

**GUIDANCE ON THE GENERATION AND
SUBMISSION OF CHEMISTRY DATA IN SUPPORT
OF THE APPROVAL OF NON-AGRICULTURAL
PESTICIDES**

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1. INTRODUCTION

Non-agricultural pesticides are presently regulated in Great Britain under The Control of Pesticides Regulations (COPR) 1986, as amended, and require approval before they can be sold, supplied, stored, used or advertised. The term non-agricultural pesticide covers wood preservatives, wood treatment products, biocidal paints, surface biocides, rodenticides and insecticides/acaricides for use in public hygiene situations, avicides, bird stupefying baits and antifouling products.

This guidance document is one of a series of documents that has been developed by HSE's Biocides and Pesticides Assessment Unit (BPAU) to support the approval of non-agricultural pesticides under COPR.

1.1 Background

Following agreement of the Advisory Committee of Pesticides, the BPAU produced a guidance document "Data requirements for non-agricultural pesticides products and their active substances" (found in Part Three/A of the Registration Handbook). The requirements published in July 1993 establish a consolidated (core) set of data requirements for all non-agricultural pesticides.

The core data requirements apply to the registration of a non-agricultural pesticide containing a new active ingredient and also to support the review of older active ingredients and their products.

1.2 New Guidance document

The chemistry data requirements outlined within the consolidated core data requirements are summarised in Appendix 1 of this document.

This additional guidance is intended to supplement the information found within BPAU's Consolidated core data requirements and also aims to promote consistency, transparency and high scientific standards in the generation and reporting of these data.

This document provides:

- Background on why these data are needed and how they are used
- Guidance on data waiver and reasoned cases
- Amplification of the individual test requirements for physical and chemical data
- Guidance on reporting standards

1.3 Guidance on data waiver and the preparation of reasoned cases

The consolidated data requirements are regarded as a minimum set for all non-agricultural pesticidal active ingredients and products. However there will be occasions where data requirements can be waived.

Valid reasons for not submitting a complete core data set fall into the following categories:

- (i) *The study is not technically possible to perform*

In some cases the intrinsic physico-chemical properties of the substance or product are such that not all the core data set tests can be performed (e.g. on very volatile or unstable substances). Information on technical limitations detailed in test guidelines for a specific method should always be respected.

(ii) Other existing data can be used instead of required data

Information on an active substance or product may be derived in certain circumstances from other sources. For example, with certain isomers or structurally similar compounds, it may be possible to read-across from existing data.

(iii) The study is not scientifically necessary

In some cases it is not scientifically justified to perform a study due to the intrinsic properties of the active substance or product. In some cases the characteristics of the active substance or product are such that a study is simply not relevant, for example if the water solubility is less than 1 mg l^{-1} then the surface tension study need not be performed.

Other reasons may also be valid and it is up to the applicant to decide the basis for the preparation of a reasoned case against providing the data

In those instances when an applicant is considering providing a reasoned case for extrapolation (see (ii) above) or non-submission of data, it is highly recommended that they contact the BPAU to discuss the situation before beginning any work.

It is stressed that the onus is on the applicant to make the case for not generating new data. Applicants should base their case on scientific arguments or other information which demonstrates that the generation of new data is unnecessary. It is understood that applicants may wish to comment briefly on the commercial implications, but such concerns should not form the main basis of the case.

Arguments should be supported by reference to appropriate data and a full list of the references cited should be provided to BPAU. Any literature cited to support a reasoned case should be summarised in sufficient detail to determine the validity of the arguments presented. If an applicant refers to any literature owned by another company and these data are not in the public domain, they will be required to demonstrate that they are entitled to make use of the data, for example, by submission of a letter of access.

A reasoned case should not just present a description of data but should also explain how these data relate to the data requirements. Applicants will be required to interpret their data and make their own case.

2. AMPLIFICATION OF THE DATA REQUIREMENTS

The list of consolidated (chemistry) data requirements is presented in Appendix 1. This section presents an overview of these requirements and provides amplification of the individual requirements including information on test guidelines and methodologies that are available to applicants.

2.1 Overview

Data submitted to meet the physico-chemical data requirements fall into two main categories: Information on identity, composition, analysis and information on specific physical and chemical characteristics of pesticidal active ingredients and products.

2.1.1 Identity, Composition and analysis

Composition data are used in several ways. BPAU will examine the composition of a technical active ingredient or formulated product to determine whether the active ingredient or product contains any ingredient in an amount that may cause unreasonable adverse effects on human health or the environment.

2.1.2 Physical and Chemical characteristics

Data on the physical and chemical characteristics of pesticidal active ingredients and products are required. Some characteristics confirm or provide supportive information on the identity of ingredients and products. This is particularly true for such properties as colour, odour, physical state, melting and boiling points, density, solubility, vapour pressure and pH.

Such information as colour, odour, physical state, pH and viscosity is also needed to respond to emergency requests for identification of unlabelled pesticides involved in accidents or spills. Medical Practitioners, hospitals and poison control centres will, on occasion, also request such information.

Physical and chemical characteristics data are used directly in hazard assessment. These include pH, stability, oxidising and reducing action, flammability, explosive properties, corrosivity and storage stability. For example, BPAU require storage stability data on a pesticidal formulation as this provides data on change (or lack of change) in product composition over time, which gives an indication of the shelf life of the product; if certain active ingredients decompose, then potentially other new chemicals are formed whose toxicity and other properties may need to be considered.

Determination of the UV/Visible absorption spectrum of a pesticide provides some indication of the wavelengths at which a compound may be susceptible to photodegradation. Since photochemical degradation is likely to occur in both the atmosphere and aquatic environment, spectra appropriate to these media will provide information concerning the need for further persistence testing.

Additionally, certain physico-chemical data are needed as basic or supportive evidence in initiating or evaluating studies in other areas, e.g. The octanol/water partition coefficient is used as a criterion in determining whether certain aquatic organism and wildlife toxicity studies are needed.

Data on vapour pressure may be used in support decisions as to appropriate re-entry intervals for some pesticidal products in situations where residues in air pose a potential hazard or there is a potential for inhalation exposure arising from handling the active ingredient

2.2 . IDENTITY OF THE ACTIVE INGREDIENT

Identification necessitates the provision of a variety of information:

2.2.1 BSI Common Name

Where available the commonly used International Organisation for Standardisation (ISO) name or alternatively the British Standard Institute (BSI) name should be provided or, if not yet established, the proposed name.

Principles for determining these appear in ISO 257:1988 and BS 1831 Part 1:1985.

2.2.2 Chemical Name

The International Union of Pure and Applied Chemistry (IUPAC) name should be provided. If applicable, each stereoisomer listed as an active ingredient must be individually identified and a corresponding structure supplied (see section 2.2.8)

2.2.3 Other Codes or synonyms

Development codes, company codes, any other name by which the active ingredient is also known must be provided.

2.2.4 Chemical Abstracts Service (CAS) Registry Number

The Chemical Abstract Service number must be provided. Each CAS number is unique to one chemical. If none allocated then applicants must state "not yet allocated"

2.2.5 EINECS/ELINCS Number

For substances 'on the market' prior to 1981 an EINECS (European Inventory of Existing Chemical Substances) number will have been allocated and should be reported. For 'new' substances (i.e. Those notified after 1981) an ELINCS (European List of New Chemical Substances) number should be available and should be reported.

2.2.6 Molecular Formula

In the order C, H, alphabetical for carbon containing molecules, otherwise alphabetical

2.2.7 Molecular mass

This must be provided and given to one decimal place

2.2.8 Empirical and Structural formula

Structures should be drawn to show 3-dimensional aspects where possible, for example in the case of stereoisomers.

2.2.9 Composition of Technical Grade Active Ingredient(s):

The following information should be supplied:

Typical batch purity:

- The mean value of the 5-batch analysis (see Section 2.5.1.1) should be reported

Minimum Purity

- The certified manufacturing limit should be reported

Purity Range

- This should encompass the certified manufacturing limits

Isomeric content

- Where applicable the isomer ratios should be reported along with tolerance limits (e.g. 80:20 +/- 5%)

2.2.10 Discussion of impurities/substances of concern

Information on impurities or additives present in the technical grade material together with any by-products of synthesis, degradation products (if the substance is unstable) etc. Common names and chemical names in accordance with 2.2.1 and 2.2.2 should be provided, together with CAS and EC numbers if available.

BPAU will require this information when considering a risk assessment for the material.

For example:- certain substances are currently or have in the past been the subject of regulatory action because of the risks posed by their presence as impurities in non-agricultural pesticide products (e.g. certain compounds have been found to be sensitizers and their presence is excluded from products made available to amateur users). In other cases they are identified because historically they are known to contribute to the toxic profile of an active ingredient.

2.2.11 Spectral data:

Discussion of results arising from absorption spectra (UV/VIS, IR, NMR) and a mass spectrum should be provided, and the relevant spectra should be included. The spectra should be of the technical active ingredient where possible. Where appropriate spectra should be provided with the same specification as used in other testing. If the purified active ingredient is used, the purity must be stated and spectra provided. The following details should also be provided.

Batch Number

- The batch numbers of each sample used in the spectral analysis should be included.

Purity (% w/w)

- The purity of each sample used in the spectral analysis should be included

Laboratory

- The name of the laboratory performing the analysis and their address should be provided

Date:

- Date of analysis

Reference

- Test report numbers, literature references (where applicable).

2.3 PHYSICO-CHEMICAL PROPERTIES OF THE ACTIVE INGREDIENT

2.3.1 Appearance (physical state, colour and odour) of the active ingredient

- *Physical state* - The description of the physical state of the active ingredient shall be based on a visual inspection of the substance at 20 °C or 25 °C. This should be described qualitatively using conventional terms such as solid, granular, crystalline solid, amorphous solid, semi-solid, liquid, gas etc. And similar terms used to describe compounds in for example "The Handbook of Chemistry and Physics" (ref: CRC Publishing Co. Latest edition)
- *Colour* - A visual description of the colour (or lack of colour) of each opaque substance should be reported qualitatively. The Munsell colour system described in, ASTM D-1535" may be used. This system is based on the colour-perception attributes hue, lightness and chroma and offers a systematic visual method for solids (opaque substances) viewed in daylight by an observer with normal colour vision. The Gardner Colour Scale described in ASTM D1544 may also be used. This method is based on the comparison of samples of the test substance against colour reference standards.
- *Odour* - The determination of odour is to be qualitative and made at room temperature. Comparison may be made to other substances of characteristic odours. The odour, if any, should be reported qualitatively using descriptive terms such as "garlic like", "characteristic of sulfur-containing compounds", "characteristic of aromatic compounds" etc.

2.3.2 Melting point/Freezing point/Boiling point/ /Relative density

These data may be used to assess the potential for movement of material in the environment, to determine the physical state of the substance under environmental conditions and to evaluate possible health and environmental effects.

- If the melting point or boiling point cannot be determined, the sublimation or decomposition temperature should be given
- Measurements of the melting point and boiling point should be taken up to 360°C
- The boiling point should be measured at normal atmospheric pressure unless decomposition occurs, in which case reduced pressure can be used
- Usually the freezing point of liquid substances should be determined if above 20 °C. An indication that no freezing has occurred during preliminary tests is also acceptable. For viscous liquids the pour point is an acceptable alternative.
- The density of gas should be calculated from its molecular weight and the Ideal Gas Law. Polymer density should be determined by buoyancy methods, where appropriate.

Recommended test guidelines:

Melting point/melting range Temperature: - OECD Guideline No. 102 (OECD 1995)

Boiling point temperature: - OECD Guideline No. 103 (OECD 1995)

Density of liquids and solids: - OECD Guideline No. 109 (OECD 1995)

Or a suitable equivalent e.g. the test methods specified in Official Journal of European Communities L383A, Annex V 92/69/EEC (hereafter in this document referred to as "Annex V tests methods") – see also section 3.1 regarding acceptable test methodology

2.3.3 Surface Tension

This measurement is required for all liquids to determine whether they are surface active.

The surface tension should be measured using an aqueous solution of sufficient concentration such that any surface activity potential is expressed, i.e. At 90 % of saturation (the concentration must be quoted) to maximum concentration of 1 g l⁻¹ (where viscosity permits). Inconsistencies between the water solubility result and the solubility reported should be fully addressed

Under the conditions of the test, the method is required for substances that are soluble in water at concentrations greater or equal to 1 mg l⁻¹

A recommended test guideline for determining the surface tension of an aqueous solution is outlined in OECD Guideline No. 115 (OECD 1995) or a suitable equivalent e.g. Annex V test method (EC Method A5)

2.3.4 Vapour pressure

This is a key parameter for the estimation of inhalation exposure

- Vapour pressure gives an indication of the probability of the phase transitions liquid/gas and solid/gas
- Vapour pressure, together with the solubility in water is a major variable for calculating the volatility of a substance from an aqueous solution
- Vapour pressure is a significant factor for predicting likely atmospheric concentrations
- The vapour pressure of a substance can furthermore be useful as a basis for deciding whether or not a photochemical induced degradation (in the homogeneous gas phase or in an absorbed phase) is necessary
- Vapour pressure at two temperatures (at 20 °C and at 25 °C) or as a vapour pressure curve must be submitted for the substance of stated specification
- Where the vapour pressure is $< 10^{-5}$ Pa, the vapour pressure at 20 °C and 25 °C may be estimated by a vapour pressure curve
- The vapour pressure need not be measured if calculations indicate that the value is significantly less than 10^{-5} Pa
- The study needs not to be conducted (unless there are minor volatile impurities or degradation products etc. in the substance) if the melting point is above 300 °C. A limit value based on measurement or a recognised calculation method is sufficient where melting point is between 200 °C and 300 °C
- The Henry's law constant must always be stated for solids and liquids if it can be calculated. The Henry's law constant depends on the water solubility and vapour pressure of a substance, and expresses the tendency of a substance to evaporate from aqueous solutions. The unit should be stated as $\text{Pa} \times \text{m}^3 \times \text{mol}^{-1}$
- There is no single vapour pressure measurement procedure applicable to the entire range of vapour pressures. Therefore several methods are recommended for the measurement of vapour pressure from $< 10^{-3}$ Pa to 10^5 Pa. The OECD Laboratory Intercomparison Testing Programme showed that the gas saturation method may allow measurements of considerably lower vapour pressure (as low as 10^{-5} Pa).
- The dynamic method, static method and isoteniscope method can be applied to pure and technical grade substances although impurities will affect the results. The vapour pressure balance method and the gas saturation method can only be applied to pure substances
- Vapour pressure testing is not required for chemicals with a standard boiling point of < 30 °C

Further guidelines on testing the vapour pressure of a substance can be found within OECD Test Guideline 104 (July 1995) or a suitable equivalent e.g. Annex V test method (EC Method A4)

2.3.5 Solubility in water

- The studies must include the effect of pH (5 to 9) and temperature on solubility
- Water solubility of the active ingredient should be studied at or near 20 °C and for a substance whose solubility is temperature dependent the solubility at 10 °C and 30 °C should be reported where relevant.
- Water solubility should be measured unless the active ingredient is hydrolytically unstable. Statements such as “insoluble in water” will not be sufficient; instead a limit test should be performed so that a positive statement can be made (e.g. until analytical limit). For complex mixtures, a mass balance may be the only practical method. However, the extract should be compared (e.g. HPLC) with the mixture to check for differential solubilities of components
- Where the stability of the active ingredient in aqueous media is such that the water solubility cannot be determined, a justification based on test data must be submitted
- Colloid and micelle formation and other possible observations should be reported as appropriate.

No single method is available to cover the whole range of solubilities in water

Two methods are outlined with OECD Guideline Number 105 (July 1995), these two methods cover the whole range of solubilities, but are not applicable to volatile substances

- One which applies to essentially pure substances with low solubilities ($<10^{-2} \text{ g l}^{-1}$), and which are stable in water, referred to as the “Column elution method”
- The other which applies to essentially pure substances with higher solubilities ($> 10^{-2} \text{ g l}^{-1}$), and which are stable in water, referred to as the “Flask method”

N.B. Analytical methods used as part of the test method to measure water solubility should be validated in accordance with the BPAU guidance document “Guidelines for validation of analytical methods for non-agricultural pesticidal active ingredients and products”.

It should be noted that a requirement of The Drinking Water Directive (80/778/EEC) is provision of an analytical method capable of measuring pesticides in drinking water to $0.1 \mu\text{g l}^{-1}$.

2.3.6 Partition Coefficient (n-octanol/water)

Partition coefficient measurements are used as an indicator of the bioaccumulation potential of a pesticide in the aquatic environment. A high Log P_{ow} indicates that a substance will be highly fat soluble and may bioaccumulate in aquatic species.

- Where the stability of the active ingredient in aqueous media is such that the partition coefficient cannot be determined a justification based on test data must be submitted
- For those substances which are extremely soluble in one of the phases a limit value should be provided. If necessary it can be based on the individual solubilities in n-octanol and water
- *If a test cannot be performed or it is impracticable to do so, a calculated value for Log P should be provided together with details of the method of calculation. One method is that due to Hansch and Leo (see C Hansch, A J Leo in Substituent Constants for Correlation Analysis in Chemistry and Biology, John Wiley, New York, 1979 and W J Lyman, WF Reehl, D H Rosenblatt (ed), Handbook of Chemical Property Estimation Methods, McGraw-Hill, New York, 1983.)*

Recommended test guidelines

OECD Guideline No 107 - Partition Coefficient (n-Octanol/Water): Shake Flask Method (July 1995)

OECD Guideline No 117 - Partition Coefficient (n-Octanol/Water) High Performance Liquid Chromatography (HPLC) Method (Original Guideline, adopted 30th March 1989)

OECD Guideline No 122 - Partition Coefficient (n-Octanol/Water) pH-Metric Method for Ionisable Substances (Draft New Guideline, November 2000)

or a suitable equivalent e.g. Annex V test method (EC Method A8)

2.3.7 Dissociation Constant in water

The dissociation of an active ingredient in water is of importance in assessing its impact upon the environment. It governs the form of the substance which in turn determines its behaviour and transport. It may affect the adsorption of the active ingredient on soils and sediments and absorption into biological cells.

This test is required when the active ingredient contains an acid or a base functionality. For products that are salts, data are required for the corresponding acid/base.

There are two basic approaches to the determination of pKa. One involves titrating a known amount of substance with standard acid or base as appropriate; the other involves determining the relative concentrations of the ionised and un-ionised forms and their pH dependence. Methods based on those principles may be classified as titration, spectrophotometric and conductometric procedures.

Further guidance can be found within OECD Guideline No 112 (dissociation constant in water)

2.3.8 Oxidising properties

The method is not applicable to liquids, gases, materials that are explosive or highly flammable or to organic peroxides.

The oxidising properties do not have to be determined if examination of the structural formula establishes beyond reasonable doubt, that the active ingredient is incapable of reacting exothermically with combustible materials. In such cases it will be acceptable to provide such information as justification for non-determination of this test requirement

Recommended test guidelines

Annex V test method A17: (Solids)

2.3.9 Corrosion characteristics

Data not required if an explanation of lack of corrosivity is reasonable (e.g. Lack of extreme pH, lack of reaction with container material)

2.3.10 Explosive Properties

The test can be exempted when available thermodynamic information (heat formation/decomposition) or absence of certain reactive groups in the structural formula or its "oxygen balance" establishes beyond reasonable doubt that the substance is incapable of decomposing, forming gases or releasing heat very rapidly.

Recommended test guidelines

Annex V test method A14: Explosive Properties

2.4. INFORMATION ON THE PRODUCT/FORMULATION

2.4.1 Nature of the product/formulation

The nature of the product formulation/coating; for example pre-pressurised handheld aerosol, emulsifiable concentrate, suspension concentrate, water based ready-for-use, wettable powder, ready to use bait, gel etc. should be stated.

Where the product/formulation is in the form of an antifouling coating, the coating type should be stated as one of the following: Soluble matrix; Insoluble matrix; TBT self polishing co-polymer, TBT-free self polishing

N.B. Where the product/formulation is a powder, dust or other particulate formulation information on particle size distribution is required. e.g. for granular products size, weight, shape (qualitative description such as grit, cylindrical shape or precise dimensions of granules should be reported)

Further guidance can be found within OECD Guideline No 110: Particle Size Distribution/Fibre length and diameter distributions (May 1981)

2.4.2 Type of product

Currently applications for approval of non-agricultural pesticide products will fall into one of the following categories:

- Antifouling product
- Insecticides and acaricides (including insecticidal paints)
- Insect repellents
- Rodenticides
- Avicides
- Bird stupefying baits
- Wood preservatives
- Wood treatment products
- Biocidal paints
- Surface biocides

2.4.3 Composition

Information and a statement of composition, identifying each active ingredient, co-formulants, stabilisers, inerts and, in certain cases impurities is required

This information is required so that BPAU are able to obtain a comprehensive listing of the components that may be present in a product and the amounts of such ingredients.

The composition information will be used primarily in subsequent evaluations of the safety and classification of the product. The identifying information will be used as an aid in locating data in the public domain concerning the human health and environmental properties of the product and/or its ingredients.

2.4.3.1 Composition details - active ingredients

- *Name of component*

For each active ingredient present in the formulation, a common name should be given (according to BSI or ISO); should this not be available, the IUPAC name should be given instead. **Trade names alone are not sufficient.** For biological agents the scientific name, strain/serovar (as appropriate) should be stated.

- *Source of active ingredient*

The source or sources of each active ingredient should be stated. For some active ingredients BPAU will only accept recognised manufacturers. Additionally for certain active ingredients which attract data protection BPAU will require a letter of access from the data holder granting BPAU appropriate authorisation to access to these data on the applicant's behalf before approval can be granted. In these circumstances it is the responsibility of the applicant to approach the data holder for such a letter. Applications for approval will not be completed without a valid letter of access. For further information on sources and technical specifications of active ingredients please see the BPAU guidance document "Guidelines concerning the requirements for technical specifications of active ingredients in non-agricultural pesticide products". This document is also available on BPAU's website:

<http://www.hse.gov.uk/hthdir/noframes/bpau.htm>

- *Concentration*

This should be stated as a percentage in terms of weight/weight of the technical material; in addition, for liquid products (excluding pre-pressurised handheld aerosol packs) each active ingredient concentration should be stated in grams per litre (g l^{-1}). For biological products the concentration should be stated as % w/w and the number of activity units/units of potency (as appropriate) relating to a defined unit of formulation [e.g. per gram (g^{-1}) or per litre (l^{-1})] should be stated.

2.4.3.2. Composition details- Non-active ingredients

- Name of component

For each component, the IUPAC name should be given where possible. However, if a CAS or EINECS Number is given then the trade name is acceptable. Material Safety Data Sheets (MSDS) should also be provided where applicable.

- *Structure*

Where possible the structural formula or chemical description of the non-active ingredient should be provided

- *Concentration*

The concentration of each component should be presented. This should be stated as a percentage by weight (% w/w). A concentration range should be given if adjustment is required, e.g. for dyes and/or pigments

- *Function*

e.g. Emulsifier, filler, antifreeze, dispersing agent, stabilisers, dye/pigment

2.4.4 Stability during storage

The purpose of storage stability testing is to provide evidence on how the quality of a product varies with time under the influence of environmental factors such as temperature, humidity and light. The evidence provided by such studies will give an indication of the effect these factors may have on product quality, safety and performance (efficacy). The main objective of testing is to determine the extent of active ingredient breakdown within the formulation contained in its packaging¹.

Storage stability studies provide data on change (or lack of change) in product composition over time. If certain ingredients decompose under conditions of high (or low) temperature and humidity, then other new chemicals may be formed whose toxicity may need to be considered. The results are used to establish storage conditions and determine a suitable shelf-life for the product.

Additionally, pesticide containers have an important effect on storage and shelf-life. If the product is corrosive then lids, liners, seals, seams or container sides may be damaged over time causing the contents to leak during storage, transportation, handling or use. Labels may also become illegible or damaged. In such instances the corrosion characteristics of a pesticide will be needed to evaluate the effects of the product formulation on the container.

In order to fully characterise the stability of a pesticide formulation, standard test methods may be used. Subjective judgement and/or familiarity with the formulation and its intended use are needed in selecting the appropriate test(s)

The test requirement for stability during storage can normally be established in one or more of the following ways:

- accelerated testing (provisional approval only)
- ambient testing
- cold stability testing
- testing for reactivity towards container material

More detailed guidance on test requirements and available test methods is contained within the BPAU guidance document "Guidance on the storage stability data requirements for non-agricultural pesticide products"

This document is also available on the BPAU website:
<http://www.hse.gov.uk/hthdir/noframes/bpau.htm>

2.4.5 Flammability or flash point as appropriate

¹ This requirement is increasingly being set as a post review data requirement by the Advisory Committee on Pesticides (ACP). Although not specified in the Core data requirements for non-agricultural pesticides additional requirements examining the technical properties of a non-agricultural pesticide formulation (e.g. emulsion stability, wettability, suspensibility, friability etc) as appropriate may also be requested by the ACP following a review of an existing active ingredient and its products

The flash point determination should be conducted on the formulated product.

- **All formulations except aerosols**

A case may be made for non-submission of data if it can be shown that the individual components of the formulation are not flammable.

Further guidance on test methods can be found in the following references:

Annex V test method A9 Flashpoint

- This method is only required for formulations that contain flammable liquids. Only data generated using a closed cup method are considered acceptable.
- N.B. The formulation is classified as “Extremely Flammable” where the flash point is $< 0\text{ }^{\circ}\text{C}$ and the boiling point less than or equal to $35\text{ }^{\circ}\text{C}$
- The formulation is classified as “Highly Flammable” if the flashpoint is $< 21\text{ }^{\circ}\text{C}$ but is not within the definition of extremely flammable
- Preparations are classified as “Flammable” where the flashpoint is $< 21\text{ }^{\circ}\text{C}$ but $< 55\text{ }^{\circ}\text{C}$

Table 1:summary of classifications for flammable substances:

| Flash point $^{\circ}\text{C}$ | Boiling Point $^{\circ}\text{C}$ | Classification |
|-----------------------------------|-------------------------------------|---------------------|
| <0 | ≤ 35 | extremely flammable |
| $\geq 0 < 21$ | n/a | highly flammable |
| $\geq 21 \leq 55$ | n/a | flammable |
| >55 | n/a | None |

Annex V test methods: A10 Flammability (Solids) and A11 (Gases)

- Solid formulations are classified as “highly flammable” if they readily catch fire after brief contact with a source of ignition and which continue to burn or to be consumed after removal of the source of ignition. This is further defined in Annex V of Council Directive 67/548/EEC.
- Gaseous substances and formulations are classified as “Flammable” if:
(a) they are flammable in contact with air at ambient temperature and pressure
(b) substances and formulations in liquid form that have a flashpoint less than or equal to $100\text{ }^{\circ}\text{C}$
- For gases the lower explosion limit and the upper explosion limit, or a statement that the gas is non-flammable over a full range of mixtures with air, must be submitted.

Annex V test methods : A12 Flammability (contact with water)

- These data are only required if the formulation is designed to liberate a gas on contact with water or if the data on the active substance or co-formulants show the individual components may release a gas on contact with water.

Auto-flammability

Annex V test method : A15 Liquids and gases

- The self-ignition temperature is the lowest temperature at which the formulation will ignite when mixed with air in defined conditions

Annex V test method: A16 - Solids

- The temperature of the oven at which the sample temperature reaches 400 °C by self heating is the self-ignition temperature

- ***Aerosols***

Aerosols are classified for their flammability according to the updated (94/1/EC) "aerosols directive" (75/324/EEC). This allows classifications of extremely flammable, highly flammable, flammable and not classified. The directive makes the flame symbol mandatory for extremely flammable and highly flammable products.

In addition to the directive's requirements, industry has agreed that under certain circumstances, where an aerosol's base concentrate has a flash point between 56 and 100 °C inclusive, it should continue to carry the flammability related precautionary phrases, even though it will not be formally classified as flammable.

Standard method of classification of aerosols

Aerosols consist of a liquid base and a gaseous propellant. To determine the overall classification of the product both the base and propellant must be checked for their flammability. The component with the highest flammability, i.e. the lowest flash point, determines the product's overall classification. The flashpoint flammability criteria are as per non-aerosol products (see Table 1).

Step 1: Determine the classification of the propellant from its flash point. If the propellant is classified as extremely flammable, e.g. butane, propane or liquefied petroleum gas (LPG), then the product is classified as extremely flammable and steps 2 and 3 can be omitted. If the propellant is not extremely flammable then the rest of the formulation must be considered.

Step 2: Determine the classification of the base from its flash point. If the flashpoint is not given then the base's individual components should be examined for flammability. Since it is not possible to calculate the base's flammability classification from its composition, the component with the lowest flash-point will determine the base's classification.

Step 3: determine the component (base or propellant) with the highest classification. This determines the product's overall classification.

A flammability classification can be challenged using the derogation tests as described below.

Classification of aerosols via derogation tests:

Derogation tests allow a classification assigned using the standard method to be removed. If these tests are used to remove a classification then the applicant must submit the test data to BPAU. These tests do not distinguish between the degrees of flammability, but instead are simply a pass/fail test to remove the flammability classification completely.

A case may be made based on test results or data which show that aerosols containing flammable contents do not present a risk under normal conditions of use.

Other available guidance include:

American Society for Testing and materials: Standard Test methods for flammability of aerosol products, D-3065, ASTM Philadelphia, PA, 1994 Annual Index

American Society for Testing and Materials: Flash Point by Tag Closed Tester, D-56, ASTM Philadelphia, PA, 1994 Annual Index

American Society for Testing and Materials: Flash Point by Pensky-Martens Closed tester, D-93, ASTM Philadelphia, PA, 1994 Annual Index

American Society for Testing and Materials: Flash Point of Liquids by Setaflash Closed-cup Apparatus, D-3278, ASTM Philadelphia, PA, 1994 Annual Index

Collaborative International Pesticide Analytical Council (CIPAC) Handbook: MT12 Flash Point. CIPAC, Hatching Green, Harpenden, Hertfordshire (1970)

2.4.6 Additional Product Data requirements

2.4.6.1 Viscosity and surface tension

Kinematic viscosity is required for substances and formulations containing > 10 % aliphatic, aromatic or alicyclic hydrocarbons, to classify them for the aspiration hazard. The surface tension is only required where the product meets the aspiration Hazard criteria and it is used to remove the classification.

Viscosity of ULVs

The data may be used to demonstrate that ULV formulations have acceptable physical characteristics for application through relevant equipment.

Further guidance on testing can be found within OECD Guidelines No 114

Viscosity of non-newtonian liquids

The measurement is required for all non-Newtonian liquids and the results should be reported with full details of the test methodology.

The criteria for classification are:

(a) Liquid substances and formulations containing aliphatic, alicyclic and aromatic hydrocarbons in a total concentration equal to or greater than 10 % and having either:

(i) a flow time of less than 30 seconds in a 3 mm ISO cup according to EN 535 **{ISO 2431}**

Or

(ii) a kinematic viscosity measured by a calibrated glass capillary viscometer in accordance with ISO 3104/3105 of less than $7 \times 10^{-6} \text{ m}^2 \text{ s}^{-1}$ at 40 °C

Or

(iii) a kinematic viscosity derived from measurements of rotational viscometry in accordance with ISO 3129 of less than $7 \times 10^{-6} \text{ m}^2 \text{ s}^{-1}$ at 40 °C

Note that substances and formulations meeting these criteria need not be classified if they have a mean surface tension > 25 **[33]** mN m^{-1} at 40 °C **[25°C]** **[as measured by the du Nuoy tensiometer or by the test methods shown in Annex V Part A.5]**

(b) For **[other]** substances and formulations **[not subject to the above criteria]**, based on practical experience in humans

Note:

Details **[in bold and square brackets]** taken from: Commission Directive 98/8/EC of 15 December 1998 adapting to technical progress for the 25th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, OJ NoL355, 30.12.98, pp1-624. This Directive came into force on 1 July 2000. For the purposes of classification, the surface tension data should be generated on the formulation data before dilution.

2.5. ANALYSIS

Analytical data are required for the determination of the active ingredient, impurities, degradation products and residues in the product/formulation, in water and in certain circumstances in other materials. The limits of quantification should be $0.1 \mu\text{g l}^{-1}$ in water and as appropriate for other media

2.5.1. Analytical requirements for the determination of pure active substance and where appropriate relevant degradation products, isomers and impurities

2.5.1.1: Five-Batch Analysis

Applicants are required to report the results of analyses of five or more production batches of the active ingredient.

Record of five batch analysis study for each active ingredient (representative samples of the active ingredient, inactive isomers, impurities and additives, as appropriate; the analytical results reported must be designed to measure and to identify and quantify (if present) any impurity associated with an active ingredient which is expected to constitute 0.1 percent or more of total content and typically should account for at least 98 % of the material analysed; the actual content of components which are particularly undesirable because of their toxicological, ecotoxicological or environmental properties, must be determined and reported; data reported must include the results of the analysis of individual samples and a summary of that data, to show the minimum or maximum and typical content of each relevant component, as appropriate).

2.5.1.2 Guidance on methods of analysis

Analytical methods used to obtain the results of the 5-batch analysis are required. For each of the methods the following must be provided:

- Sample, standard and calibration preparation methods.
- Conditions, e.g. for chromatographic methods, details of column, eluent (including gradients where applicable) temperature (including gradients where applicable) detector and retention times
- **Validation data for the methods of analysis must be included** e.g. calibration, repeatability, linearity, recovery.
- All results, calculations, and raw data (e.g. chromatographic traces) should be submitted.

More detailed guidance on method validation can be found within the BPAU guidance document "Guidelines for validation of analytical methods for non-agricultural pesticidal active ingredients and products".

*This document is also available on the BPAU website:
<http://www.hse.gov.uk/hthdir/noframes/bpau.htm>*

2.5.2. Analytical requirements for determination of the concentration of the active ingredient in the product or in environmental media such as water, air soil etc.

- A quantitative, and if possible, also a qualitative method for defining the active ingredient in the formulated product must always be stated.
- In the case of a product/formulation containing more than one active ingredient, a method of determining each, in the presence of the other, should be provided. If a combined method is not submitted, the technical reasons must be stated
- In so far as not covered by Section 2.5.1 (analysis for active ingredient), details of analytical methods including recovery rates and limits of determination for toxicologically and ecotoxicological relevant components of the formulated product and/or residues should be provided.

3. GUIDANCE ON REPORTING STANDARDS FOR DATA SUBMISSION AND REPORT FORMAT

3.1 General Points

For a critical scientific assessment of these data to be undertaken, each study must be reported in sufficient detail.

The applicant should submit all available data that may be relevant for decision making **including original reports**. Data from published literature or other sources will only be considered where a clear description of the method and detailed presentation of results are provided.

All reports should show that experiments have been carried out systematically using sound scientific procedures. The methodology used in each test must be thoroughly described, or if the study has been conducted to an internationally recognised protocol without significant deviation then a reference to this method will be sufficient. Test conducted in accordance with internationally recognised guidelines (e.g. OECD, EPA, ASTM, AOAC, ISO, Annex V, CIPAC) are accepted and recognised by BPAU.

3.2 Good Laboratory Practice

Good Laboratory Practice (GLP) is concerned with the organisational process and the conditions under which studies are planned, performed, monitored, recorded and reported. The regulations are not concerned with the interpretation and evaluation of test results. The EC Directive 87/18/EEC required member States to take all measures necessary to ensure that safety studies submitted to regulatory authorities in support of notification or registration of certain classes of chemicals were in accordance with GLP. With regard to the position of COPR the following points are relevant.

COPR does not make reference to GLP since it pre-dates Directive 87/18/EEC and the UK GLP regulations. However, with respect to the principles of GLP and its applicability to the current statutory scheme for pesticides, the following arrangements were drawn up following a consultation exercise with Approval Holders and interested parties (Pesticides Newsletter, September 1992 and the Pesticide Register Issue 3, 1992 refer)

- (i) Mammalian toxicology studies started after 30th June 1988 must be carried out in compliance with the principles of GLP
- (ii) Physico-chemical studies and ecotoxicology studies after 1st January 1993 must be carried out in compliance with the principles of GLP
- (iii) All other safety studies started after 1st January 1993 must be carried out in compliance with the principles of GLP

Conditions (i), (ii) and (iii) apply to studies submitted either in support of an application for approval under COPR; or to satisfy a requirement for new data arising out of a review of a pesticide active ingredient or co-formulant.

In those cases where studies have not been conducted under the principles of GLP this must be justified and the quality assurance procedures used for the study must be described.

Further information on the applicability of GLP for physico-chemical studies can be found in Appendix 1

3.3 Reporting format

The following paragraphs describe guidance on presentation of data and study reports. ***Whilst these paragraphs present a preferred reporting format for applicants submitting test reports, they do not set out a style that is to be followed verbatim since BPAU recognise the need for flexibility in presentation.***

Preliminary pages

- Title/cover page:
Title and additional documentation requirements (i.e. Requirements for data submission and statements concerning confidentiality if applicable), if relevant to the study report, should precede the content of the study.
- Table of contents
- Signed GLP compliance statement
- Signed QA statement

Introduction and summary

- Scope-procedure/test used
- Source of method - include references to a published method
- Principles of the procedure/test used - provide a brief description including any references which may be applicable

Materials and Methods

- Equipment - if applicable
- Reagents and Standards (if applicable)
- Procedures - detailed stepwise description of procedure employed in test
- Instrumentation - detailed description of equipment employed in the test
- Methods of calculation (if applicable)
- Other - any and all additional information that the applicant considers appropriate and relevant

Results and discussion

Discussion of the adequacy of procedures or tests as well as whether the results provide acceptable accuracy and precision. Discussion of any other points that may have a bearing on the information/data provided.

Certification

Certification of authenticity by the sponsor and study director (including signature, typed name, affiliations, address, telephone number and date)

Tables and Figures (as appropriate)

References

Appendices

These should include any representative chromatograms etc. or other relevant material not placed elsewhere in the report.

APPENDIX 1

SUMMARY OF THE CHEMISTRY DATA REQUIREMENTS FOR NON-AGRICULTURAL PESTICIDES

| Study/test property | GLP | Additional Comments |
|--|-----|--|
| Identity of the active ingredient | | |
| BSI Common name | | See Section 2.2.1 |
| Chemical name (IUPAC nomenclature) | | See Section 2.2.2 |
| Other names (common name, trade name, synonyms) | | See Section 2.2.3 |
| CAS Number (if available) | | See Section 2.2.4 |
| EINECS or ELINCS number (if available) | | See Section 2.2.5 |
| Empirical Molecular and structural formula | | See Sections 2.2.6 and 2.2.8 |
| Molecular mass | | See Section 2.2.7 |
| Percentage purity of the active substance | | See Section 2.2.9 |
| Identity (IUPAC nomenclature) and percentage of impurities including isomers and additives together with their structural formulae | | See Section 2.2.10 |
| Spectral data (e.g. UV, IR, NMR, MS as appropriate) | | See Section 2.2.11 |
| Analytical profile of batches (5-batch analysis) | v | See Section 2.5.1.1 |
| Physico-chemical properties of the active ingredient | | |
| Appearance (physical state, colour, odour) | | See Section 2.3.1 |
| Melting point | v | See Section 2.3.2 |
| Boiling point | v | See Section 2.3.2 |
| Relative density | v | See Section 2.3.2 |
| Surface tension | v | See Section 2.3.3 |
| Vapour pressure | v | See Section 2.3.4 |
| Solubility in water | v | See Section 2.3.5 |
| Partition coefficient (n-octanol/water) | v | See Section 2.3.6 |
| Dissociation constant in water (pKa) | v | See Section 2.3.7 No longer considered to be a "core" data requirement but depending on circumstances and/or results of other studies this data may be requested |
| Oxidising properties | v | Test can be exempted see Section 2.3.8 |
| Corrosion characteristics | v | Data not always required see Section 2.3.9 |
| Explosive properties | v | Test can be exempted see Section 2.3.10 |

| Study/test property | GLP | Additional Comments |
|---------------------|-----|---------------------|
|---------------------|-----|---------------------|

| | | |
|---|---|--|
| | | |
| Information on the formulation | | |
| Physical characteristics (e.g. colour, odour, particle size) | | See Section 2.4.1 *GLP will be required for those studies that investigate potential hazardous properties (e.g. particle size) |
| Nature of the formulation | | See Section 2.4.2 |
| Type of product | | See Section 2.4.2 |
| The percentage by weight of the active ingredient(s) and all non-active ingredients | | See Section 2.4.3 *For classified liquid formulations the concentration in g/l must also be specified |
| Stability during storage | | See Section 2.4.4 *GLP for chemical stability only if on the basis of theoretical considerations hazardous compounds may be formed on storage |
| Flammability or Flash point as appropriate | v | See Section 2.4.5 |
| Viscosity and surface tension | v | Not a "core" data requirement See Section 2.4.6 for when this data is required |
| Analytical methods | | |
| Analytical requirements for the determination of the concentration of the active ingredient impurities, degradation products and residues in the product, and in certain circumstances in other materials. N.B. The limits of quantification should be 0.1 µg l ⁻¹ in water and as appropriate for other media | v | See Section 2.5.2 *It should be noted that method validation is considered to be an intrinsic part of method development and as such does not have to be carried out to GLP. However such work should be carried out using robust scientific principles |

GLOSSARY

| | |
|-------------------|---|
| Active ingredient | The component of a product which fits it for use as a pesticide |
| Annex V | Test methods described in Annex to Commission Directive 92/69/EEC of 31 July 1992 adapting to technical progress for the seventeenth time Council Directive 67/548/EEC on the approximation of laws regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances |
| Approval | An approval given jointly by Ministers under Regulation 5 of the Control of Pesticides Regulations 1986 (as amended) (COPR) |
| AOAC | AOAC International, formerly known as the Association of Official Analytical Chemists |
| ASTM | American Society for Testing and Materials |
| Batch | A defined quantity of material produced in a single series of operations |
| BPAU | The Biocides and Pesticides Assessment Unit of HSE that deals with the approval of non-agricultural pesticides and biocides |
| BSI | British Standards Institute |
| CIPAC | Collaborative International Pesticides Analytical Council |
| EEC | European Economic Community |
| EINECS | European Inventory of Existing Commercial Chemical Substances |
| ELINCS | European List of (New or Notified) Chemical Substances |
| EPA | Environmental Protection Agency (of the United States of America) |
| Formulation | A pesticide preparation containing technical active ingredient(s) and formulant(s) in a form suitable for use |
| GC | gas chromatography |
| GLP | good laboratory practice |

| | |
|----------------------------|--|
| HPLC | high performance liquid chromatography |
| IR | Infra-red (spectroscopy) |
| ISO | International Organisation for Standardisation |
| LC | Liquid chromatography |
| MS | Mass spectrometry |
| NMR | Nuclear magnetic resonance (spectrometry) |
| Non-agricultural pesticide | non-agricultural pesticides normally used in domestic situations or in aquaculture and include wood preservatives, wood treatment products, biocidal paints, surface biocides, antifouling products, rodenticides and insecticides/acaricides for use in public hygiene situations, bird stupefying baits and avicides |
| OECD | Organisation for Economic Co-operation and Development |
| Pesticide | As defined in the Food and Environment Protection Act 1985 (FEPA) (Part III., section 16 (15) + (16) and COPR (section 3, (1))). |
| Pesticide Newsletter | This is a quarterly newsletter on non-agricultural pesticides issues produced by BPAU. Copies of the Newsletter can be downloaded from BPAU's website |
| pH | pH-value, potential hydrogen value, negative logarithm (to the base 10) of the hydrogen ion concentration |
| pKa | negative logarithm (to the base 10) of the acid dissociation constant |
| P _{ow} | Partition coefficient of a substance between water and n-octanol |
| ULV | Ultra Low Volume |
| UV/VIS | Ultraviolet/Visible spectroscopy |
| w/w | weight for weight ratio |

REFERENCES

SUMMARY OF GUIDELINES AND TEST METHODS CITED IN THIS DOCUMENT

1. OECD Test Guidelines for the Testing of Chemicals (OECD, Paris)

OECD 102: Melting Point/Melting Range (updated guideline, adopted 27 July 1995)

OECD 103: Boiling Point (updated guideline, adopted 27th July 1995)

OECD 104: Vapour Pressure (updated guideline, adopted 27th July 1995)

OECD 105: Water Solubility (updated guideline, adopted 27th July 1995)

OECD 107: Partition Coefficient (n-octanol/water): Shake Flask Method (updated guideline, adopted 27th July 1995)

OECD 109: Density of Liquids and Solids (updated guideline, adopted 27th July 1995)

OECD 110: Particle Size Distribution/Fibre length and Diameter Distributions (Original Guideline, adopted 12th May 1981)

OECD 112: Dissociation Constants in Water: (Original Guideline, adopted 12th May 1981)

OECD 114: Viscosity of Liquids (Original Guideline, adopted 12th May 1981)

OECD 115: Surface Tension of Aqueous Solutions (Updated guideline, adopted 27th July 1995)

OECD 117: Partition Coefficient (n-octanol/water), HPLC Method (Original guideline adopted 30th March 1989)

OECD 122: Partition Coefficient (n-octanol/water) pH-Metric Method for Ionisable Substances (**Draft New Guideline**, November 2000)

2. Official Journal of the European Communities - Annex V Test Methods

EC Method A1 Melting/Freezing Temperature

EC Method A2 Boiling Temperature

EC Method A3 Relative Density

EC Method A4 Vapour Pressure

EC Method A5 Surface Tension

EC Method A6 Water Solubility

EC Method A8 Partition Coefficient

EC Method A9 Flashpoint

EC Method A10 Flammability (Solids)

EC Method A11 Flammability (Gases)

EC Method A 12 Flammability (contact with water)

EC Method A 14 Explosive Properties
EC Method A15 Auto-ignition temperature (liquids and gases)
EC Method A16 Relative self-ignition temperature for solids
EC Method A17 Oxidising Properties – (Solids)

**American Society for Testing and Materials (ASTM), Philadelphia, PA, 1994 (?)
Annual Index**

ASTM D-56: Flash Point by Tag Closed Tester

ASTM D-93: Flash Point by Pensky-Martens Closed Tester

ASTM D-1535 Standard Method of Specifying Colour by Munsell System

ASTM D-1544 Standard Test Method for Colour of Transparent Liquids (Gardner Colour Scale)

ASTM D-3065: Standard Test Methods for Flammability of Aerosol Products

ASTM D-3278 Flash Point of Liquids by Setaflash Closed-cup Apparatus

OTHER REFERENCES

Collaborative International Pesticide Analytical Council (CIPAC) Handbook Volume F Physico-chemical methods for technical and formulated pesticides: MT12 Flash Point: CIPAC, Hatching Green, Harpenden, Hertfordshire (1995)

ISO 257:1988 Pesticides and other agrochemicals. Principles for the selection of common names.

BS 1831, Part 1 1985: Common Names for pesticides. Guide to the principles for selection of common names

Handbook of Chemistry and Physics, CRC Publishing, Latest Edition

Hansch, C and Leo, A J in Substituent Constants for Correlation Analysis in Chemistry and Biology, John Wiley, New York 1979

Lyman, W J, Reehl, W F, and Rosenblatt, D H (ed), Handbook of Chemical Property Estimation Methods, McGraw-Hill, New York, 1983.