Chemistry and Manufacture of Agricultural Chemicals

ACVM Registration Information Requirements No 12

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Chemistry and Manufacture of Agricultural Chemicals

1 NZFSA assesses chemistry and manufacture to manage risks

To register an agricultural chemical in New Zealand, you must provide formulation and product specifications so that NZFSA can assess risk potential. This requirement stems from section 4 of the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997, which provides for prevention or management of risks associated with the use of agricultural compounds:

- risks to trade in primary produce
- risks to animal welfare
- risks to agricultural security
- risks to public health.

Chemistry and manufacturing information that you must provide is printed in bold. Guidance and optional information are in regular print. If required information is not provided, you must justify this by scientific argument.

Provision of electronic data: If you wish to provide data electronically, please contact us first to discuss.

All documentation provided must be in English.

If you are not sure about the meaning of any terms in this document, use our website glossary http://www.nzfsa.govt.nz/publications/glossary

Contact us if you have any questions (acvm@nzfsa.govt.nz)

2 Active Ingredient

The following information must be provided for each active ingredient unless a waiver has been granted or the active fits a category for which reduced information may be acceptable.

2.1 Manufacturer of the active ingredient

An active ingredient manufacturer is defined as any site of manufacture of the active ingredient that is intended for use in the manufacture of the trade name product.

The following details must be provided for every site of manufacture of the active ingredient(s):

- **name of organisation**
- **postal address**
- **physical address**
- **telephone, fax and email details**
- **name of contact person**
- **name and CAS number of the active ingredient.**

The Approvals and ACVM Group reserves the right to enquire into the manufacturing process of active ingredient(s) where it needs to satisfy issues relating to the suitability of the process or the adequacy of quality assurance procedures.

Refer to Annex 4 for a list of active ingredients that are exempt from notification of the manufacturer, and the alternative information that needs to be provided for them.

2.2 Identification of the active ingredient(s)

Identification of the active ingredient must include:

- **chemical or IUPAC, ISO and common (INN) or proposed name**
- **Chemical Abstracts Service (CAS) registry number (if assigned)**
- **empirical molecular formula and molecular weight**
- **two-dimensional chemical structure**.

2.3 Active ingredient specification

The active ingredient specification must include the following:

2.3.1 Manufacturer's specifications

The manufacturer's specifications are the specifications that the active ingredient will be within when it is used in the manufacture of the trade name product. These may include chemical and physical characteristics (see below).

These specifications include minimum content of pure active ingredient[#], isomeric ratio (where applicable) and maximum impurity content. If the active substance is produced at more than one plant, specifications must be provided for each plant separately.

For minimum active content, New Zealand is harmonising with Australia. Refer to the Australian Pesticides and Veterinary Medicines Authority (APVMA) publication *Standards for Active Constituents* (link below) for the minimum purity limit for the active. If no limit exists or the active is not on the list, then justification for the appropriateness of the proposed minimum content should be supplied.

Requests for exemptions from conforming to the APVMA specifications will need to be supported by arguments, and will be considered on a case-by-case basis.

Standards for Active Constituents
http://www.apvma.gov.au/products/constituents/standards/index.php

2.3.2 Description of chemical and physical characteristics

Physical and chemical characteristics relevant to the active ingredient(s) must include the appropriate characteristics from those listed below:

Physical characteristics:

- **state**
- **colour**
- **melting point range for solids**
- **boiling point/freezing point/range (atmospheric pressure) for liquids**
- **specific gravity**
- **vapour pressure**
- **particle size (sieve tests, median, range)**
- **odour.**

Chemical characteristics

- **isomeric content (enantiomeric, rotational, diastereomeric and/or geometric)**
- **solubility (in water and organic solvents)**
- **hydrolytic properties**

- **photolytic properties**
- **pKa and (aqueous) pH values**
- **n-octanol/water partition coefficient.**

2.3.3 Impurities related to the active ingredient(s)

The issue of significant impurities (including degradation products and contaminants) present in the active ingredient(s) must be addressed.

Any impurities where the toxicology and ecotoxicology is known and of no concern and which are present at a concentration of 10 g/kg or more, must be identified, quantified and reported.

Any impurities of toxicological/residue concern present at any level, including those present at less than 10 g/kg (1%), must be identified, quantified and reported.

Any impurities where the toxicology or ecotoxicology is unknown and which are present at any level, must be identified, quantified and reported.

Details of significant impurities must include:

- **name(s)**
- **CAS number (if available)**
- **quantity (S.I. units)**
- **maximum allowable limits.**

For impurity specifications, New Zealand is harmonising with Australia. Refer to the APVMA publication *Standards for Active Constituents* (link in 2.3.1) for the maximum impurity limit for the active. Please note that it is only the stated impurities and minimum active content that are applicable.

Requests for exemptions from conforming to the APVMA specifications will need to be supported by arguments, and will be considered on a case-by-case basis.

In some cases this publication may not list the active or all impurities of toxicological/residue concern that are found in an active. Therefore the likelihood of such compounds (eg, dioxins, dibenzofurans, hexachlorobenzene and nitrosamines) being present should be considered.

2.3.4 Additives

Any additives (eg, stabilisers) must be identified.

2.3.5 Manufacturing concentrate

A manufacturing concentrate is a form of active ingredient that contains intentionally added inert ingredients, such as stabilisers or solvents.

If a manufacturing concentrate is used, the following information must be provided:

- **the final concentration of the active constituent present**
- **methods used to confirm the active concentration, and**
- **identification of the diluents and/or any additives used, and their concentrations.**

2.4 Batch analysis of the active ingredient

At least one batch analysis of the active ingredient must be provided for each site of manufacture. Provision of the results from analyses of three different batches from each site is preferable if they are available.

Batch analysis of the active ingredient must include:

- **the date of manufacture**
- **batch size**
- **site of manufacture**
- **results for appropriate parameters (eg, active content and impurities as specified above) using appropriate determinative analytical methods (including counter ions when present), and**
- **identification of the analytical method(s) used.**

If the active ingredient is a manufacturing concentrate, batch analysis must also include:

- **the minimum concentration of the active ingredient in the manufacturing concentrate**
- **the minimum purity of the active ingredient**
- **the maximum concentration of all impurities on a dry weight (solvent/additive free) basis, and**
- **the concentrations of diluents and/or additives.**

3 Formulation

3.1 Formulation type

The formulation type of the trade name product must be stated. Select from the list given in section A9 of the Guideline: Product Data Sheet for Registration of an Agricultural Chemical (http://www.nzfsa/govt/nz/acvm/publications/forms/ac-registration-pds-guideline.htm).

3.2 Composition

The formulation declared in the chemistry dossier, and on the product data sheet, must be a complete and accurate list of the ingredients and their concentrations in the trade name product.

Concentrations must be expressed in g/L or g/kg (milligrams or micrograms may be substituted for grams as appropriate). For non-chemical formulations, biological units are acceptable for the active ingredient.

Nominal (discrete) concentration values of ingredients must be given. For excipients, variations within the following limits are considered acceptable.

Nominal concentration of excipient (N) in g/kg or g/L	% Allowable variation relative to N
N ≤ 10	± 10%
10 < N ≤ 200	± 5%
200< N ≤ 1000	± 3%

These limits may be included next to the nominal value within the formulation table (for example, excipient A 6 (5.4-6.6) g/kg, excipient B 100 (95-105) g/kg and excipient C 400 (388-412) g/kg.

If the product contains separate formulations (eg, coatings), show these as separate distinguishable formulations.

3.2.1 Overage

Where an overage (small excess) of an active ingredient has been deliberately added, the actual concentration (nominal plus overage) must also be stated. State whether the overage is intended to cover losses during manufacture, storage, or both.

3.2.2 Multiple formulations

An alternative formulation for a trade name product can be registered when the proposed changes to the formulation do not alter the following properties of the registered trade name product:

- identity and concentration(s) of the active ingredient(s)
- formulation type
- hazard status of the product
- physical and chemical characteristics of the formulated product to the extent that the risk profile under the ACVM Act changes.

3.3 Excipient (non-active ingredient) requirements

3.3.1 Identification of each excipient must include:

- **chemical or IUPAC, ISO and common name (INN)**
- **CAS registry number.**

For any excipient where no CAS number has been assigned (or a CAS number is not applicable), full details of the excipient must be supplied. The details must include:

- **name**
- **the safety data sheet (SDS), and**
- **where the excipient is a mixture, its full formulation information, including the name, CAS number and % of each component in the mixture.**

When a trade name excipient which is a mixture is specified in the product formulation, it cannot be exchanged for any other trade name excipient unless their formulations are identical. If they are not, a formulation change application must be submitted.

3.3.2 Impurities

Any impurities of toxicological/residue concern must be identified, quantified (where appropriate) and reported.

Consider the likelihood of compounds such as dioxins, dibenzofurans, heavy metals, organo-chlorine compounds, PCBs and nitrosamines being present.

We recommend that you identify and quantify, where practical, any impurities present at greater than 10g/kg in the excipients.

3.3.3 Additives

Any additives (eg, stabilisers) must be identified, quantified and reported.

3.4 Batch analysis of the formulation

At least one batch analysis of the formulation must be provided for each site of manufacture.

This can be an analysis of a laboratory, pilot or production batch, provided argument is provided as to why a laboratory or pilot batch can be considered to be representative of a production batch. If there are any concerns in relation to the analysis of a laboratory or pilot batch, results of the analysis of the first commercial batch may be required to be provided post-registration.

Each batch analysis of the formulation must include:

- **the date of manufacture**
- **batch size**
- **site of manufacture, and**
- **results for all the parameters that are included in the release specifications, using the specified methods.**

The time zero analysis from the stability study can be used as the formulation batch analysis.

4 Product specifications

4.1 Release specifications

The release specifications are the specifications which the product must meet before it is released for sale. They include active content (including any impurities formed during manufacture) and the relevant chemical and physical characteristics of the product. Refer to Annex 1 for the recommended chemical and physical parameters based on formulation type.

You must set the release specifications, which should include identification of the method that will be used to test each parameter.

The active content must be at least within the following tolerances (as accepted by the FAO group of experts):

Declared content g/kg or g/L at 20°C	Tolerance

Up to 25	± 15% of the declared content for homogeneous formulations (EC, SC, SL, etc.), or ±25% for heterogeneous formulations (GR, WG, etc.)
Above 25 and up to 100	± 10% of the declared content
Above 100 and up to 250	± 6% of the declared content
Above 250 and up to 500	± 5% of the declared content
Above 500	± 25 g/kg or g/L

Where the proposed release specifications for an active ingredient are outside the above tolerances, this must be fully justified.

Where the formulation contains more than one active ingredient, a release specification must be provided for each active ingredient.

4.2 Expiry specifications

The expiry specifications are the specifications within which the product must be maintained during its approved shelf life.

You must set and justify the expiry specifications, which should include identification of the method that will be used to test each parameter.

The expiry specifications will usually be justifiably wider than the release specifications, particularly where the formulation has a degree of instability. The reason for this is that if the product is released at the low end of a specification and the release and expiry specifications are the same, there is a likelihood the expiry specifications will be breached during the product's shelf life.

The appropriate specifications would usually include the relevant parameters based on formulation type and any appropriate limits for degradation products.

The active content must be at least within the following tolerances:

Declared content g/kg or g/L at 20°C	Tolerance
Up to 25	± 15% of the declared content for homogeneous formulations (EC, SC, SL, etc) or ±25% for heterogeneous formulations (GR, WG, etc)
Above 25 and up to 100	± 10% of the declared content
Above 100 and up to 250	± 6% of the declared content
Above 250 and up to 500	± 5% of the declared content

Above 500	± 25 g/kg or g/L

Where the proposed expiry specifications for an active ingredient are outside the above tolerances, this must be fully justified.

Where the formulation contains more than one active ingredient, an expiry specification must be provided for each active ingredient.

Note that the tolerances stated above refer to percentages of the declared (label) content in both release and expiry specifications. They are not cumulative – for example, the expiry tolerance of ± 5% is considered against the active content stated on the label (100%) and not against the release specification (100% ± 5%).

4.3 Packaging specifications

Details of size, shape, construction material and lining of all packaging to be marketed must be supplied. New component packaging materials must be used unless approval for the use of second hand materials for the packaging of the trade name product has been granted by NZFSA.

Comments on the packaging must be included when the inherent chemical characteristics of the formulated product are such that the packaging must be designed to manage the associated risks (eg, high acidity).

The comments could include notes on inherent chemical or physical characteristics that impact on packaging, for example:

- porosity
- permeability
- impact strength
- closure type
- stability (photolytic and hydrolytic stability of biodegradable packaging).

The pack sizes to be marketed must be specified.

In addition to the pack sizes to be marketed, you may request a pack size range. If we consider that there is no additional risk, pack sizes within the assessed range and specifications (such as construction material) will be considered approved. When additional pack sizes within the approved range and specifications are to be marketed, we only require a letter of notification of the marketed pack sizes.

5 Manufacturing

5.1 Manufacturer of the trade name product

The following details must be provided for every site of manufacture (including repackers/relabellers) of the trade name product:

- **name of organisation**
- **postal address**
- **physical address**
- **telephone, fax and email details**
- **name of contact person.**

5.2 The responsible manufacturer*

The following details must be provided for the responsible manufacturer of the trade name product:

- **name of organisation**
- **postal address**
- **physical address**
- **telephone, fax and email details**
- **name of contact person.**

*The responsible manufacturer is the entity who ensures that the formulated agricultural chemical is in compliance with NZFSA registration and releases it for sale. There are occasions where more than one manufacturer is involved in the manufacturing process (split manufacture). For example, one manufacturer may fill a product that has been manufactured by another.

5.3 Manufacturing process

Provide a description of all stages involved in the manufacture of the trade name product. This should be in the form of a *simple* flow diagram (see below) with explanations. The description must identify the manufacturing process from the starting materials through to the packaged and labelled product.

Provide sufficient detail to cover at least the essential steps and processes—for example, when the product or its ingredients are exposed to heat or processes likely to lead to toxic impurities.

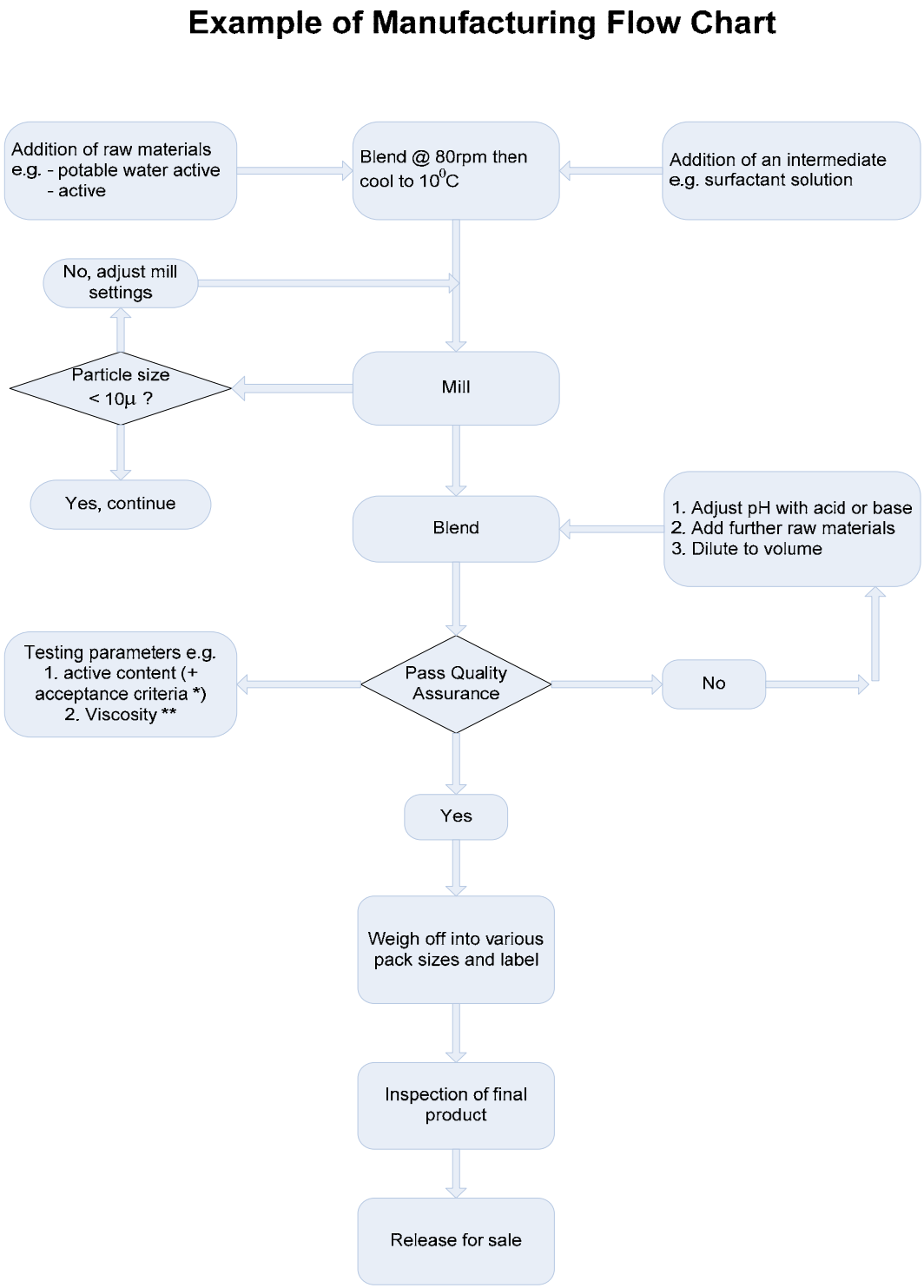
5.3.1 Flow diagram requirements

The flow diagram of the manufacturing process represents the sequence of the manufacturing steps and the process controls used during the production to monitor and, if appropriate, adjust the process to ensure the trade name product meets the release specifications. If alternatives processes can be used, the information is to be provided for each alternative.

- **The flow chart must show where starting materials enter the manufacturing process. The entire manufacturing process must be included (starting materials through to trade name product release.) Each manufacturing step must be included.**
- **Critical manufacturing control points must be identified on the process flow diagram. The critical control points identified should be the relevant ones that are controlled during the manufacturing process by objective measurement.**
- **In-process and final product quality control testing**
  In-process and final product quality control testing steps must be identified on the process flow diagram. Include a reference to the analytical method at the particular step (eg, HPLC method Ref 01). If methods are published in a monograph or similar the reference is adequate. If in-house methods are used, the test reference should be clearly traceable to the information supplied in section 7, Analytical Methods. All quality control tests must be supported by ranges, limits or acceptance criteria.
- **Filling, packing and labelling**
  The flow diagram must also include a description of the filling process into the final product container and associated closure system (eg, cap), the attachment of market labels with required batch number and expiry date.
- **Final release for sale**
  Brief description of the final inspection to ensure compliance with the NZFSA registration, approved label and release for sale.
- **Typical batch size must be stated**.

If the manufacturing process is complex, you may need to provide more details than you can show on the flow diagram.

5.3.2 Flow Diagram



* Active concentration determined by HPLC method1 (reference section 7)
** Viscosity is determined by Brookefield cup method

5.4 Labelling requirements

Refer to the labelling information requirements on our website.

6 Stability testing of the trade name product

The purpose of stability testing is to provide evidence on how certain specified characteristics of the product vary with time under the influence of a variety of environmental factors, such as temperature, humidity and light. This enables recommended storage conditions and shelf lives to be established.

A proposed shelf life must be nominated.
This is the length of time supported by the stability data.

The proposed storage conditions for the product, including temperature range and any other specific conditions, must be stated both on the label and in any product literature. This is particularly important for products where the risk characteristic inherent in the product is one that is affected by storage conditions—for example, freezing, high temperatures or exposure to water, light or oxygen (air).

Stability studies must incorporate identification and quantitative analysis of any toxic degradation products.

Provide discussion on any observed variations from the expiry specifications and the likely impact of these variations on the proposed shelf life of the trade name product.

For example, if the formulated trade name product is altered before use (eg, diluted or dissolved), you must confirm that any changes occurring over the shelf life of the product do not adversely affect that process.

Provide discussion on any unusual results and any significant changes within a given parameter even if the product remains within specification

6.1 Stability study requirements

Stability studies must be conducted on the trade name product.
This means the formulation of the product used in the stability studies must be the same formulation as stated on the registration application form. Confirmation that this is the case must be given.

Stability studies must be conducted on at least one batch of the product. This must be either a production batch or representative of a production batch in terms of process (for example a

laboratory or pilot scale batch which simulates the equipment, procedures and controls which will be used in a production batch). When a production batch is not used, argument must be provided to support how the batch represents a production batch.

Each batch tested must be uniquely identified, including

- **the batch identifier**
- **the date of manufacture**
- **the batch size, and**
- **the site of manufacture.**

All the recommended parameters for the formulation type (as listed in Annex 1) must be tested before and after storage. Any deviation must be fully justified.

The stability study must be conducted on the product in the packaging for sale, and in one of the proposed marketed packaging sizes which is representative of all those that are to be sold. If multiple formulations and/or packaging types are proposed to be used, data must be generated for each formulation and packaging type. Any variations from this must be fully justified.

Non-compliance with the stated procedure (temperature, time or other conditions) must be fully justified.

Exemption from conducting a stability study for actives listed in Annex 2 will be considered by NZFSA. Requests for the exemption must be fully supported and batch analysis from at least one batch must be provided. No shelf life greater than five years will be granted under this waiver.

6.2 Stability study conditions

The stability trials may be conducted as either accelerated and/or real time studies.
However, please note that a real time study is required for trade name products containing actives listed in Annex 3.

6.2.1 Accelerated studies

These must be performed for a minimum of 14 days duration at 54°C. Some preparations may not be stable under these conditions. In these cases, alternative time/temperature regimes may be proposed but the choice must be supported by a reasoned, scientific case. Each batch tested must include initial (Time=0 days) and final readings.

If samples analysed in the accelerated stability study do not exceed the expiry specifications*, then a two-year shelf life will usually be deemed applicable.

* If the active content differs by ≥5% of the initial reading or there is a change of concern in one of the physical parameters, then a suitable interim shelf life will be granted and a real time study to two years will be required. This study must be performed on a sample retained in its market packaging from the first production batch produced. Readings must be taken initially (at release of the batch) and at specified time intervals, usually 6 monthly. The approval letter will state the parameters that are to be measured and when this information must be supplied. If the interim readings suggest the product will be outside specifications prior to the specified time period results must be supplied immediately.

An application for an extension beyond two years may be requested. To achieve this, the stability trial of 14 days duration at 54°C, would be conducted on samples that had been stored at ambient temperature in their market packaging for a given length of time. If approved, the new shelf life of the product would then become the time spent at ambient temperature plus two years. For example, if the product was stored for three years at ambient temperature and an accelerated stability study was then performed, a five year shelf life would be granted providing the expiry specifications were not exceeded.

6.2.2 Real time studies

These studies are to be performed at either ambient temperature or at, or above, 25°C. Ambient temperature studies must reflect the minimum and maximum temperature that the trade name product is likely to face throughout its lifetime. However if the product is to be stored under special conditions during use (eg, frozen or under refrigeration), the stability data must be generated under the same conditions. Each batch tested must include initial (Time = 0 days) readings and final readings.

Where appropriate for the product, registrants can propose their own storage conditions to reflect how the product will actually be stored. Supporting argument should be provided.

It is recommended the frequency of testing is every three months over the first year, every six months over the second year and then annually thereafter. If interim readings are not taken and the final readings are considered unsatisfactory, a very conservative shelf life will be assigned as no interim data exist.

If the data submitted as part of the real time stability study do not exceed the expiry specifications, then a shelf life equivalent to the length of time to which the batch/es are tested will be deemed applicable.

An argument for a shelf life up to 1.5 times longer than this time period, up to a maximum of 5 years, may be acceptable assuming packaging integrity is maintained and there is minimal change in all parameters tested. This is not applicable for products with actives listed in Annex 3.

7 Analytical methods

The analytical methods used for testing of the technical active ingredient, stability testing and finished product testing (those methods used to test the product to ensure it meets the required specifications) must be described.

It is not necessary to supply a copy of the method if it is a published method from FAO, CIPAC or AOAC. A summary or abstract of the method may be provided with the reference citation attached.

Any variations from nominated standard methods (eg, FAO, CIPAC or AOAC, and other internationally recognised standards) must be provided.

The analytical methods used to determine the concentration(s) of the active ingredient(s) in the formulation must be validated in the testing laboratory prior to implementation. A copy of the method validation report must be provided.

The EU guideline SANCO/3030/99 rev.4 11/07/00 and the APVMA Guideline (links below) may be useful in respect of the validation of the analytical method used for determining the concentration of the active ingredient.

Internal methods are acceptable where these have been validated and all reference materials used are traceable. Where internal methods are used or referenced, an authorised copy of the methods and the validation itself must be provided. Where an active ingredient is a stereoisomer or geometrical isomer of a molecule then the method must demonstrate the required specificity.

It must be demonstrated that all analytical methods used to determine the concentration(s) of the active ingredient(s) are specific to the active ingredient(s) and have acceptable specificity, linearity, range, precision and accuracy. It must be demonstrated that all analytical methods used to determine the concentration(s) of any of the impurities are specific to that compound.

EU Guideline
http://ec.europa.eu/food/plant/protection/evaluation/guidance/wrkdoc13_en.pdf

APVMA Guideline
http://www.apvma.gov.au/publications/guidelines/docs/gl_69_analytical_methods.pdf

Annex 1: Recommended Chemical and Physical Parameters Based on Formulation Type

Any variations from the tests must be explained and justified.

In some cases it may be applicable to test for additional parameters.

Further guidance can be found in the *FAO Pesticide Management Manual on Development and Use of FAO and WHO Specifications for Pesticides* (March 2006 revision of the first edition) (link below).

This also contains information on the testing of some of the formulation types that are not listed below.

If the formulation type is not listed in the tables below or in the *Manual on Development and Use of FAO and WHO Specifications for Pesticides (March 2006 revision of the first edition)*, use the one that bears the closest resemblance to the formulation type required. In such cases consideration should be given to whether it may be appropriate to add additional parameters.

FAO Manual

Collaborative International Pesticide Analytical Council (CIPAC) methods are published in the CIPAC Handbooks. Details of the CIPAC handbooks may be obtained from Black Bear Press, Kings Hedges Road, Cambridge, UK.

AEROSOL (AE)

Recommended Test Parameters	Relevant CIPAC Method/Comments
Active content	Appropriate validated method
Packaging stability	Observation of packaging stability (no corrosion and no nozzle blockage)

AQUEOUS CAPSULE SUSPENSION (CS)

Recommended Test Parameters	Relevant CIPAC Method/Comments
Appearance (physical state, colour)	
Active content	Appropriate validated method
Acidity/alkalinity or pH	MT 75 or MT 191
Pourability	MT 148
Suspensibility	MT 184
Spontaneity of dispersion	MT 160
Wet sieve test	MT 185
Persistent foam	MT 47.2
Particle size distribution (if required)	MT 187

Viscosity (if required)	MT 192
Packaging stability	Observation of packaging stability and integrity

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
Pourability	MT 148
Wet sieve test	MT 185
Packaging stability	Observation of packaging stability to include a statement on claying, sedimentation and re-dispersibility

GELS

Recommended Test Parameters	Relevant CIPAC Method/Comments
Appearance (physical state, colour)	Evidence the physical state has been maintained and there has been no phase separation
Active content	Appropriate validated method
Acidity/alkalinity or pH	MT 31, MT 75 or MT 191
Kinematic viscosity	MT 22, MT 192, OECD 114
Miscibility	Only required if to be dispersed in water
Emulsion characteristics	MT 36.3 (0.1-5% dilution) or MT 183 (1% dilution) or MT 180 ; only required if to be emulsified in water
Wet sieve test	MT 185; Only required if to be dispersed in water
Suspensibility	MT 184; Only required if to be suspended in water
Packaging stability	Observation of packaging stability

GRANULES (GR)

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
Particle size distribution	MT 58.*2* or 58.3
Dust content	MT 171
Friability and attrition characteristics	MT 178
Release rate of active constituent	Suitable validated method/ Only applicable to controlled release granules
Packaging stability	Observation of packaging stability; there should be no loss of granule integrity or caking on storage

LIQUID (READY TO USE)

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
Packaging stability	Observation of packaging stability

OIL MISCIBLE LIQUID (OL)

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

Miscibility with hydrocarbon oil	MT 23
Packaging stability	Observation of packaging stability

POWDER FOR DRY SEED TREATMENT (DS)

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
Adhesion to seeds	MT 83 may be applicable; if not, the company should supply an alternative procedure
Dry sieve test	MT 59.1
Packaging stability	Observation of packaging stability

SMOKE GENERATOR (FU)

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
Burning time	
Evidence of combustibility	The quantity of material remaining after combustion should be determined
Packaging stability	Observation of pack integrity

SOLUBLE CONCENTRATE (SL)

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
Packaging stability	Observation of packaging stability

SUSPENSION CONCENTRATE (SC)

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
Pourability	MT 148
Suspensibility	MT 184
Spontaneity of dispersion	MT 160
Wet sieve test	MT 185
Packaging stability	Observation of packaging stability to include a statement on

	claying, sedimentation and re-dispersibility

TABLETS (TB)

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
Tablet Integrity	The data should demonstrate the mechanical robustness of the tablets
Degree of dissolution and solution stability *	MT 179
Suspensibility #	MT 184
Wet sieve test	MT 185
Disintegration time	
Packaging stability	Observation of packaging stability

* Where the table is water-soluble then degree of dissolution and solution stability should also be tested.

Where the tablet is water-dispersible then suspensibility should also be tested.

ULTRA LOW VOLUME LIQUID (ULV)

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
Kinematic viscosity	MT 22, MT 192, OECD 114
Packaging stability	Observation of packaging stability

WATER-DISPERSIBLE GRANULES (WG)

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
Wet sieve test*	MT 185
Suspensibility*	MT 184
Wettability*	MT 53.3
Dispersibility	MT 174
Dust content	MT 171
Flowability	MT 172
Dissolution of water-soluble bags	MT 176/ Only for the product packaged in a sealed water-soluble bag
Packaging stability	Observation of packaging stability

*Where the product is packaged in a water-soluble bag then the wet sieve test, suspensibility and wettability test must be carried using a solution of the product and water-soluble bag in the same ratio as in the recommended application.

WATER-DISPERSIBLE POWDER (WS)

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
Wet sieve test	MT 185
Wettability	MT 53.3
Packaging stability	Observation of packaging stability

WATER-SOLUBLE GRANULES (SG)

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
Degree of dissolution and solution stability*	MT 179
Dissolution of water-soluble bags	MT 176/ Only for the product packaged in a sealed water-soluble bag
Packaging stability	Observation of packaging stability

*Where the product is packaged in a water-soluble bag then the wettability, degree of dissolution and solution stability test must be carried using a solution of the product and water-soluble bag in the same ratio as in the recommended application.

WATER-SOLUBLE POWDER (SP)

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
Persistent foam	MT 47.2
Wettability*	MT 53.3
Degree of dissolution and solution stability*	MT 179
Dissolution of water-soluble bags	MT 176/ Only for the product packaged in a sealed water-soluble bag
Packaging stability	Observation of packaging stability

*Where the product is packaged in a water-soluble bag then the wettability, degree of dissolution and solution stability test must be carried using a solution of the product and water-soluble bag in the same ratio as in the recommended application.

WETTABLE POWDER (WP)

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
Wet sieve test*	MT 185
Suspensibility*	MT 184
Wettability*	MT 53.3
Dissolution of water-soluble bags	MT 176/ Only for the product packaged in a sealed water-soluble bag
Packaging stability	Observation of packaging stability: include a statement no caking on storage

*Where the product is packaged in a water-soluble bag then the wet sieve test, suspensibility and wettability test must be carried using a solution of the product and water-soluble bag in the actual ratio of application.

Annex 2: Stability Study Exemptions for Agricultural Chemicals Compounds

The following compounds, pure or in any combination with each other or excipients, may be appropriate for an application of exemption from conducting stability studies:

- Copper sulphate (any degree of hydration)
- Copper oxychloride
- Sulphur
- Carbonate, sulphate and phosphate salts of calcium, magnesium or zinc (any degree of hydration)
- Mineral oils
- Chitosan
- Iron phosphate
- Iron EDTA
- Canola oil / methyl canolate

Annex 3: Active Ingredients that Require Real Time Stability Studies of the Trade Name Product

- Organisms (including, in particular, nematodes, bacteria, viruses, algae or protozoa) (will be placed in Biological Standard once completed)
- Mancozeb, including testing for ethylene thiourea
- Acephate, including testing for O,O,S-trimethylphosphorothioate
- Diazinon, including testing for 0,0,0',0'-tetraethyl thiopyrophosphate (0,S-TEPP) and 0,0,0',0'-tetraethyl dithiopyrophosphate (S,S-TEPP)
- Dimethoate, including testing for 0,0,S-trimethyl phosphorodithioate

Note: The need to conduct real time studies on formulated products containing Maldison has been removed due to an accelerated stability test recently published by the FAO being considered appropriate.

Annex 4: Active Ingredients Exempt from Notification of the Manufacturer

- Calcium carbonate
- Copper sulphate (any degree of hydration)
- Copper oxychloride, copper hydroxide
- Sulphur
- Food quality ingredients.

Evidence of a quality system needs to be provided for these actives if the manufacturer is not notified. A quality system should provide assurance that the active will meet ACVM approved specifications prior to its inclusion in the formulated product.

An internal record of the active manufacturers used and batch analysis certificates which confirm that the active is fit for purpose must be available for immediate inspection.