agriculture

Department:
Agriculture
REPUBLIC OF SOUTH AFRICA

CHEMISTRY DATA REQUIREMENTS GUIDELINE

ISSUED BY THE REGISTRAR: ACT NO. 36 OF 1947, PRIVATE BAG X343, PRETORIA, 0001

REPUBLIC OF SOUTH AFRICA

JUNE 2026

Table of Contents

INTRODUCTION 4
USE OF THIS GUIDELINE 5
DEFINITION OF TERMS / GLOSSARY 6
Active ingredient (see TC or TK) 6
Analytical standard 6
Co-formulant or formulant 6
Formulation 6
Manufacturer 6
OECD GLP 6
Packaging 6
Reference profile 6
Reference specification 6
Relevant impurities 6
Significant impurities 7
Technical Grade Active Ingredient (TGAI) 7
Technical material (TC) 7
Technical concentrate (TK) 7
1. DATA REQUIREMENTS FOR THE REGISTRATION OF TECHNICAL GRADE ACTIVE INGREDIENTS: NEW ACTIVE INGREDIENTS 8
1.1. General description of the batch 8
1.2. Identity of the active ingredient (TGAI) 9
1.3. Physical and chemical properties of the active ingredient (TGAI) 9
1.4. Manufacturer and manufacturing site 10
1.5. Description of the manufacturing process 10
1.6. Active ingredient content (TGAI) 11
1.7. Impurities 11
1.8. Analytical methods 12
1.9. Method validation 13
1.10. Mass accountability 13
1.11. Declaration of composition 14
1.12. Toxicological data 14
2. DATA REQUIREMENTS FOR THE REGISTRATION OF TECHNICAL GRADE ACTIVE INGREDIENTS: ALTERNATIVE SOURCES 15
2.1. Determination of equivalence 16
2.2. General description of the batch 17

2.3. Identity of the active ingredient (TGAI) 18
2.4. Physical and chemical properties of the TGAI 18
2.5. Manufacturer and manufacturing site 19
2.6. Description of the manufacturing process 19
2.7. Active ingredient content 20
2.8. Impurities 20
2.9. Analytical methods 21
2.10. Method validation 22
2.11. Mass accountability 22
2.12. Declaration of composition 23
2.13. Toxicological data (if required see Paragraph E & F) 23
2.14. Steps to be followed to determine equivalence 24
3. DATA REQUIREMENTS FOR THE REGISTRATION OF A FORMULATION 25
3.1. Physical and chemical properties of the formulation type 25
3.2. Shelf-life (storage stability conditions) 26
3.3. Stability of the packaging material 27
3.4. Low temperature stability testing 27
3.5. Active ingredient content 28
3.6. Analytical methods 28
3.7. Method validation 29
4. DATA REQUIREMENTS FOR THE REGISTRATION OF A FORMULATION SITE 29
4.1. New formulator requirements 29
4.2. Physical and chemical studies 29
5. REFERENCES 30
ANNEXURE A: Active ingredients for which a Certificate of Analysis is required 31

INTRODUCTION

This Guideline details the chemistry data requirements for registration of agricultural remedies under the Act No. 36 of 1947. This is the revised document which replaces the "Chemistry Data Requirements Guidelines" from March 2021. Applications submitted prior to the date of implementation may conform to the previous version of the guideline. Applications submitted after the publication of the guideline must conform to the latest version of the guideline, unless it can reasonably be demonstrated that studies were initiated prior to the publication of the latest version of the guideline. This document is aimed at clearing any ambiguity around the registration of a technical material itself or incorporated in any formulation and to provide clear understanding to applicants on what information is required for registration purposes. This guideline should be read in conjunction with all other relevant guidelines published by the office of the Registrar (Act No. 36 of 1947). Applicants are advised to consult the relevant technical adviser for full details on registration requirements before submitting a registration application.

The Department of Agriculture (DoA), through Act No. 36 of 1947 is required to approve active ingredient(s) contained in an agricultural remedy intended for distribution, sale or use in South Africa. This applies regardless of whether the product is formulated in South Africa or overseas.

The chemical equivalence of a source of a technical grade active ingredient (TC/TK) must be determined and established to be compliant with European Regulation (EC) No. 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market. This regulation repealed the Council Directives 79/117/EEC and 91/414/EEC. Regulation (EC) No. 1107/2009 as amended, sets out the data requirements for the approval of a source of a technical grade active ingredient.

The storage stability of the formulated product must be determined in accordance with the Manual on Development and Use of FAO and WHO Specifications for Pesticides (latest version) and the Australian Pesticides and Veterinary Medicines Authority (APVMA) Guidelines for the Generation of storage stability data of agricultural chemical products (latest version). Results must be in line with active ingredient specific FAO specifications, where available.

To ensure data submitted to the Registrar (Act No. 36 of 1947) for evaluation is unbiased and true, it is imperative that laboratories function impartially of the applicant applying for registration and there is no conflict of interest. Impartial means the presence of objectivity and will be determined in accordance with the 'General requirements for the competence of testing and calibration laboratories' (section 4.1, general requirements, ISO / IEC 17025 International Standard):

- Laboratory activities shall be undertaken impartially and structured and managed so as to safeguard impartiality.
- The laboratory management shall be committed to impartiality.
- The laboratory shall be responsible for the impartiality of its laboratory activities and shall not allow commercial, financial or other pressures to compromise impartiality.
- The laboratory shall identify risks to its impartiality on an on-going basis. This shall include those risks that arise from its activities, or from its relationships, or from the relationships of its personnel. However, such relationships do not necessarily present a laboratory with a risk to impartiality.

NOTE: A relationship that threatens the impartiality of the laboratory can be based on ownership, governance, management, personnel, shared resources, finances, contracts, marketing (including branding), and payment of a sales commission or other inducement for the referral of new customers, etc.

- If a risk to impartiality is identified, the laboratory shall be able to demonstrate how it eliminates or minimizes such risk.

USE OF THIS GUIDELINE

These guidelines are to be used by Technical Advisers of Act No. 36 of 1947, new applicants, existing registration holders and testing facilities.

It is incumbent on manufacturers of the technical material to supply the information required under section 2 and to follow the steps for determination of equivalence or to supply whatever information they may have on the chemical composition of the product. The demonstration of chemical equivalence does not suggest that the formulated product will result in the same efficacy, phytotoxicity or residue trends as compared to the original reference standard. Therefore, registration holders will be required to conduct such tests as per the guidelines published by the Office of the Registrar.

This guideline is specific to conventional agricultural remedies, such as synthetic, chemical pesticides. In the case of non-conventional agricultural remedies, such as biological products or semiochemicals, this guideline may be used to provide guidance on the type of data to be submitted in support of registration. Where a guideline specific to the type of remedy exists, such guideline should be used preferentially to determine the data required for registration. Where a guideline specific to the type of remedy does not exist, the current guideline should be used as guidance.

DEFINITION OF TERMS / GLOSSARY

Active ingredient (see TC or TK)	The part of the product that provides the agricultural remedy action as claimed.
Analytical standard	Also named the purified active ingredient. It is a material resulting from any manufacturing process, industrial or from laboratory, which is purified enough to reach a minimum purity of 980 g/kg. It is accurately characterized, comprising the active ingredient, together with very low amounts of associated impurities.
Co-formulant or formulant	Any substance, other than a technical grade active ingredient, intentionally incorporated in a formulation.
Formulation	The combination of various ingredients designed to render an agricultural remedy useful and effective for the purpose claimed and for the envisaged mode of application.
Manufacturer	Manufacturer means a corporation or other entity in the public or private sector (including any individual) engaged in the business or function (whether directly or through an agent or entity controlled by or under contract) of manufacturing a pesticide active ingredient or preparing its formulation or product.
OECD GLP	The Organisation for Economic Co-operation and Development series on the Principles of Good Laboratory Practice, which is a managerial quality control system covering the organisational process and the conditions under which non-clinical health and environmental studies are planned, performed, monitored, recorded, reported and retained (or archived).
Packaging	The container together with the protective wrapping used to contain formulations.
Reference profile	The composition of a technical material (TC), or technical concentrate (TK) where appropriate, upon which the reference specification is based, including active ingredient content (range and specified minimum), impurity profile and impurities identified as relevant (with maximum limits), together with the corresponding toxicological and ecotoxicological profiles. Reference profiles are confidential to Act No. 36 of 1947. Where appropriate, a reference profile may incorporate data submitted by more than one applicant or registration holder.
Reference specification	The current published Food and Agricultural Organization of the United Nations (FAO) and World Health Organization (WHO) specification for a pesticide, where this has been developed according to the evaluation procedure of the FAO/WHO or the specification submitted by the original registration holder. The reference specification is used to determine the equivalence of a technical material and/or formulation of a subsequent manufacturer.
Relevant impurities	Those by-products of the manufacturing process or storage of a pesticide which, compared with the active ingredient, are toxicologically significant to health or the environment, are phytotoxic to treated plants, cause taint in food crops, affect the stability of the

	pesticide, or cause any adverse effect. Relevant impurities are usually disclosed on reference specifications.
Significant impurities	Those by-products of the manufacturing or storage of a pesticide which are present in material accountability studies in quantities equal or above 1 g/kg and as a consequence shall be specified.
Technical Grade Active Ingredient (TGAI)	This refers to either technical material (TC) or technical concentrate (TK).
Technical material (TC)	A material resulting from a manufacturing process comprising the active ingredient, together with associated impurities. This may contain small amounts of necessary additives.
Technical concentrate (TK)	A material resulting from a manufacturing process comprising the active ingredient, together with associated impurities. This contains small amounts of necessary additives and appropriate diluents.

1. DATA REQUIREMENTS FOR THE REGISTRATION OF TECHNICAL GRADE ACTIVE INGREDIENTS: NEW ACTIVE INGREDIENTS

Batch analysis results for at least five commercial-scale production batches of the technical grade active ingredient (TGAI) should be submitted to demonstrate routine compliance with the Declaration of Composition of the TGAI and to demonstrate that the manufacturer is in control of the process. The 5-batch analysis should be conducted by an OECD GLP compliant laboratory within the last 10 years (at the date of submission), provided a declaration by the manufacturer accompanies the 5-batch analysis if it is older than 5-years but younger than 10 years, to confirm that the manufacturing process and facility have not changed since the 5-batch analysis was conducted and quality control (QC) data for recent batches are provided in support (i.e., results of analysis of batches of the technical grade active ingredient analysed under GLP or non-GLP conditions, including information on all relevant impurities).

- Results from QC data need to conform to the same specifications as the 5-batch analysis.
- Where QC data is performed by a different laboratory that conducted the 5-batch analysis, QC data should include method validation.
- QC data should be submitted for 5-batches produced in the last 5 years, or if less than 5 batches were produced during this time, QC data for all batches produced in the last 5 years should be submitted.
- QC data should include chromatograms (or equivalent, depending on the method of analysis used).

The age of the 5-batch analysis is determined by considering the completion date of the study. Explanations of amendments are mandatory.

In case of multiple sources of production, one 5-batch analysis report should be submitted per manufacturing site. If data on commercial scale batches are not available, data of laboratory scale or pilot scale batches (manufactured using the same process as intended for commercial scale batches) may be submitted. Once registration has been granted, data on commercial scale batches should be provided within one year. If this data is not available within one year, a justification shall be provided.

The batch results should be provided based on the following parameters:

1.1. General description of the batch

- Batch size
- Batch number
- Date of manufacture
- Date of analysis
- Date of expiry – if the product is not stable, it must be stated and an expiry date is compulsory.

1.2. Identity of the active ingredient (TGAI)

- ISO English common name (and its status)
- Chemical name (IUPAC and CA)
- Chemical Abstracts Service (CAS) No.
- CIPAC No. (if applicable)
- Structural formula
- Molecular formula
- Molecular mass

1.3. Physical and chemical properties of the active ingredient (TGAI)

Please note: The following properties must be determined and reported.

- A general description, for example, appearance, colour, odour, physical state
- If a new active ingredient contains one or more chiral centres, a specification of whether the active constituent is a pure enantiomer, racemate or fixed combination of non-enantiomeric isomers.
- If a new active ingredient contains geometric isomers (*cis/trans, E/Z*), a specification of whether the active constituent is a pure geometric isomer, or a fixed combination of geometric isomers.
- The melting point or range (for solids)
- The boiling point or range (for liquids)
- If the melting and/or boiling point cannot be determined because of decomposition or sublimation, the temperature at which decomposition or sublimation occurs.
- The flash point (where the melting point is below 40°C)
- The flammability including auto-flammability
- Explosive properties
- Photochemical properties
- Oxidising properties
- The auto-ignition temperature
- Corrosion characteristics

1.4. Manufacturer and manufacturing site

The manufacturer should provide the name and business address of the manufacturing plant of the technical grade active ingredient (TGAI) and the street address in which the TGAI is manufactured. If a toll or contract manufacturer is involved, the name and business address of the manufacturing plant of the active ingredient and the street address in which the active ingredient is manufactured should be provided.

The manufacturer together with the applicant should familiarize themselves with all relevant guidelines published by the office of the Registrar (Act 36 of 1947) before manufacturing any agricultural remedy that is intended to be registered in South Africa under Act No. 36 of 1947.

1.5. Description of the manufacturing process

An accurate and detailed description of the manufacturing process and process controls should be provided for each manufacturing site and include the following information:

- An introductory paragraph detailing the number of chemical steps, whether the process is a batch or continuous process, and significant purification steps.
- A flow-diagram of the synthetic processes that outlines the sequence of all the steps.
- A reaction scheme that outlines the sequence of all the chemical reactions including molecular formulae.
- Chemical structure of starting materials, intermediates, reagents and catalysts.
- The final products formed.
- Amounts used or formed.
- Yields obtained.
- The relative amounts of each starting material and their order of addition.
- The reaction conditions (temperature, pressure, pH, reaction times and addition rate, etc.)
- The duration and yield of each step of the process.
- Information on intermediates that are isolated and purified.
- A description of any purification procedure for the active ingredient, including procedures to recover starting materials, intermediates or the final product.
- If a Technical Concentrate is produced, details must be provided of the final specified concentration of the active ingredient present including justified range, methods used to confirm the concentration, and details of the diluents and/or any additives used.
- Description of compounds intentionally added to the Technical Material (TGAI) (e.g., stabilizers). The synthetic process should be described in sufficient detail to enable the evaluators to assess the potential presence of impurities of toxicological relevance.

1.6. Active ingredient content (TGAI)

1.6.1. The following analytical results shall be reported:

- Identification of the active ingredient
- The active ingredient content, determine with a validated analytical method according to international criteria for validation and the results on the same sample should not deviate more than authorised by the validation of the method.

1.6.2. The following information must be included in the analytical report (for chromatographic methods – where other methods of analysis were used, equivalent data of relevance must be included):

- Reference to the analytical methods and validation reports used to generate the data.
- The batch number of the tested batches.
- The analytical reference standard(s) used for the determinations.
- Copies of the original data and images from the chromatographic system which include a software-generated table with retention time, peak areas or peak-height of the associated peaks and relevant chromatogram tables.
- Chromatograms should be clearly labelled with the following:
    - Batch number (or internal laboratory reference number/code linked to the specific batch)
    - Peak identity, e.g. retention time or compound name
    - Peak integration
- Worked examples of all calculations.

1.7. Impurities

1.7.1. All impurities

Information on impurities that are, or may be, present in the technical grade active ingredient (TGAI) at levels greater than or equal to 1 g/kg should be provided (i.e., significant impurities). Note that toxicologically relevant impurities at any level must be characterised and reported. The concentration of impurities should be quantified against their own reference standards. The use of analogue standards must be justified.

Potential sources of impurities or related substance include:

- Impurities in the starting materials from incomplete or side reactions, or isomerisation, residual solvents, reagents and immediate precursors.
- Trace elements arising from the use of catalysts or other sources
- The degradation of the active ingredient that may occur after manufacture.

1.7.2. Impurities of toxicological relevance (relevant impurities)

If there is potential for the formation of toxic impurities and/or by-products, this must be declared and quantified. Details of the conditions leading to their formation and the steps taken to control the formation of toxic impurities should be provided. All impurities identified as toxicologically relevant must be properly analysed regardless of manufacturing process used or non-appearance during screening process. Area normalization is not accepted.

1.7.3. Data to be submitted

Data to be submitted with respect to impurities must include:

- Structural formula
- CAS number
- A scheme for the formation of the impurity, followed by a text discussion of its formation.
- A justification of the limits of these impurities should be provided.
- Results of the analytical determination of the content of each impurity present at a concentration of 1 g/kg or more (significant impurities), using specific methods. Actual numerical results should be provided rather than vague statements such as "within limits" or "conforms".
- Content of toxicological relevant impurities (present at any level)
- Chromatograms or spectroscopic data (or any suitable data depending on the method of analysis) of batches showing separation of impurities. Chromatograms should be clearly labelled with
    - Batch numbers (or internal laboratory reference number/code linked to the specific batch)
    - Peak identity
    - Peak integration data
    - A software-generated table with retention time and peak area of associated peaks
    - A copy of all raw data used to generate the final results.

1.8. Analytical methods

1.8.1. Full details of the test methods used for determining the following:

- Active ingredient
- All impurities at or above 1 g/kg (significant impurities)

- Relevant impurities (even when present at less than 1 g/kg should be submitted)

1.8.2. The following information should be included in a written analytical method:

- A copy of the actual laboratory method. If this laboratory method is not in English, please include an English version.
- The principle of the method.
- The method summary
- Sample preparation techniques
- Equipment or reagents (for example, for chromatographic methods, details of the column including column name, manufacturer, packing material and dimensions)
- Eluent (including gradients, where applicable)
- Column temperature
- Detector and retention times of all components where chromatographic techniques are used.

1.9. Method validation

Validation data for the method(s) used to assay the active constituent and impurities should be provided. The following parameters should be addressed:

- Selectivity
- Linearity
- Precision
- Recovery (accuracy)
- Limit of detection (LOD) for impurities
- Limit of quantitation (LOQ) for impurities

Note that LOD and LOQ may not be required for the quantitation of the active ingredient, only the determination and quantitation of the impurities.

1.10. Mass accountability

The sum of the quantitative level of the active ingredient and impurities is often referred to as the mass balance. Mass balance is an important parameter in batch analysis to ensure that all major impurities have been detected. The mass balance need not add up to exactly 100 percent, because of analytical error associated with each analytical procedure; however, it is expected to be in the range of 98 – 102 percent. In other words, the unidentified fraction of each batch must not exceed 2 percent (20 g/kg).

1.11. Declaration of composition

A comprehensive declaration of composition (DoC) for the active ingredient should be submitted. The DoC should be signed and dated and include the following information:

- The minimum purity of the active ingredient (in grams per kilogram [g/kg] or grams per litre [g/L], as appropriate) on a dry weight basis, as well as the ratio of the content of isomers or diastereoisomers (where relevant) and according to the active ingredient definition. For active ingredients listed in Annexure A: Active ingredients for which a Certificate of Analysis is required (no 5-batch analysis), the maximum content of all impurities present in quantities of 1 g/kg or more and any toxicologically relevant impurities present at any level (including less than 1 g/kg).

When the active ingredient is a Technical Concentrate (TK):

- The minimum and maximum concentration of the active ingredient in the technical concentrate
- The minimum purity of the active ingredient and the maximum content of all impurities on a dry-weight (solvent or additive free) basis
- The content of diluents and/or any additives in g/kg

The chemical names with company code numbers, CAS registry numbers where they exist, empirical formula, molecular weight, structural formula for all identified impurities.

All impurities present at or above 1 g/kg level must be identified. If identification of an impurity is not feasible, a summary of laboratory studies demonstrating the unsuccessful effort should be included in the application. There is no need to identify impurities that are not of toxicological relevance and are below levels of 1 g/kg.

1.12. Toxicological data

1.12.1. Toxicological profile of the TGAI based on acute oral, dermal and inhalation toxicity, skin and eye irritation, skin sensitization.

1.12.2. Toxicological profile of the TGAI based on repeated administration (from sub-acute to chronic) and studies such as reproductive and developmental toxicity, genotoxicity, carcinogenicity, developmental and adult neurotoxicity, etc.

1.12.3. Ecotoxicological profile of the TGAI based on toxicity to aquatic and terrestrial organisms (e.g., fish, crustaceans, algae, birds, bees) as appropriate to the intended use, and information on persistence.

1.12.4. Environmental fate profile of the TGAI based on exposure to the environment (e.g., biodegradation in water, abiotic degradation, bioaccumulation in aquatic and terrestrial environment and behaviour in soil and sediments).

2. DATA REQUIREMENTS FOR THE REGISTRATION OF TECHNICAL GRADE ACTIVE INGREDIENTS: ALTERNATIVE SOURCES

This chapter covers the following cases:

1. When TGAI comes from a new/different manufacturer other than the applicant of the reference specification.
2. When the production is switched from a laboratory or pilot scale to an industrial scale commercial production, the latter is regarded as a different source.
3. When there is a change of the manufacturing location, and/or the addition of one or more alternative manufacturing locations (production sites).
4. When the method of manufacture (e.g., process or quality of starting materials) change.

Batch analysis results for at least five commercial-scale production batches of the active ingredient should be submitted to demonstrate routine compliance with the Declaration of Composition of the TGAI and to demonstrate that the manufacturer is in control of the process.

The 5-batch analysis should have been conducted by an OECD GLP-compliant laboratory within the last 10 years (at the date of submission), provided a declaration by the manufacturer shall accompany the 5-batch analysis if it is older than 5 years but younger than 10 years, to confirm that the manufacturing process and facility have not changed since the analysis was conducted and QC data for recent batches are provided in support (i.e., results of analysis of batches of the technical grade active ingredient analysed under GLP or non-GLP conditions, including information on all relevant impurities).

- Results from QC data need to conform to the same specification as the 5-batch analysis.
- Where QC is performed by a different laboratory than the laboratory that conducted the 5-batch analysis, QC data should include method validation.
- QC data should be submitted for 5 batches produced in the last 5 years, or if less than 5 batches were produced during this time, QC data for all batches produced in the last 5 years should be submitted.
- QC data should include chromatograms (or equivalent depending on the method of analysis used).

The age of the 5-batch analysis is determined by considering the completion date of the study. Explanations of amendments are mandatory.

In case of multiple sources of production, one 5 batch analysis report should be submitted per manufacturing site. If data on commercial-scale batches are not available, data of laboratory scale or pilot scale batches (manufactured using the same process as intended for commercial scale batches) may be submitted. Once registration has been granted, data on commercial scale batches should be provided within one year. If the data is not available within one year, a justification shall be provided.

Please note: Some active ingredients do not require the submission of five batch chemical equivalence, but only a certificate if analysis of 5 manufactured batches. For a detailed list, please see the latest edition of “ANNEXURE A: Active ingredients for which a Certificate of Analysis is required” (no 5-batch analysis).

2.1. Determination of equivalence

Equivalence is determined in a two-tiered approach.

2.1.1. Tier 1 (A – D)

A. Technical grade active ingredient (TGAI) from different manufacturers or manufacturing processes are deemed to be equivalent if:

    1. The materials meet the requirements of the existing FAO/WHO specifications

    2. Assessment of the manufacturing process used, the impurity profile and results of mutagenicity testing (bacteria, *in vitro*) have been carried out with the result that the profiles meet the requirements of section C below.

B. Where a producer changes the manufacturing process for a technical grade active ingredient which has previously been evaluated and incorporated into a specification, equivalence may be determined on the basis of paragraphs A.1 and A.2 above.

C. Equivalence of the impurity profiles of technical grade active ingredients (TGAI), determined by comparison of the manufacturing specification limits.

    1. Where (i) the maximum level (manufacturing limit) of no non-relevant impurity is increased by more than 50% (relative to the maximum level in the reference profile), or the maximum absolute level (manufacturing limit) is not increased by more than 3 g/kg (whichever represents the greater increase); (ii) there are no new relevant impurities; and (iii) the maximum level of the relevant impurities is not increased; the technical grade active ingredients will normally be considered equivalent.

    2. Where these limits for differences in maximum non-relevant impurity concentration are exceeded, the proposer will be asked to provide a reasoned case, with supporting data as required, as to why the particular impurities remain “non-relevant”. The technical advisor will evaluate the case to decide whether or not the technical active ingredient is considered to be equivalent.

    3. Where new impurities are present at or above 1 g/kg, the proposer will be asked to provide a reasoned case, with supporting data if available, as to why these impurities are “non-relevant”. The technical advisor will evaluate the case to decide whether or not the technical active ingredient is equivalent.

    4. The mutagenicity (bacteria, *in vitro*) profile is considered equivalent to that of the reference material if the assessment compares endpoint to endpoint and the outcome is not worse for the material under consideration.

    5. Information about the assessment of the proposed material by a competent registration authority is taken into account in Tier 1.

    6. Where relevant, impurities are increased in maximum concentration and/or where new relevant impurities are present, appropriate toxicological, ecotoxicological or other information on the technical grade active ingredient or

the impurities in question should be submitted, if available, for evaluation in Tier 2.

D. Where the Tier 1 information is insufficient to decide on equivalence or is insufficient to decide non-equivalence, further evaluation should proceed with information and data available under Tier 2.

Technical grade active ingredients from different manufacturers or manufacturing processes are deemed to be equivalent if Tier 1 non-equivalence is uncertain and the Tier 2 assessments of the toxicological/ecotoxicological profiles have been carried out with the result that the profiles meet the requirements of sections E and F below.

2.1.2. Tier 2 (E – F)

E. Equivalence of the toxicological profiles of a technical grade active ingredient.

1. The toxicological profile will be considered equivalent to that of the reference profile, where the data required by section 2.13 below (referring to the requirements of section 2.13, paragraph 2.13.1) do not differ by more than a factor of 2 compared to the reference profile (or by a factor greater than that of the appropriate dosage increments, if more than 2). There should be no change in the assessment in those studies which produce categorical results (e.g., category 1, 2, or 3 skin irritant, not a skin irritant).

2. Where necessary (see 2.13), additional toxicological data (see paragraph 2.13.2) will be assessed by the criterion applied in paragraph E.1, provided that, where appropriate, the organ affected are the same. The benchmark dose should not differ by more than a factor of two, or the “no observable effect levels” (NOELs) or “no observable adverse effect levels" (NOAELs) should not differ by more than the differences in the dose levels used.

F. Equivalence of the ecotoxicological profiles for the technical active ingredient (as appropriate to the intended use of the active ingredient). Where required (see section 2.13 below), the ecotoxicological profile (paragraph 2.13.3 below) will be considered equivalent to that of the reference profile if the data do not differ by more than a factor of 5 compared to the reference profile (or by a factor more than that of the appropriate dosage increments, if greater than 5), when determined using the same species.

2.2. General description of the batch

- Batch size
- Batch number
- Date of manufacture
- Date of analysis
- Date of expiry – if the product is not stable, it must be stated and an expiry date is compulsory.

2.3. Identity of the active ingredient (TGAI)

- ISO English common name (and its status)
- Chemical name (IUPAC and CA)
- CAS no.
- CIPAC no. (if applicable)
- Structural formula
- Molecular formula
- Molecular mass

2.4. Physical and chemical properties of the TGAI

Please note: The following properties may be obtained from open-source data but must be reported. Reference must be credible and clearly described.

- A general description, for example, appearance, colour, odour, physical state
- If a new active ingredient contains one or more chiral centres, a specification of whether the active constituent is a pure enantiomer, racemate or fixed combination of non-enantiomeric isomers.
- If a new active ingredient contains geometric isomers (*cis/trans*, *E/Z*), a specification of whether the active constituent is a pure geometric isomer, or a fixed combination of geometric isomers.
- The melting point or range (for solids)
- The boiling point or range (for liquids)
- If the melting and/or boiling point cannot be determined because of decomposition or sublimation, the temperature at which decomposition or sublimation occurs.
- The flash point (where the melting point is below 40° C)
- The flammability including auto-flammability
- Explosive properties
- Photochemical properties
- Oxidising properties
- The auto-ignition temperature
- Corrosion characteristics

2.5. Manufacturer and manufacturing site

The applicant should provide the name and business address of the manufacturing plant of the active ingredient and the street address in which the active ingredient is manufactured. If a toll or contract manufacturer is involved, name and business address of the manufacturing plant of the active ingredient and the street address in which the active ingredient is manufactured should be provided.

The manufacturer together with the applicant should familiarize themselves with all relevant guidelines published by the office of the Registrar (Act 36 of 1947) before manufacturing any agricultural remedy that is intended to be registered in South Africa under Act 36 of 1947.

2.6. Description of the manufacturing process

An accurate and detailed description of the manufacturing process and process controls should be provided for each manufacturing site and include the following information:

- An introductory paragraph detailing the number of chemical steps, whether the process is a batch or continuous process, and significant purification steps.
- A flow diagram of the synthetic processes that outlines the sequence of all the steps.
- A reaction scheme that outlines the sequence of all the chemical reactions including molecular formulae
- Chemical structure of starting materials, intermediates, reagents and catalysts
- The final products formed
- Amounts used or formed
- Yields obtained
- The relative amounts of each starting material and their order of addition
- The reaction conditions (temperature, pressure, pH, reaction times and addition rate, etc.)
- The duration and yield of each step of the process
- Information on intermediates that are isolated and purified.
- A description of any purification procedures for the active ingredient, including procedures to recover starting materials, intermediates or the final product.
- If a TK is produced, details of the final specified concentration of the active ingredient present, including justified range, methods used to confirm the concentration, and details of the diluents and/or additives used.
- Description of compounds intentionally added to the technical material (e.g. stabilizers). The synthetic process should be described in sufficient detail to enable the evaluators to assess the potential presence of impurities and impurities of toxicological relevance.

2.7. Active ingredient content

2.7.1. The following analytical results shall be reported:

- Identification of the active ingredient (TGAI)
- The active ingredient content, determined with a validated analytical method according to international criteria for validation and the results on the same sample should not deviate more than authorised by the validation of the method.

Please note: The active ingredient content of all the batches must comply with the minimum purity stated in all the international specifications, e.g., FAO specifications, APVMA specifications, or minimum purity specified by the European Food Safety Authority (EFSA).

2.7.2. The following information must be included in the analytical report (for chromatographic methods – where other methods of analysis were used, equivalent data of relevance must be included):

- Reference to the analytical methods and validation reports used to generate the data
- The batch numbers of the tested batches
- The analytical reference standard(s) used for the determinations
- Copies of the original data and images from the chromatographic system which include a software-generated table with retention time, peak areas or peak-height of the associated peaks and relevant chromatogram tables.
- Chromatograms should be clearly labelled with the following:
    - Batch number or internal laboratory reference number / code linked to the specific batch
    - Peak identity e.g., retention time or compound name
    - Peak integration
- Worked examples of all calculations

2.8. Impurities

2.8.1. All impurities

Information on impurities that are, or may be, present in the active ingredient at levels greater than or equal to 1 g/kg should be provided (significant impurities). Note that toxicologically relevant impurities at any level must be characterized and reported. The concentration of impurities should be quantified against their own reference standards. The use of analogue standards must be justified.

Potential sources of impurities or related substances include:

- Impurities in the starting materials from incomplete or side reactions, or isomerisation of residual solvents, reagents and immediate precursors.

- Trace elements arising from the use of catalysts or other sources.
- The degradation of the active ingredient that may occur after manufacture.

2.8.2. Impurities of toxicological relevance (relevant impurities)

If there is potential for the formation of toxic impurities and/or by-products, this must be declared and quantified. Details of the conditions leading to their formation and steps taken to control the formation of toxic impurities should be provided. All impurities identified as toxicologically relevant must be analysed regardless of manufacturing process used or non-appearance during screening process. Area normalization is not accepted.

2.8.3. Data to be submitted

Data to be submitted with respect to impurities must include:

- Structural formulae
- CAS number
- A scheme for the formation of the impurity, followed by a text discussion of its formation.
- A justification of the limits of these impurities should be provided.
- Results of the analytical determination for the content of each impurity present at a concentration of 1 g/kg or more (significant impurities) using specific methods. Actual numerical results should be provided rather than vague statements such as "within limits" or "conforms".
- Content of toxicologically relevant impurities (present at any level).
- Chromatograms of the batches showing separation of impurities. Chromatograms should be clearly labelled with
    - Batch numbers
    - Peak identity
    - Peak integration data
    - A software-generated table with retention time and peak area of associated peaks
- A copy of all raw data used to generate the final results.

2.9. Analytical methods

2.9.1. Full details of the test methods used for determining the following:

- Active ingredient
- All impurities at or above 1 g/kg (significant impurities)

- Toxicologically relevant impurities (even when present at less than 1 g/kg should be submitted).
- Where possible, the active ingredient must be identified by means of various techniques / instruments in order to confirm identity.

2.9.2. The following information should be included in a written analytical method:

- A copy of the actual laboratory method. If this laboratory method is not in English, please include an English version.
- The principle of the method
- The method summary
- Sample preparation techniques
- Equipment or reagents (for example, for chromatographic methods, details of the column include column name, manufacturer, packing material and dimensions).
- Eluent (including gradients, where applicable)
- Column temperature
- Detector and retention times of all components where chromatographic techniques are used.

2.10. Method validation

Validation data for the method(s) used to assay the active constituent and impurities should be provided. The following parameters should be addressed:

- Selectivity or specificity
- Linearity
- Precision
- Recovery (accuracy)
- Limit of detection (LOD) for impurities
- Limit of quantitation (LOQ) for impurities

Note that LOD and LOQ may not be required for the quantitation of the active ingredient, only the determination and quantitation of the impurities.

2.11. Mass accountability

The sum of the quantitative level of the active ingredient and impurities is often referred to as the mass balance. Mass balance is an important parameter in the batch analysis to ensure that all

major impurities have been detected. The mass balance need not add up to exactly 100 percent, because of the analytical error associated with each analytical procedure; however, it is expected to be in the range of 98 – 102 percent. In other words, the unidentified fraction of each batch must not exceed 2 percent (20 g/kg).

2.12. Declaration of composition

A comprehensive declaration of composition (DoC) for the active constituent should be submitted. The DoC should be signed and dated and include the following information:

- The minimum purity of the active ingredient (in grams per kilogram [g/kg] or grams per litre [g/L], as appropriate) on a dry weight basis, as well as the ratio of the content of isomers or diastereisomers (where relevant) and according to the active ingredient definition. For active ingredients listed in Annexure A: Active ingredients for which a Certificate of Analysis is required (no 5-batch analysis), the active ingredient content and the maximum content of all impurities present in quantities of 1 g/kg or more (significant impurities) and any toxicologically relevant impurities present at any level (including less than 1 g/kg) should be included.

When the active ingredient is a TK:

- The minimum and maximum concentration of the active ingredient in the Technical Concentrate
- The minimum purity of the active ingredient and the maximum content of all impurities on a dry-weight (solvent or additive free) basis.
- The content of diluents and/or any additives in g/kg.

The chemical names with company code numbers (where applicable), CAS registry numbers where they exist, empirical formula, molecular weight, structural formula for all identified impurities are required.

All impurities present at or above 1 g/kg level must be identified (significant impurities). If identification of an impurity is not feasible, a summary of laboratory studies demonstrating the unsuccessful effort should be included in the application. There is no need to identify the impurities that are not toxicologically relevant, and which are below levels of 1 g/kg.

2.13. Toxicological data (if required see Paragraph E & F)

2.13.1. Toxicological profile of the TGAI based on acute oral, dermal and inhalation toxicity, skin and eye irritation, skin sensitization.

2.13.2. Toxicological profile of the TGAI based on repeated administration (from sub-acute to chronic) and studies such as reproductive and developmental toxicity, nontoxicity, carcinogenicity, developmental and adult neurotoxicity, etc.

2.13.3. Ecotoxicological profile of the technical material or technical concentrate based on toxicity to aquatic and terrestrial organisms (e.g., fish, crustaceans, algae, birds, bees), as appropriate, to the intended use, and information or persistence.

2.13.4. Environmental fate profile of the technical material or technical concentrate based on exposure to the environment (e.g., biodegradation in water, abiotic degradation, bioaccumulation in aquatic and terrestrial environment and behaviour in soil and sediments).

Please note: New testing is not required in order to determine/confirm endpoints where the applicant can demonstrate that endpoints are very likely not impacted by the new (or increased) relevant impurity.

2.14. Steps to be followed to determine equivalence

A. The applicant supplies all the applicable information listed under point 2.2. to 2.3. to the Registrar (Act No. 36 of 1947). The applicant should also consider the FAO header note given in italics which states that "*This specification, which is PART ONE of the publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report. It should be applicable to relevant products of these manufacturers but it is neither an endorsement of those products, nor a guarantee that they comply with the specifications. The specifications may not be appropriate for the products of other manufacturers*."

B. The technical advisor (Act No. 36 of 1947) determines whether all the required information is supplied and then decides on equivalence using the following criteria:

1. All the data required were supplied and the comparative analyses and tests show that the product of the applicant is equivalent in all respects to the national specification of reference (original when complete) as well as to international specification of reference when available (FAO or WHO).
    - Recommend registration
2. All the data required were supplied but the comparative analyses and tests show that the product of the applicant is not equivalent due to:
    a) New or higher relevant impurities in the product but full toxicological summaries were presented on the relevant impurities.
        - Refer to a recognised toxicologist in the Department of Health for an opinion or phyto-toxicologist in the Agricultural Research Council (ARC) where necessary.
        - Recommend registration or not, based on the findings of the Department of Health with or without efficacy tests.
    b) New or higher relevant impurities in the product but full toxicological summaries were not presented.
        - Refer back to applicant to supply additional information
3. All the data were supplied but the comparative analyses and tests were done by a laboratory not recognised by OECD GLP authority.

- Refer back to applicant for new tests. Applicant can apply to South African National Accreditation System (SANAS) for evaluation of the test laboratory and the findings of SANAS must be supplied with the comparative test results to Act 36 of 1947.
- Refuse the application based on the principle of "non-tested compliance".

4. Insufficient or incomplete data is supplied as stipulated in this document.
    - Refer back to the applicant, the client should supply studies within 30 days, and the study should have been done before the submission date. Substitution or replacement of studies is not allowed.
    - Refuse application outright based on the "not in the public interest" principle.

3. DATA REQUIREMENTS FOR THE REGISTRATION OF A FORMULATION

The stability profile of a formulation is determined by monitoring physical and chemical properties before and after storage. Monitoring active ingredient content alone is insufficient to make any reliable prediction about the stability of the formulation. On prolonged storage, a formulation may exhibit negligible changes in active ingredient content, yet the important physical properties (e.g., wettability, suspensibility, etc.) may have changed to such an extent that the performance of the formulation can be compromised.

Relevant test parameters for each formulation type are given in the FAO/WHO specifications (Manual on the development and use of FAO and WHO specifications for chemical pesticides). It is expected that all relevant parameters will be tested during a storage stability study. If certain parameters are not addressed, then relevant scientific arguments must be provided in advance (not during evaluation) as to why testing for certain parameters are not relevant.

Relevant test parameters for horticultural mineral oils for use on agricultural crops are stipulated in South African National Standards (SANS) codes.

All storage stability studies must be conducted in the correct packaging material.

3.1. Physical and chemical properties of the formulation type

Formulation type should be identified as in the latest Manual on development and use of FAO and WHO specifications for pesticides. The main countries where these formulations are registered and sold should be listed and if there are many, give the number of countries in each region or continent.

Physical, chemical properties and storage stability studies should be done according to the most recent edition of the "Manual on Development and use of FAO and WHO Specifications for Pesticides" or the "FAO Specification for Agricultural Pesticides for the active ingredient." Detailed reports, including raw data and summary on the physical, chemical properties and storage stability studies of the formulated product, should be submitted. Studies need to be

conducted by facilities with either OECD GLP or ISO 17025 accreditation. Studies must be less than 10 years old at the time of submission. Results must be in line with active ingredient-specific FAO specifications, where available.

In cases where an applicant claims that the formulation type is not available in the list of the latest Manual on development and use of FAO and WHO specifications for pesticides, a close match of that formulation should be used to establish which tests should be done. Also, in cases where the applicant is of the opinion that there is no specific active ingredient in the formulation, it will be sufficient to analyse the physical and chemical properties of the formulation before and after storage to ensure chemical properties of the formulation have not changed. The applicant should provide a Safety Data Sheet (SDS) or certificate of analysis (CoA) for all co-formulants of the product. Formulation composition should have the name of the ingredient, CAS number, function and concentration.

This document should be read in conjunction with the document listing some of the active ingredients and co-formulants that are phased out and some that are identified as potentially toxic or hazardous by Act No. 36 of 1947.

3.2. Shelf-life (storage stability conditions)

Storage stability trials may include accelerated or real-time tests, or both. Real-time testing is generally conducted for a formulation that may be unstable at high temperatures and is generally a requirement for date-controlled products. For example, products containing microbiologically active ingredients are date-controlled and are not generally stable at the elevated temperatures typically used for accelerated testing, and real-time testing is almost always necessary. Where a formulation has a shelf-life of less than 2 years, this must be fully justified, and the label must identify both the manufacturing date and the “use by” date.

For some formulations, studies at lower temperatures may be necessary due to the instability of the formulation at higher temperatures (this should be reflected in the recommended storage conditions).

3.2.1. Two-year shelf life

A two-year shelf life can be obtained by submitting supporting data (chemical analysis, physical and technical properties, as well as packaging stability data) from one of the following storage conditions:

- 2 weeks 54 ± 2 °C
- 4 weeks at 50 ± 2 °C
- 6 weeks at 45 ± 2 °C
- 8 weeks at 40 ± 2 °C
- 12 weeks at 35 ± 2 °C
- 18 weeks at 30 ± 2 °C
- 2 years at 20 °C

- 2 years at 25 °C
- 2 years at 30 °C

3.2.2. Shelf life of more than two years

Real time stability data carried out at 20 °C, 25 °C or 30 °C for x number of years (where: 2 < x < 5) must be submitted. Samples should be tested as soon as practicable following manufacture (time zero) and after suitable time intervals (e.g., 2, 3, 4 years). The dates of product testing should be recorded and reported with stability results.

Please note that the above shelf-life assignment is granted when the active ingredient content is still within the FAO tolerance levels. There must also not be significant changes in the physical and chemical properties of the formulation before and after storage.

3.3. Stability of the packaging material

The packaging, storage or shipping containers must be appropriate for the characteristics of the formulation.

A description of the packaging materials used for the formulation and information regarding the corrosive effect, if any, of the formulation on the packaging materials should be provided. The effect of the formulation on the packaging material and *vice versa* is important and, therefore, the product should be stored in the same packaging (materials and pack sizes) that are proposed for the marketing of the final product.

If the product is to be marketed only in containers in which stability testing would be impractical (e.g., too large), then stability trials in smaller containers of the same materials and construction may be used to extrapolate to the larger containers.

Containers should be examined to ensure that no significant interaction with the formulation (affecting the stability/integrity of the packaging material) has taken place during storage. The examination should be done by performing the storage stability studies according to the recent "Manual on development and use of FAO and WHO specifications for pesticides" on that particular packaging material. If the product is marketed in the same packaging material but in different pack sizes, it is advisable that the storage stability study should be done on the smallest pack size. In cases where the formulation is marketed in different packaging material, the storage stability studies should be done on each packaging material.

3.4. Low temperature stability testing

Liquid formulations (capsule suspensions, emulsifiable concentrates, oil-in-water emulsions, micro-emulsions, soluble concentrates, suspension concentrates, and so on) may be adversely affected by storage at low temperatures. Storage at low temperatures may result in crystallization of active ingredient(s), significant changes in viscosity or phase separation of emulsions. Therefore, liquid formulations should also be tested at 0 °C ± 2 °C for seven days.

For capsule suspension formulations, in which capsule walls may break as a result of repeated freezing and thawing (thus releasing the active into the suspending liquid), freeze-thaw cycling testing should also be undertaken. Unless otherwise stated, the freeze/thaw stability test shall cycle the formulation between room temperature (e.g., 20 °C ± 2 °C) and -10 °C ± 2 °C on 18-hour-freeze/6-hour-melt cycles for a total of 4 cycles.

3.5. Active ingredient content

3.5.1. The following analytical results shall be reported:

- Identification of the active ingredient
- The active ingredient content, determined with a validated analytical method according to international criteria for validation and the results on the same sample should not deviate more than authorised by the validation of the method.

3.5.2. The following information must be included in the analytical report (for chromatographic methods – where other methods of analysis were used, equivalent data of relevance must be included):

- Reference to the analytical methods and validation reports used to generate the data
- The batch numbers of the tested batches
- The analytical reference standard(s) used for the determinations
- Copies of the original data and images from the chromatographic system which include a software-generated table with retention time, peak areas or peak-height of the associated peaks and relevant chromatogram tables.
- Chromatograms should be clearly labelled with the following:
    - Batch number or internal laboratory reference number / code linked to the specific batch
    - Peak identity e.g., retention time or compound name
    - Peak integration
- Worked examples of all calculations.

3.6. Analytical methods

3.6.1. Full details of the test method(s) used for determining the active ingredient content.

3.6.2. The following information should be included in a written analytical method:

- A copy of the actual laboratory method. If this laboratory method is not in English, please include an English version

- The principle of the method
- The method summary
- Sample preparation techniques
- Equipment or reagents (for example, for chromatographic methods, details of the column include column name, manufacturer, packing material and dimensions)
- Eluent (including gradients, where applicable)
- Column temperature
- Detector and retention times of all components where chromatographic techniques are used

3.7. Method validation

Validation data for the method(s) used to assay the active constituent and impurities should be provided. The following parameters should be addressed, where appropriate:

- Selectivity or specificity
- Linearity
- Precision
- Recovery (accuracy)

4. DATA REQUIREMENTS FOR THE REGISTRATION OF A FORMULATION SITE

4.1. New formulator requirements

All the requirements as stipulated in the "Guidelines on the data and documents required for registration of agricultural remedies in South Africa" should be submitted.

4.2. Physical and chemical studies

Physical and chemical properties, active ingredient concentration and visual inspection of packaging material of a minimum of one batch of formulated product should be submitted. No storage stability study is required. The visual inspection of the packaging material should be done in the same packaging in which the agricultural remedy will be marketed and sold and may be done directly after decanting. Feedback should be provided on the following visual parameters, where applicable: sealing, leakage, holes, dents, and perforations. Studies need to be conducted by facilities with either OECD GLP or ISO 17025 accreditation. Studies must be less than 10 years old at the time of submission.

Note: If data on commercial-scale samples are not available, data of laboratory scale or pilot scale samples (manufactured using the same process as intended for commercial-scale samples) may be submitted. Once registration has been granted, data on commercial-scale

formulation should be provided within one year. If this data is not available within one year, a justification shall be provided.

5. REFERENCES

5.1. Food and Agriculture Organization of the United Nations and World Health Organization, 2016. Manual on development and use of FAO and WHO specifications for pesticides. First edition, third revision, Rome.

5.2. Collaborative International Pesticides Analytical Council (CIPAC), Handbooks E to L. Analysis of technical and formulated pesticides.

5.3. Australian Pesticides and Veterinary Medicines Authority (APVMA). Validation of analytical methods for active constituents and agricultural products.

5.4. European Commission: Directorate General Health and Consumer Protection, 22 March 2019. Technical Active Substance and Plant protection products: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex (Section 4) of Regulation (EU) No. 283/2013 and Annex (Section 5) of Regulation (EU) No 284/2013. SANCO/3030/99 rev. 5.

5.5. Registrar (Act 36 of 1947), November 2000. Guidelines on Equivalence of agricultural remedies (pesticides).

5.6. Registrar (Act 36 of 1947), 2015. Guidelines on the data and documents required for registration of agricultural remedies in South Africa.

5.7. CropLife International, June 2009. Guidelines for specifying the shelf life of plant protection products. Technical monograph no. 17, 2nd edition.

5.8. Australian Pesticides and Veterinary Medicines Authority (APVMA), 24 February 2020. Generation of storage stability data for agricultural chemical products.

5.9. SANS 1367-1. Horticultural mineral oils for use on agricultural crops, Part 1: Base oils.

5.10. SANS 1367-2. Horticultural mineral oils for use on agricultural crops, Part 2: Monophase emulsifiable concentrates.

5.11. OECD, 5 April 2017. Guidance document on botanical active substances used in plant protection products. Series on pesticides, No 19, ENV/JM/MONO(2017)6.

5.12. Convention on Biological Diversity, United Nations, 2011. Nagoya protocol on access to genetic resources and the fair and equitable sharing of benefits arising from their utilization to the convention on biological diversity. Montreal.

ANNEXURE A: Active ingredients for which a Certificate of Analysis is required

It should be noted that agricultural products containing active constituents included in this list below must be registered in accordance with Act 36 of 1947 before that product can be legally sold, distributed or used in South Africa. Although the chemistry evaluation may not be necessary for these active constituents, the other stages of the registration must still proceed as normal. The certificate of analysis must not be older than 10 years at the time of submission and the analysis must be conducted by an OECD GLP or ISO 17025 accredited laboratory.

Table 1: Active ingredients for which five Certificates of Analysis is required (no 5-batch analysis). An updated list should be obtained from the APVMA website. CoA's must contain information on the maximum content of all impurities present in quantities of 1 g/kg or more and any toxicologically relevant impurities present at any level (including less than 1 g/kg).

1 – 9	**A**
• 1-Aminomethanamide dihydrogen tetraoxosulfate (AMADS) • 1-Naphthylacetic acid and its salts *DoC • 2-Naphthyloxylacetic acid and its salts *DoC • 1,2-Dichlorobenzene (ortho-dichlorobenzene) • 1,4-Dichlorobenzene (para-dichlorobenzene) • 2,4-Dinitrophenol • 2-Benzyl-4-chlorophenol (Clorophene) • 2-Mercaptoethanol • 4-Aminopyridine • 4-(p-acetoxyphenyl)-2-butanone (Cue-lure) *P • 4-(p-hydroxyphenyl)-2-butanone (Frambinone) *P • 8-Hydroxyquinoline sulfate	• Acetic acid – glacial • Alkaline salts • Allyl alcohol • Alphachloralose *DoC • Alum (potassium aluminium sulfate) • Aluminium hydroxide • Aluminum ammonium sulfate (ammonium alum) • Ammonium sulfate • Ammonium thiocyanate • Ammonium thiosulphate • Arsenic • Arsenic acid • Arsenic pentoxide • Arsenic trioxide
B	**C**
• Bentonite • Benzalkonium chloride • Benzoic acid • Benzyl alcohol • Benzyl benzoate • Borax (disodium octaborate; disodium, tetraborate; sodium metaborate) • Bordeaux mixture • Boric acid • Bromine • Butanoic acid	• C9-C11 alcohol ethylene oxide condensate • Cabbage extract • Calcium carbide • Calcium dodecylbenzenesulfonate • Calcium hypochlorite • Calcium polysulfide • Calcium sulfate • Camphor • Canola oil • Capsicum oleoresin • Carbon disulfide • Chilli extract

	• Chloramine-T (N-chloro-4-methylbenzenesulfonamide sodium salt) • Chlorinated xylenols *CD • Chlorine dioxide • Chlorohexidine digluconate (chlorhexidine gluconate, chlorhexidine digluconate) • Chloropicrin (trichloronitromethane) • Chromium trioxide (chromium (VI) oxide) • Citric acid • Citronella oil • Clay – Kaolin • Copper acetate • Copper ammonium carbonate • Copper hydroxide (cupric hydroxide) *S • Copper naphthenate • Copper nitrate • Copper oxychloride *S • Copper silicate • Copper sulfate *S • Creosote • Cresols • Cresylic acid • Crotyl mercaptan • Cupric acetoarsenite • Cupric ammonium chloride • Cupric carbonate *S • Cupric chloride • Cupric oxide • Cuproammoniumfluoroborate complex • Cuprous oxide *S • Cuprous thiocyanate • Cypress wood oil
D • D-Limonene • Decan-1-ol • Denatonium benzoate (Bitrex) • Den-Co-Fume carbon monoxide fumigant cartridge • Derris dust • Diatomaceous earth • Dibenzyldimethylammonium chloride • Dibutyl phthalate • Didecyl dimethyl ammonium chloride • Dimethyl phthalate • Diphenyl • Disodium octaborate tetrahydrate • Docusate sodium *P • Dodecylbenzene sulfonic acid *CD	**E** • (E)-2-Octadecenal *P • (E)-8-Dodecenyl acetate • (E,E) 8,10 Dodecadien-1-ol • E,E-9,11-Tetradecadien-1-yl acetate • (E,Z)-2,13-Octadecadienal *P • E-11-Tetradecen-1yl acetate *P • EDTA and its sodium salts • Ethanolamine complex of copper salts • Ethoxylated lanolin • Ethyl and methyl esters of fatty acids produced from food grade canola oil *DoC • Ethyl formate • Ethyl hexanediol • Ethyl oleate • Ethylene

• Dodecylbenzyltrimethylammonium chloride • Dodicin (dodecyl diethylenediamino glycine + dodecyl aminopropyl glycine)	• Ethylene dibromide • Ethylene dichloride • Ethylene oxide • Eucalyptus oil
F • Ferrous sulfate • Fatty alcohol blend • Food grade vegetable oils • Food quality ingredients • Formaldehyde • Formic acid	G • Garlic extract • Garlic oil • German cockroach pheromone *P • Glutaraldehyde *DoC • Glycolic acid
H • Hexanol • Hydrochloric acid • Hydrogen peroxide • Hydrolysed linseed fatty acid	**I** • Indole • Indol-3-acetic acid *DoC • Indol-3-butyric acid *DoC • Ingard Cotton Gene – Bacillus Thuringiensis variety Kurstaki delta endotoxin as produced by the Cry IA(C) gene and its controlling sequences • Iodine • Iodophors • Iso-amyl mercaptan • Isomate LBAM *P • Isomate OFM Rosso *P • Isostearyl alcohol ethoxylate
L • Lanolin oil • Lavender fragrance • Lead arsenate • Lecithin • Lime oil • Lime sulfur • Lithium hypochlorite	**M** • Magnesium chlorate • Melaleuca oil (tea tree oil) *DoC • Metarhizium anisopliae *DoC • Methyl nonyl ketone • Mineral oil • Mixed copper chelates or complex blend of copper salts • Mono and di 2-ethylhexyl phosphate salts with ethoxylated cocamine (Intersept Manufacturing Concentrate) [For use in • carpet manufacture only]
N • N-Alkyldimethylbenzyl ammonium chloride • n-Butyl mercaptan • Naphthalene • Nickel sulfate • Nitric acid • Nonionic surfactants (not listed elsewhere) • Nonyl phenol ethylene oxide condensate	**O** • Octanol • Orange oil

• Nuclear polyhedrosis virus of helicoverpea zea	
P • Paecilomyces Lilacinus Strain 251 • Paraffin oil • Pentachlorophenol • Peroxyacetic acid • Petroleum oil • Phenol • Phenylethyl propionate • Phosphine gas • Phosphorous (phosphonic) acid and its salts • Phosphoric acid and its salts • Pindone *V • Pine oil • Pivalyn *V • Polybutene • Poly (hexamethylene biguanide) hydrochloride • Polyoxypropylene polyoxyethylene alkyl ether • Potassium chromate • Potassium dichromate • Potassium hydroxide • Potassium nitrate • Potassium permanganate • Potassium peroxomonosulphate triple salt • Propionic acid • Pyrethrins, Pyrethrin I and Pyrethrin II (pyrethrum extract) *S	**Q** • Quassia
R • Rabbit Calicivirus • Rotenone	**S** • Salicylic acid • Sesame • Shellac • Silica gel • Silver metal • Sodium arsenite • Sodium bisulfate • Sodium bisulfite (sodium metabisulfite) • Sodium bromide • Sodium carbonate • Sodium chlorate • Sodium diacetate • Sodium dichloroisocyanurate • Sodium dichromate • Sodium fluoride • Sodium fluoroacetate

	• Sodium fluorosilicate • Sodium hydroxide • Sodium hypobromite • Sodium hypochlorite • Sodium metabisulfite • Sodium metasilicate • Sodium sulfide • Sodium thiosulfate • Sodium tripolyphosphate • Strychnine • Sulfamic acid • Sulfur • Sulfuric acid
T • Tallow amine ethoxylate • Tannic acid • Tartar emetic (antimony potassium tartrate) • Thymol • Tin Acrylate Polymers RC 626 & RC 627 [Anti-Fouling Paint Use Only] • Tributyl tin oxide • Trichloroacetic acid • Trichloroisocyanuric acid and its salts • Trichoderma Harzianum Rifai Isolate T-39 • Triclosan [5-chloro-2-(2,dichlorophenoxy)phenol]	**X** • XL High Boiling Tar Acids (boiling range 230 – 270 °C) *CD
Z • (Z)-9-Tricosene *P • (Z)-8-Dodecen-1-ol *P • (Z)-8-Dodecen-1-ol acetate *P • Zinc naphthenate • Zinc oxide	

- *DoC = actives for which declaration of composition (DoC) is required
- *P = pheromone use only
- *N = not classified as an active for anti-fouling paints
- *V= vertebrate pest management only
- *S = this active has a standard which the active must comply with
- *CD = included in products for used in cleaning and disinfection of premises only