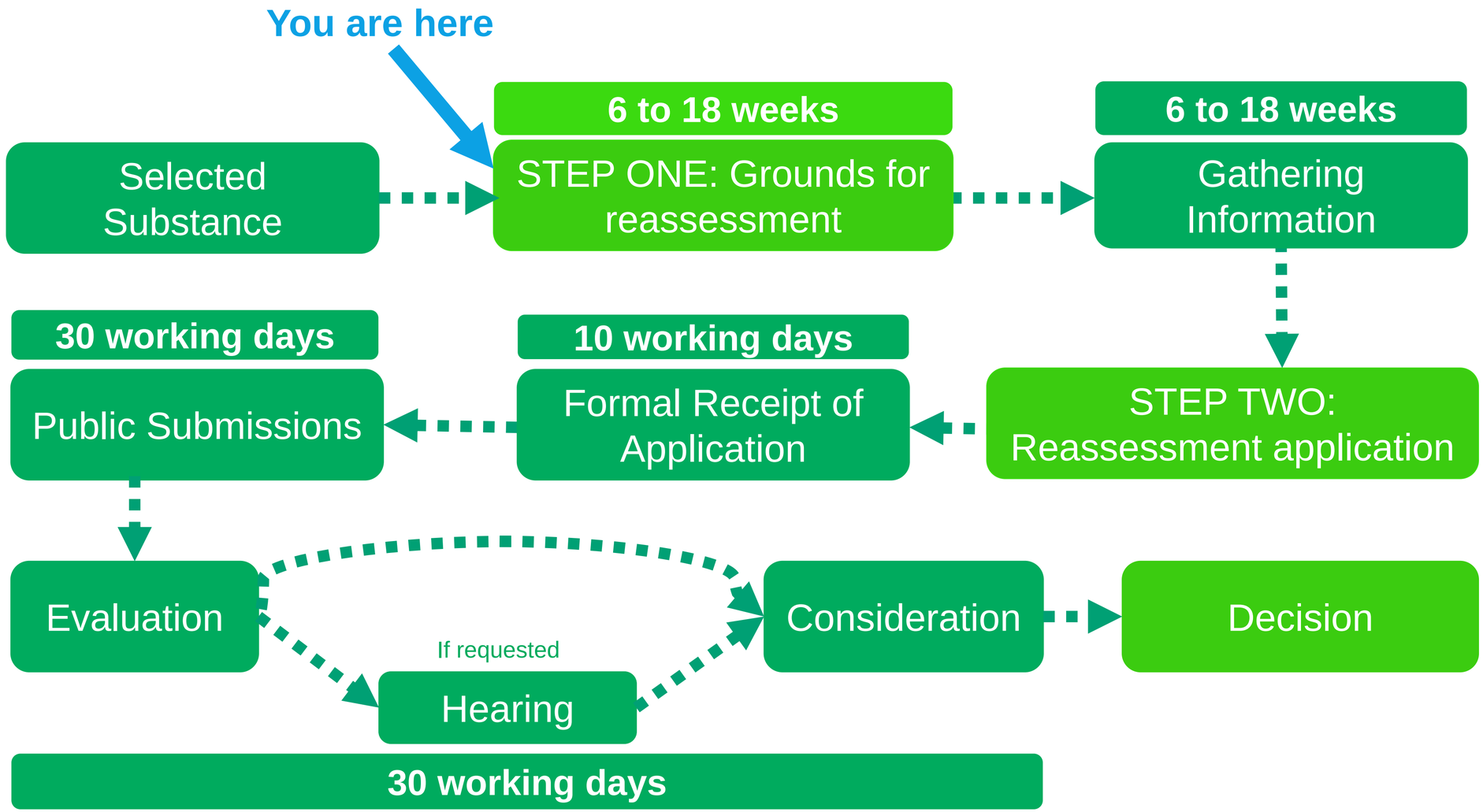
- Most reassessments follow the same two-step process.
- Step one: Grounds – grounds must be established to warrant a reassessment for a particular substance.
- Step two: Reassessment – Official reassessment of a substance including hazards, benefits, risks, use, cultural, international, controls etc…
- Anyone can apply for reassessment of hazardous substance. May include Chief Executive (CE) of EPA or external applicants (incl. individuals, industries, companies, other government agencies etc…).
- For EPA-initiated applications, EPA collects all and any information needed and then evaluates. External applications are dependent on the external applicant.

Reassessment Process



Times are estimate, may vary between reassessments

Reassessment Process

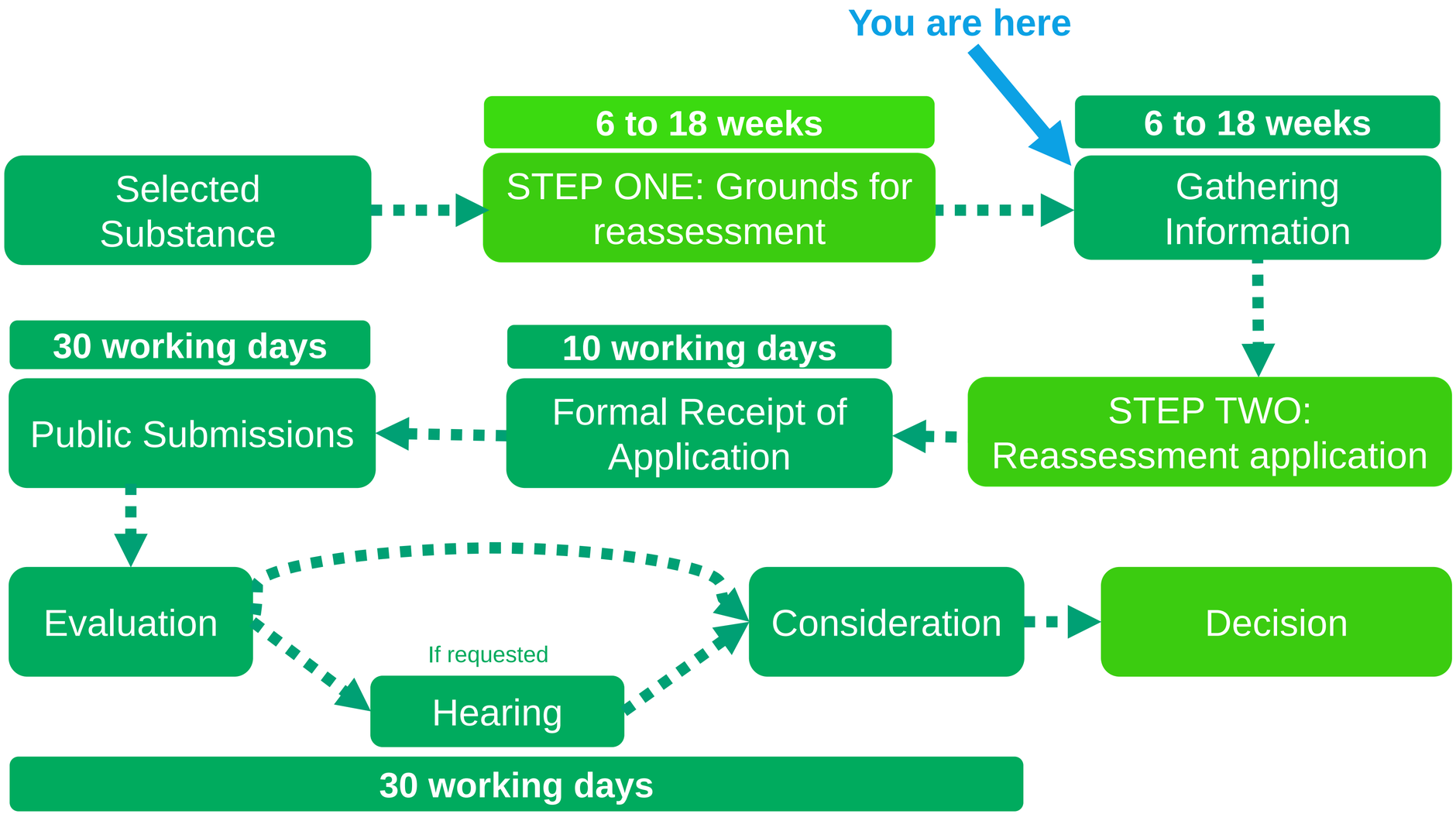


Times are estimate, may vary between reassessments

Step One: Grounds for Reassessment

- Grounds need to be established before reassessing a hazardous substance.
- Any person may request grounds for reassessment.
- Reasons could include: change in use/quantity, change in controls, similar alternative substance, new information.
- The EPA fee for a grounds for reassessment application is $1000 and it can take between 6 weeks to 3 months to complete.

Reassessment Process



Times are estimate, may vary between reassessments

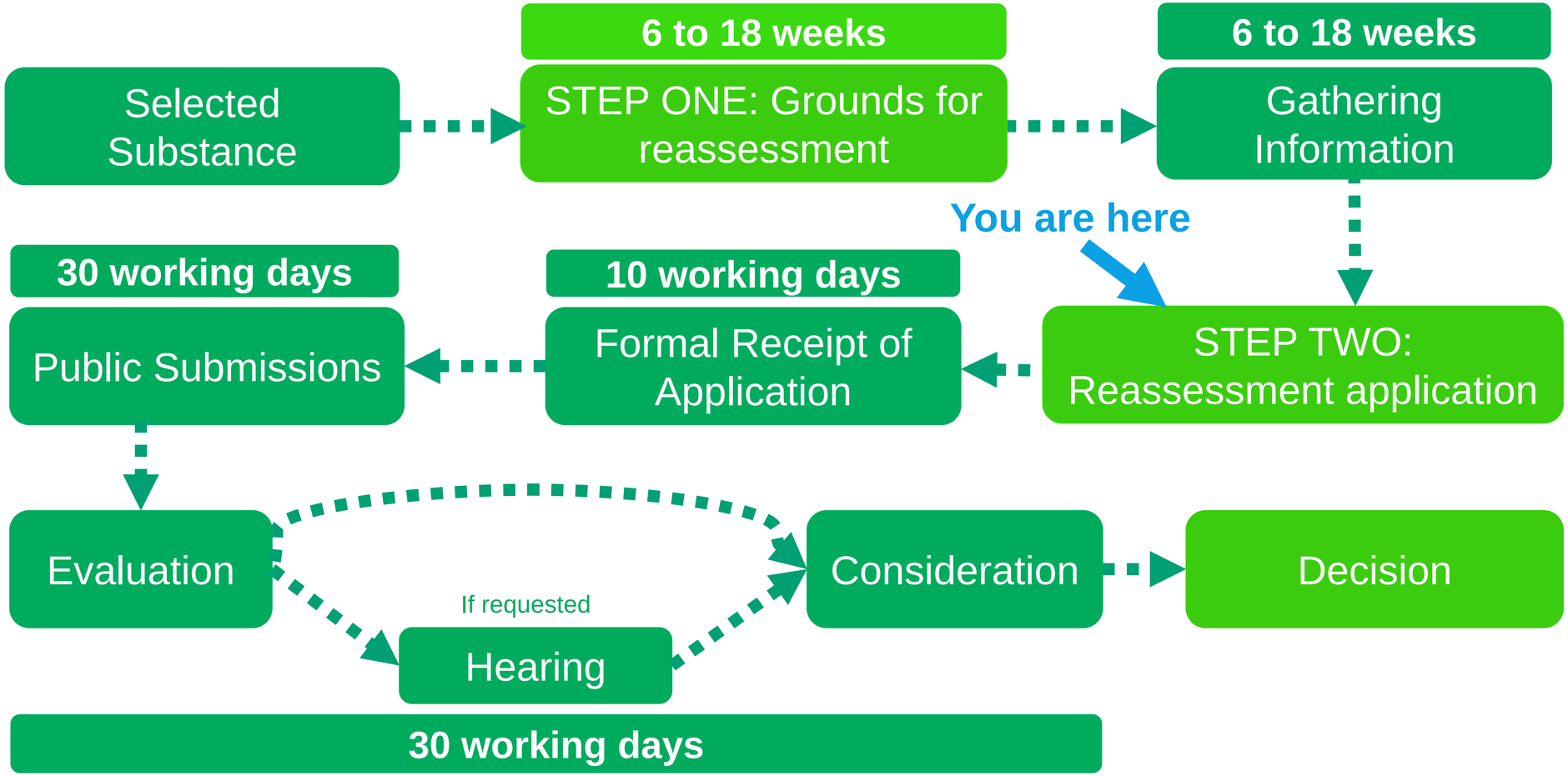
Gathering Information

- After establishing grounds, any person may request a reassessment.
- Preparing an application involves compiling all relevant information. This is the ‘Gathering Information’ step.
- The relevant information relating to the substance can include:
    - Hazard assessment
    - Risk management assessment
    - Approval status
    - Risks and benefits assessment
    - International status
    - Proposed control changes
- This step takes between 6 weeks to 3 months to complete, but it could extend.

Key points about Gathering Information

- EPA-initiated applications use a public call for information. EPA will evaluate the information provided.
- For external applications, it’s expected that the applicant sources and collects their information.
- EPA can provide support or advice to external applicants regarding cultural engagement (Māori).
- Sources of information may include: internal EPA databases, overseas agencies’ databases, external/public databases, responses to the call for information.

Reassessment Process

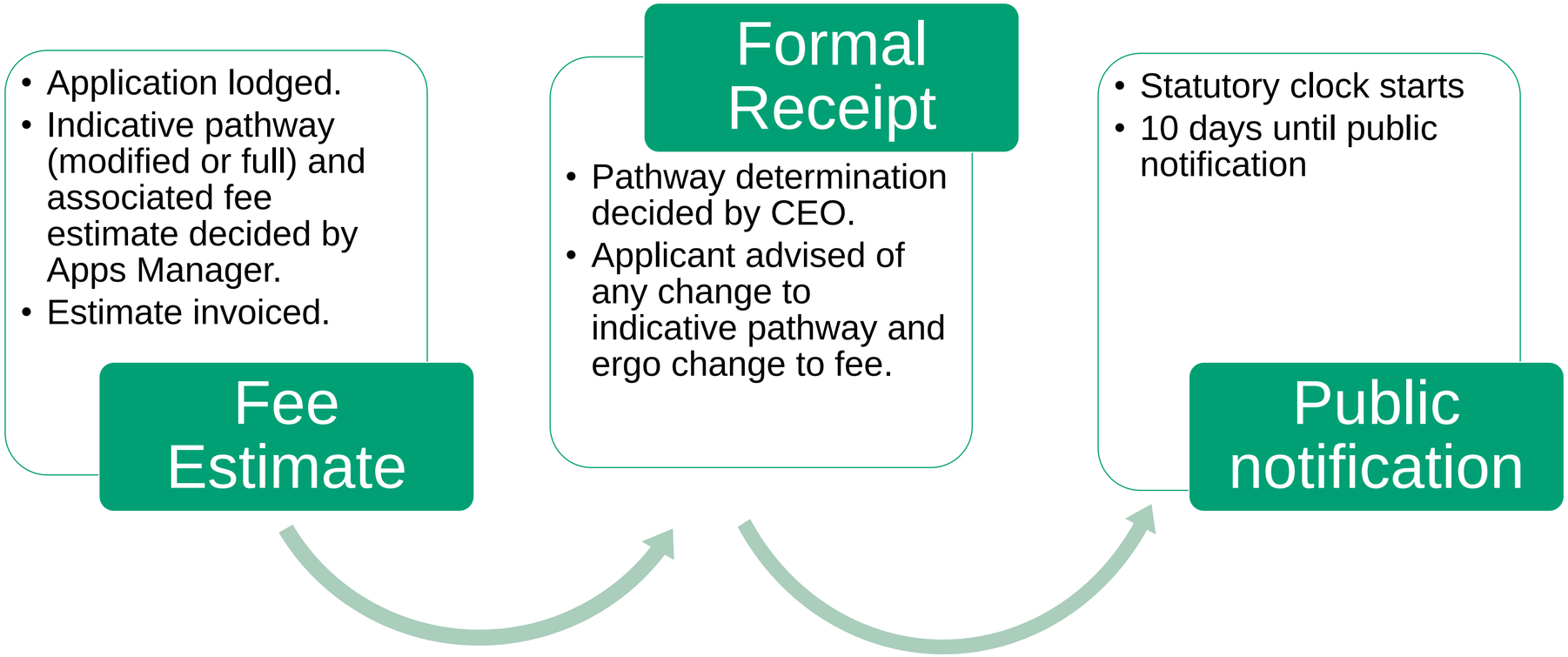


Times are estimate, may vary between reassessments

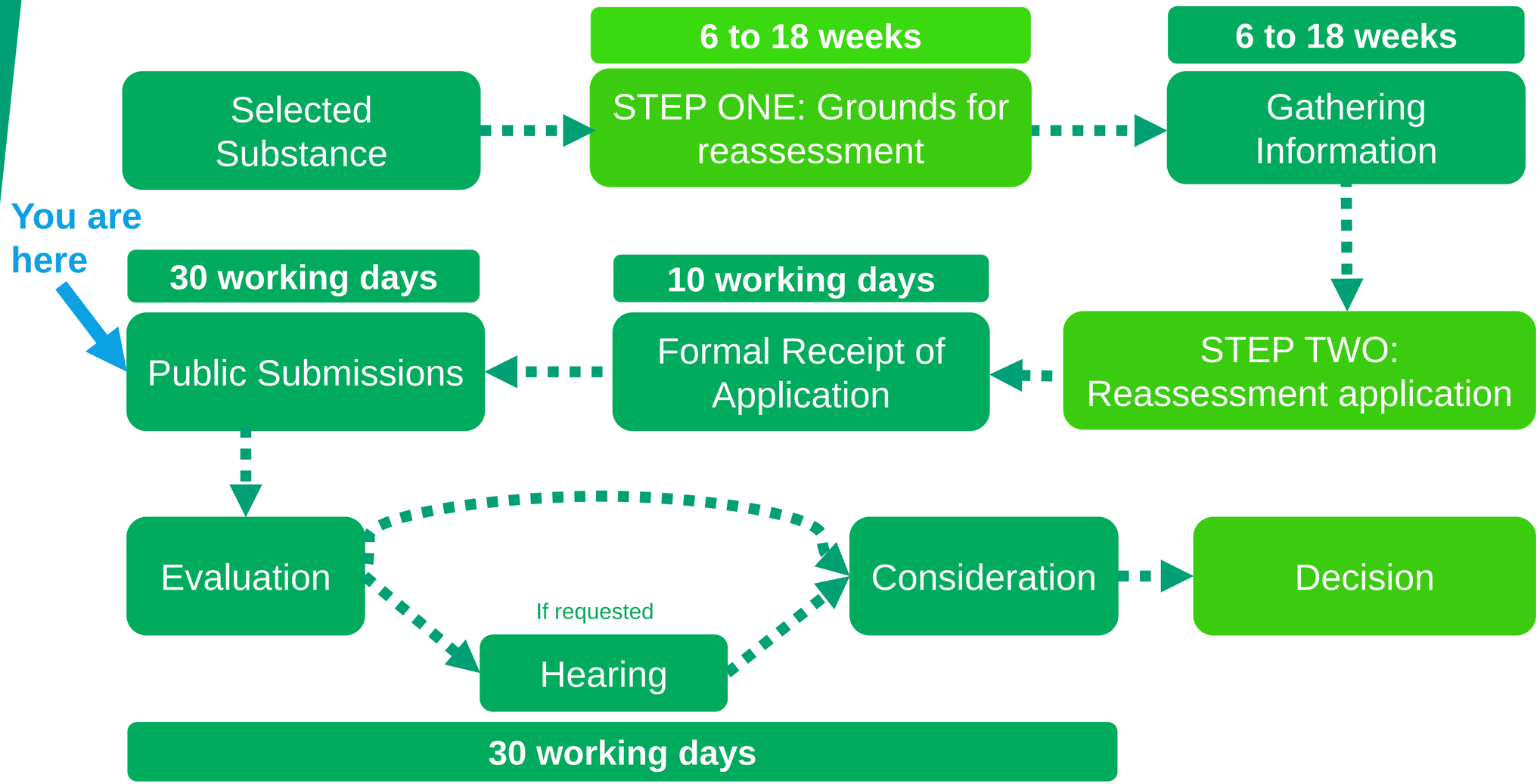
Step two: Application

- All information gathered from the previous step must be compiled into the reassessment application.
- Once the applicant is ready to submit, EPA will review the application.
- Revision of the application ensures consistency and completeness of all information submitted.

Application: From lodgement to public notification



Reassessment Process



Times are estimate, may vary between reassessments

Public Submissions and Evaluation

- A reassessment application is open for public submissions for a statutory period of 30 working days.
- The public submission period allows the general public to read and give feedback on a reassessment application.
- Public includes: individuals, companies, industries, iwi etc…
- Feedback may provide new or updated information for the applicant and for consideration by DMC.
- EPA will evaluate all submissions and report to DMC.

Hearing

- If a submitter requests to be heard publicly, then a hearing takes place.
- The hearing is a place for opinions/viewpoints/ideas/questions of the public submitter/s to discuss with applicant and DMC.
- A normal hearing will take no longer than 1 or 2 days.
- If none of the public submitters want to be heard, and the applicant and DMC do not consider a hearing necessary, then no hearing will take place. The submissions will be provided to the DMC to assist in their consideration.

Consideration and Decision

- DMC considers the application and makes a decision.
- Outcomes of the reassessment (depending on type) include:
    - no change to the existing approval
    - change to the controls or rules, around use of the substance
    - decline the existing approval.
- EPA notifies the public and uploads documents surrounding the reassessment on the EPA website.
- The decision is publicly notified within 30 working days of the conclusion of the hearing or consideration.
- Ongoing communication, compliance and monitoring is scheduled for any key dates.

EPA Reassessment Programme

- Priority Chemicals List
  - 39 individual chemicals identified using the FRCaST screening tool
  - includes industrial chemicals, fungicides, herbicides, insecticides, vertebrate toxic agents (VTAs)
  - launched mid-October 2018
- Externally-generated reassessments
- Emerging Issues
  - Chemical Reviews for hazard classification changes
  - issues raised by compliance, applications, other EPA functions
  - international concerns

Priority Chemicals List

2,4-DB
Alachlor
Amitrole
Dichlobenil
Paraquat
Diuron
Flumioxazin
Oxadiazon
Trifluralin

Paraquat

Carbendazim
Cyproconazole
Folpet

TBBPA
APFO
Benzo[a]pyrene
Tributyltin oxide

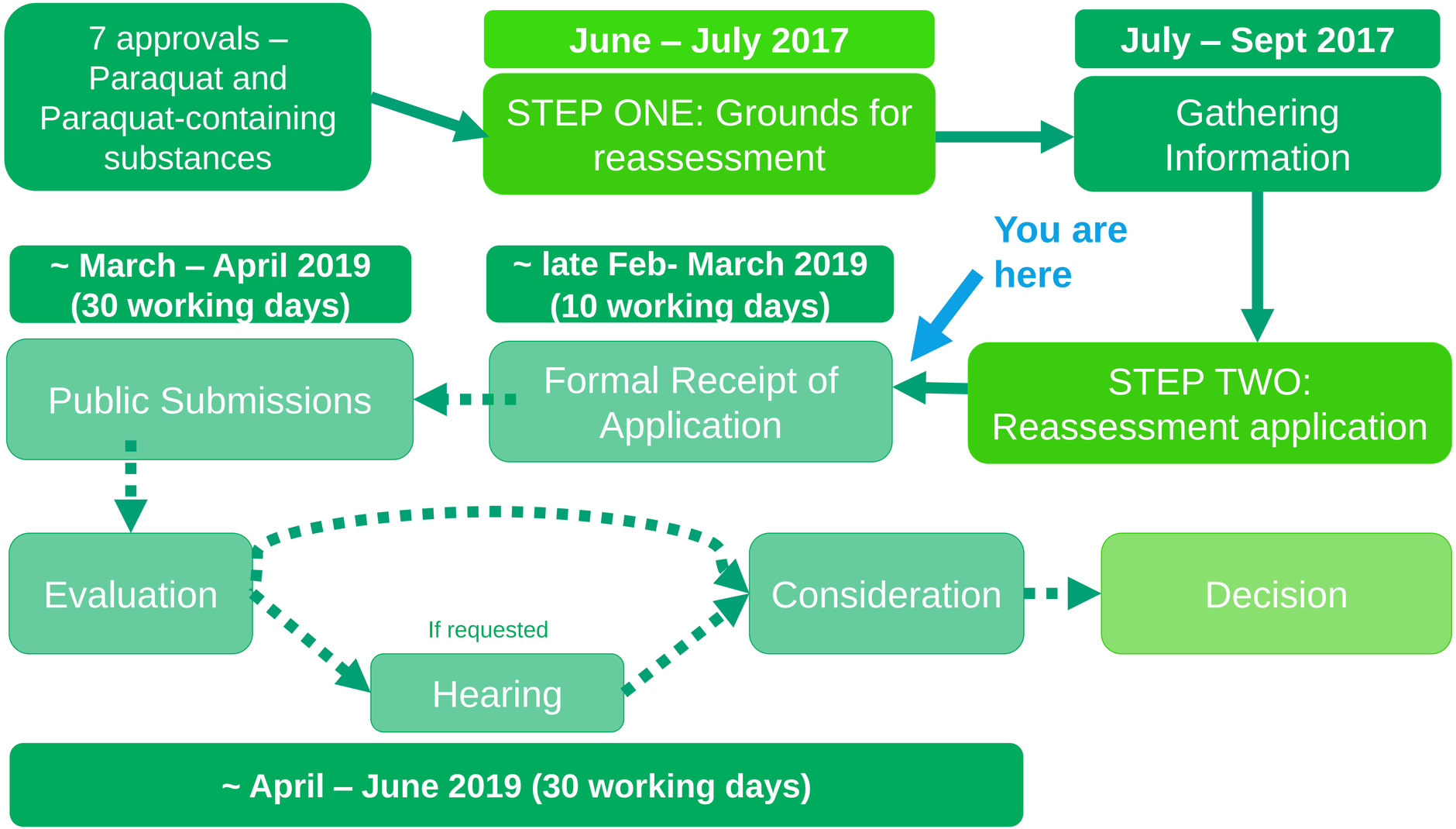
Brodifacoum
Bromadiolone
Flocoumafen

Synthetic Pyrethroids

α-Cypermethrin
Bifenthrin
Bioresmethrin
Cyfluthrin
Cyhalothrin
Cypermethrin
Deltamethrin
λ-Cyhalothrin
Permethrin

Carbaryl
Chloropicrin
Chlorpyrifos
Diazinon
Dichlorvos
Fenitrothion
Fenthion
Maldison
Pirimphos-methyl
Propargite
Propoxur

Paraquat Reassessment



Times are estimate, may vary between reassessments

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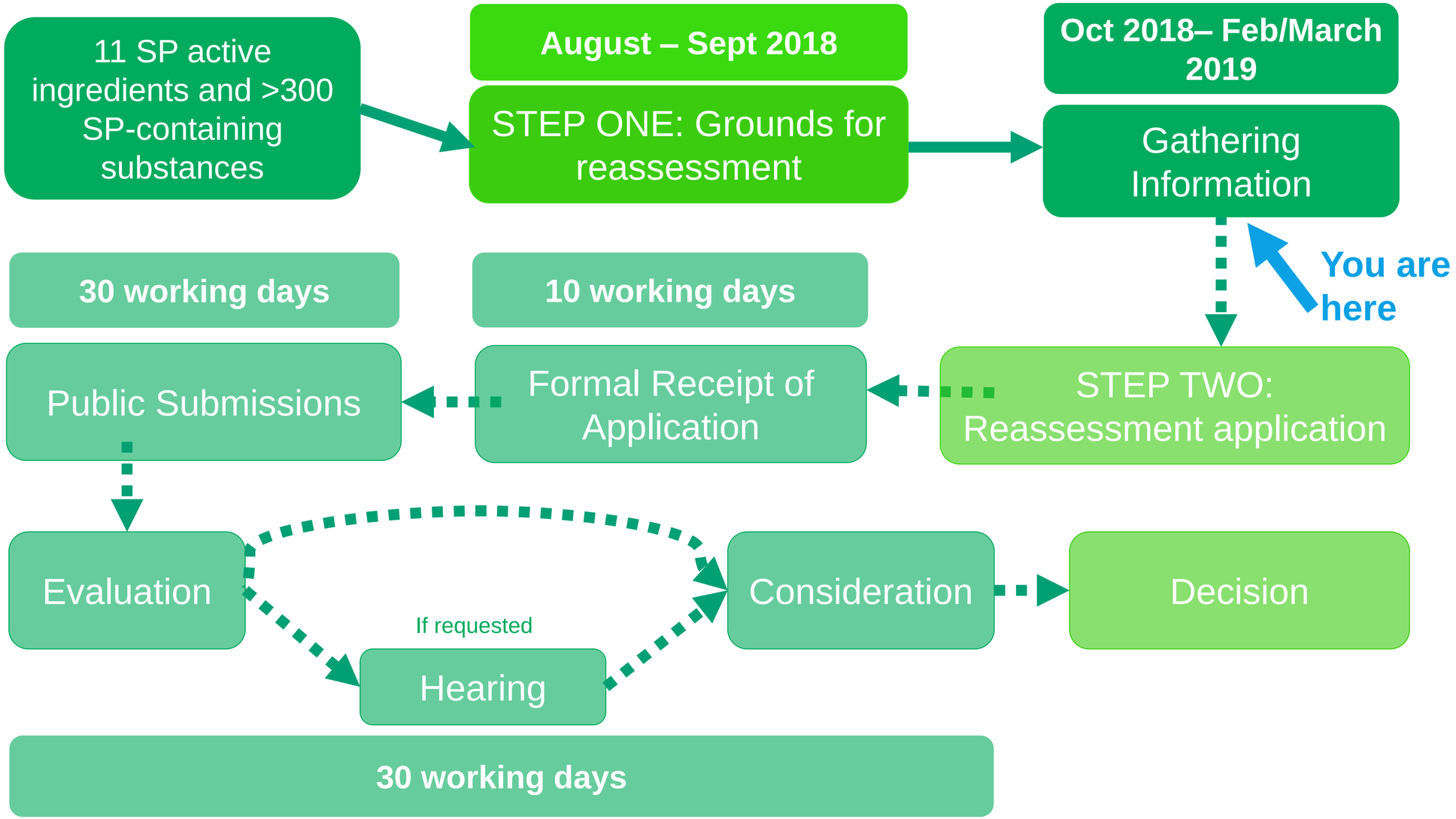
Synthetic Pyrethroids Reassessment



Times are estimate, may vary between reassessments

Summary

- Reassessments are the mechanism for the EPA to change or decline existing approvals.
- Reassessments follow a two-step process – Step One: Grounds for reassessment, Step Two: Reassessment Application
- Applications must have sufficient information for the EPA Decision-making committee.
- Decision-making committee will make the decision and EPA will notify the public.
- EPA Reassessment Work Programme for 2019 includes the paraquat reassessment and the synthetic pyrethroids reassessment.

Environmental Protection Authority

Te Mana Rauhī Taiao

Hazardous Substances Reassessments Team

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