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Guidance for Registration Requirements for Pheromones and Other Semiochemicals Used for Arthropod Pest Control

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No. 1, *Data Requirements for Pesticide Registration in OECD Member Countries: Survey Results* (1993)

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About the OECD

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation composed of 30 industrialised countries in North America, Europe and the Pacific. The OECD works to co-ordinate and harmonize government policies, address issues of mutual concern, and respond to international problems.

The Pesticide Programme was created in 1992 within the OECD's Environmental Health and Safety Division to help OECD countries:

- harmonize their pesticide review procedures,
- share the work of evaluating pesticides, and
- reduce risks associated with pesticide use.

The Pesticide Programme is directed by a body called the Working Group on Pesticides, composed primarily of delegates from OECD Member countries, but also including representatives from the European Commission and other international organisations (e.g. United Nations Food and Agriculture Organization, United Nations Environment Programme, World Health Organization, Council of Europe), and observers from the pesticide industry and public interest organisations (NGO's).

In addition to the **Series on Pesticides**, the Environment, Health and Safety (EHS) Division publishes documents in five other series: **Testing and Assessment**; **Good Laboratory Practice and Compliance Monitoring**; **Risk Management**; **Harmonization of Regulatory Oversight in Biotechnology**; and **Chemical Accidents**. More information about the Environment, Health and Safety Programme and EHS publications is available on the OECD's World Wide Web site (see next page).

This publication was produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals (IOMC). It was approved for derestriction by the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, the governing body of the Environment, Health and Safety Division.

The Inter-Organization Programme for the Sound Management of Chemicals (IOMC) was established in 1995 by UNEP, ILO, FAO, WHO, UNIDO and the OECD (the Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. UNITAR joined the IOMC in 1997 to become the seventh Participating Organization. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

**OECD Environment Directorate,
Environment, Health and Safety Division**

**2, rue André-Pascal
75775 Paris Cedex 16
France**

Fax: (33-1) 45 24 16 75

E-mail: ehscont@oecd.org

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I. Introduction

In order to facilitate the development, registration and use of pheromones and other semiochemicals for controlling pest arthropods, the OECD Working Group on Pesticides (WGP) is developing guidance and rationale for specific registration requirements for such pest control products. Harmonisation of these requirements is critical for research, and for encouraging the development, commercialisation, and use of pheromones and semiochemicals for pest control. Using similar registration requirements in different countries will make these reduced-risk, Integrated Pest Management (IPM)-compatible pest management tools more accessible by making it easier for companies to submit registration applications across countries and by making it possible for regulatory agencies to benefit from each other's reviews.

In developing a regulatory approach for arthropod semiochemicals, the inherent differences between these products and conventional chemical pesticides were taken into consideration. Semiochemicals act by modifying behaviour of the pest species rather than killing it, are more target specific than conventional insecticides, are used at concentrations close to those in nature, and dissipate rapidly. For these reasons it is expected that most semiochemical products pose lower potential risk to human health and the environment than conventional pesticides. Environmental and health studies have demonstrated that such substances may provide effective pest control at low volumes, and at minimal risk.

This document proposes rationale and guidance for registration requirements for pheromones and other semiochemicals that affect the behaviour of arthropods and which are used in pest control products. (Semiochemicals used in traps to attract and monitor arthropods are exempt from registration). Relative to conventional pesticide data, the data set proposed here is reduced. Further reductions in data requirements are proposed for the family of chemicals that comprise the Straight-Chained Lepidopteran Pheromones (SCLPs). For regulatory purposes, SCLPs are pheromones with a well-defined unbranched aliphatic structure, which is characteristic of most known pheromones produced by members of the order Lepidoptera, including moths and butterflies.

Guidance for data requirements for registration of these products is provided in a table in Appendix 1. This table also shows how data requirements differ in countries. Additional data may be required if the review of these data suggests that the use of a proposed product could pose a risk to human health or the environment. Countries may also elect to waive certain findings.

II. Background

In 1994, Canada and the United States offered to work on harmonising data requirements for pheromones as a first step towards the development of common data requirements for OECD countries. At the beginning of 1996, the European Crop Protection Association (ECPA) prepared a report that supported the harmonisation of data requirements for both micro-organisms and pheromones, and presented it to the Working Group on Pesticides (WGP). Harmonisation was considered as a means to encourage the development of new environmentally friendly pest control products for sustainable agriculture.

Later on in 1996, Canada reported on progress to the WGP and indicated that the US and Canada were harmonised in their data requirements for the registration of pheromones in the areas of chemistry, health and the environment. There was interest in establishing a common OECD position on data requirements, and WGP members reviewed the Canadian/US document. Responses were received from Australia, Austria, Germany, Japan, Sweden, the United Kingdom, the European Commission, and the International Biocontrol Manufacturers Association (IBMA).

Further discussion at the June 1997 meeting of the WGP resulted in continued support for the development of common core data requirements for pheromones. Building on the harmonisation work with the US, Canada agreed to draft a proposal that would include the rationale for common core data requirements and that would also respond to countries' comments. Comments from the Netherlands and the UK indicated a need to explore apparent differences.

In March 1999, a meeting was organised in Wageningen (the Netherlands) to compare approaches used by different countries (Canada, the Netherlands, Switzerland, and the United States). It was evident that the four countries' data requirements were similar. Key issues concerned the assumptions each country was making about the safety of these products, particularly since knowledge about their specificity, toxicity, and environmental fate had led some countries to reduce data requirements in order to reduce the regulatory burden.

Finally in September 1999, the Canadian Pest Management Regulatory Agency (PMRA) organised the *OECD Workshop on Common Core Data Requirements for Pheromones and Other Arthropod Semiochemicals* in Ottawa. The purpose of the workshop was to give pesticide regulators from OECD countries, as well as representatives from the pheromone industry and scientific experts, an opportunity to review the progress of the WGP and to work towards a consensus on common core data requirements for pheromones.

The rationale and guidance included in this document build very much on the various activities that have been undertaken since 1994 and on the conclusions of the 1999 workshop held in Canada.

III. Definitions

- *Semiochemicals* (SC) are chemicals emitted by plants, animals, and other organisms - and synthetic analogues of such substances - that evoke a behavioural or physiological response in individuals of the same or other species. They include pheromones and allelochemicals. This report pertains only to SCs that affect the behaviour of arthropods.

- *Allelochemicals* are semiochemicals produced by individuals of one species that modify the behaviour of individuals of a different species (*i.e.* an interspecific effect). They include allomones (emitting species benefits), kairomones (receptor species benefits) and synomones (both species benefit).

- *Pheromones* are semiochemicals produced by individuals of a species that modify the behaviour of other individuals of the same species (*i.e*. an intraspecific effect).

- *Straight-chained lepidopteran pheromones (SCLPs)* are a group of pheromones consisting of unbranched aliphatics having a chain of nine to eighteen carbons, containing up to three double bonds, ending in an alcohol, acetate or aldehyde functional group. This structural definition encompasses the majority of known pheromones produced by insects in the order Lepidoptera, which includes butterflies and moths.

- *Active ingredient (AI)* is the ingredient(s) of a control product to which the effects of the pest control product are attributed, such as a synergist and all active ingredient components, but does not include a solvent, diluent, emulsifier or component that by itself is not primarily responsible for the effect of the product. The AI may be a complex mixture of active and non-active components, as in a plant extract, or it may consist of well-characterised, separately synthesised chemical compounds which are blended to produce the TGAI.

- *Technical grade of the active ingredient (TGAI)* is a product containing an active ingredient that is used to manufacture pesticides. It may contain unintentionally added impurities produced as by-products of the manufacturing process but does not contain formulants

- *Active ingredient component (AIC)* is an individual chemical compound that contributes to the activity of the active ingredient. More than one component or isomer may be combined to form the active ingredient.

- *End-use product (EP)* is a pest control agent containing active ingredient(s) and usually formulant(s) that is labeled with instructions for direct pest control use or application.

- *Impurity of toxicological concern* is an unintentional ingredient that is toxic or sensitising to mammals.

IV. Rationale for Reduced Data Requirements

Arthropod semiochemicals are inherently different from conventional pesticides in their non-toxic, target-specific mode of action and natural occurrence. They are generally effective at very low rates, comparable to levels that occur naturally. They are generally volatile and usually dissipate rapidly in the environment. In addition, many end use products are formulated in passive dispensers (hollow fibres, tapes) that present little direct exposure to humans and non-target organisms. All these factors minimise the risk of adverse effects from the use of semiochemicals. The following paragraphs demonstrate the low exposure potential of arthropod semiochemicals in general, and the low toxicity of SCLPs in particular.

→ <u>The application rate is typically low and probably comparable to natural emissions.</u>

- For purposes of pest control, releases of semiochemicals (except for perhaps repellents) are unlikely to greatly exceed natural emissions because their effectiveness is dependent on arthropod olfactory systems that are tuned to natural emission rates. Male Lepidoptera typically respond to a discrete range in ambient pheromone concentration, with the consequence that a high rate of pheromone release may be less effective than an intermediate rate of release. Controlled release technology is critical to slow down and extend effective pheromone release over the flight period of the insect, which is usually 4-8 weeks (Howse, Stevens and Jones 1998).

- Measurements of natural releases of semiochemical components at the scale of g/ha/d (gramme/hectare/day) appear to be unavailable. Estimates of emissions from individual female moths during the calling period include 8.5 ng/hr (nanogramme/hour) for *Grapholitha molesta* and 880 ng/d (nanogramme/day) for *Trichoplusia ni* (Howse, Stevens and Jones 1998). Natural releases within an agricultural setting may be estimated using information on population density and emissions from individual female moths. For example, the density of codling moth females in severe outbreaks in orchards was estimated, by different methods, to be 42,500-950,000 females/ha (17,000-380,000 females/acre)[1]. If all codling moth females, containing 4 ng pheromone in each of their glands, released 240 ng/hr, then their total pheromone release would be 10-227.5 mg/ha/hr (4-91 mg/acre/hr). For comparison, the discrete pheromone dispensers used in mating disruption of this insect have a pheromone release rate of 32.5 mg/ha/hr (13 mg/acre/hr) (Touhey, unpublished report). The recommended application rates of some pheromone dispensers (including Hercon, Ecopom, and Isomate-C Plus) used to control codling moths range from 7.5-410 g ai/ha/year (3-164 g ai/acre/year).

- On labels of registered products, recommended rates of application are typically about 50 g ai/ha per application (20 g ai/acre) and annual rates of application are typically less than 375 g ai/ha (150 g ai/acre) per year. Individually placed dispensers generally give season-long control, while broadcast formulations are usually applied at lower rates more than once in a season.

- Considering the above, in 1994 the US Environmental Protection Agency (US EPA) exempted arthropod pheromones from the requirement of an experimental use permit for trials on up to 250 acres, at a rate of up to 375 g ai/ha/yr (150 g ai/acre/yr). A threshold of 375 g ai/ha/yr was established as high enough to accommodate the maximum reasonable use level that companies would require for testing. As this level is comparable to naturally occurring emissions of pheromones during an infestation, it is expected to have no impact on public health, non-target

[1] 1 acre = 0,4 ha (hectare).

organisms, or the environment. The US EPA has received no reports of adverse effects to humans or the environment arising from this policy.

→ Volatility and rapid environmental transformation minimise residues in crops and exposure of non-target organisms.

- Semiochemicals are generally assumed to dissipate rapidly in the environment, primarily by volatilisation and degradation; this is partly because persistence is counterproductive to a communication signal received by an olfactory system. Only the aerial compartment within and around the crop need be loaded and concentrations in the air are unlikely to exceed several ng/m^3 (see *e.g.* Bäckman 1997; Koch *et al* 1997).

- Many pheromones and other semiochemicals must include a UV screen (absorber) and an anti-oxidant to prevent decomposition on the shelf. Once these products are taken into the field and volatilised, they undergo photo-oxidation. SCLPs are readily transformed by oxidation of the double bonds in the carbon chain and other types of oxidative degradation. The enzymes operative during the degradation of SCLP residues are ubiquitous in nature.

- Studies of the fate of SCLPs on moistened soil and in water confirm rapid dissipation, largely due to volatilisation of the parent compounds. The half-life of gossyplure (Z,Z and Z,E 7,11-hexadecadien-1-ol acetate) at 32°C in soil was 1 day, and 7 days in water (Henson 1977). Similarly, the half-lives of (Z)-9-tetradecenal and (Z)-11-hexadecenal were reported to be 29 and 50 hours, respectively, in soil (22°C), and 30 and 90 hours in water (24°C) (Shaver 1983).

- When lepidopteran pheromones were applied in retrievably-sized dispensers, food residues from airborne transfer of pheromone were not detected; in analyses of fruit treated with 325 to 350 g ai/ha (129 – 141 g ai/acre), no pheromone residues could be found with a detection limit of 2-5 µg/kg (or ppb) (Spittler *et al*., 1988 and 1992).

- Microencapsulation of pheromones can result in a prolonged release of effective levels of pheromones at application rates that leave little, if any, food residues. In a laboratory study of volatilisation from an SCLP (tridecenyl acetate) formulated in ~35µm microcapsules, about 70% of pheromone remained after 30 days, a slower rate of loss than anticipated. Residues of the same pheromone were analysed from unwashed tomatoes from field-treated plants, with the following results: 21-72 µg/kg on the day of application, 0.9-6.8 µg/kg on day 15, and 0.29-1.2 µg/kg on day 30. Washing the tomatoes brought all the residues below the level of detection. This study demonstrates pheromone residue levels in tomatoes that are several orders of magnitude lower than previously estimated. The process of application, weathering, and other environmental transformation processes lead to a reduction in the active ingredient that approaches the system limit of detection in the expected 3-week lifetime of the raw agricultural product (Federal Register v.60, Aug.30/95).

→ SCLPs are of low toxicity to mammals.

- The US EPA, Canada's PMRA and the European Union's regulatory authorities have received no reports of adverse effects to human health or the environment associated with semiochemicals registered for use in mating disruption of arthropods and other applications. Most registered products are SCLPs.

- The data submitted for registering semiochemicals in the United States (most are SCLPs) have indicated no mammalian toxicity when mammals are exposed to high doses. Available data indicate: acute oral toxicity (LD_{50} > 5000 mg/kg - EPA category IV, non-toxic), acute dermal toxicity (LD_{50} > 2000 mg/kg - EPA category IV, non-toxic), acute inhalation toxicity (LC_{50} generally > 5 mg/L - EPA category III-IV, practically non-toxic), no evidence of mutagenicity (Ames Salmonella assay), and minimal eye and skin irritation (Federal Register v.59, Jan.26/94). Published mammalian toxicity data on SCLPs indicate no significant acute toxicity to humans (Inscoe and Ridgway 1992).

- SCLPs are biodegradable by enzyme systems present in most living organisms, and should present no problems with their normal physiology. For example, the known metabolism of long-chain fatty acids predicts that SCLPs would be metabolised either by β-oxidation yielding a series of paired carbon losses or by complexing with glucuronide and excretion by the kidneys (Federal Register v.60, Aug.30/95).

- The US EPA has used the results of two subchronic toxicity studies as bridging data for the safety assessment of other structurally similar SCLP products submitted for registration. Published results of these studies indicated no significant health effects. A 90-day feeding study (using rats) was conducted at doses up to 1 g/kg, of a commercial blend of branched acetates with an aliphatic chain length between C_{10} to C_{14}. The results indicated no significant signs of toxicity other than those expected with longer term exposure to high dose of a hydrocarbon, namely, histopathologic evidence of nephropathy in males and increased liver and kidney weights in both sexes (Daughtrey *et al*. 1990). A developmental toxicity study (using rats), involving inhalation exposure to unbranched, primary alcohols with chain length C_8 to C_{10}, indicated no detectable developmental toxicity (Nelson *et al.* 1990).

V. Data Requirements

The data required to chemically characterise a semiochemical pest control product and to demonstrate how it is most effectively used are the same as for conventional pesticides.

However, the factors described above justify substantial reductions in health and environmental data requirements, especially for SCLPs, a well-defined chemical group for which considerable data are available (Touhey 1990). Also for other classes of semiochemicals, it may be justified to waive certain required studies if the registrant can provide an adequate rationale. To date, the US-EPA has registered 20 lepidopteran and 8 non-lepidopteran active ingredient pheromones, mostly on the basis of acute toxicity and chemistry data.

A. Data Required for Product Analysis

Product analysis information should be sufficient to identify the active ingredient, formulants and impurities of toxicological concern in the pest control product, and to provide specific physical and chemical characteristics. For TGAIs, identity data are used to determine whether an active ingredient is identical or substantially similar to another active ingredient or a naturally occurring substance. Required elements include a description of starting materials, manufacturing process, discussion of the possible formation of impurities, upper and lower concentrations (certified limits) for each AIC with upper limits for impurities, and analytical data including component identity confirmation (three batches supporting specifications). For end-use products, required elements include a description of starting materials, formulation process, upper and lower concentrations (certified limits) of TGAI and formulants, and an enforcement analytical method for each AIC; no batch analyses are required. If the formulation process introduces or enhances the presence of impurities of toxicological concern, this should be identified along with upper limits and an enforcement analytical method for such impurities.

Data on physical and chemical characteristics of the pesticidal active ingredient and end-use products include, when appropriate, information on their colour, odour, physical state, stability, oxidising and reducing potential, storage stability and corrosiveness.

B. Data for Assessment of Risk to Human Health and Safety

Toxicology

Sufficient information to identify potentially hazardous products is always required. Studies of teratogenicity and subchronic exposure can generally be waived if long-term exposure above background levels can be excluded or if a substance is a member of a well-characterised chemical group, such as SCLPs, for which toxicological concerns have already been addressed. In general, the possibility of irritation, dermal sensitisation, acute toxicity, and mutagenicity should be taken into account, as well as the latest medical data.

Less information is available on the toxicity of other forms of semiochemicals that may contain ketone, epoxide, lactone, terpenoid, pyrazine, pyran, and other aromatic structures. If they have the toxicity characteristics of other chemicals with these sub-structures or functional groups, they may be more

toxic than the SCLPs, and might potentially require long-term tests (Federal Register v.59, Jan.26/94; Inscoe and Ridgway 1992).

Dietary, Occupational, and Bystander Exposure

Metabolism and residue chemistry data are designed to provide the information necessary to determine the site, nature, and magnitude of residues in or on food, feed and tobacco, so that the acceptability of crops which have been treated with a pest control product can be established. For semiochemicals, residue data may not be required if it has been determined that detectable residues on the consumable commodity are unlikely to occur, or that residue levels are unlikely to exceed natural background levels during outbreaks of the pest, and that the residues are not toxic.

In Canada and the European Union, applicants are encouraged to provide a scientific rationale for waiving residue data based on the low potential risk of any residues on a treated crop. The US EPA has established an exemption from the requirement of a food tolerance (*i.e.* Maximum Residue Limit) for most uses of arthropod semiochemicals, namely:

(i) in retrievably-sized polymeric dispensers used at a rate of no more than 375 g ai/ha/yr (150 g ai/acre/yr);
(ii) at a rate of no more than 50 g ai/ha (20 g ai/acre) per application regardless of formulation, provided no potentially adverse effects are observed during the Tier I toxicity testing; and
(iii) SCLPs at rates of up to 375 g ai/ha/yr, regardless of the mode of application.

Sufficient information is required to characterise occupational/bystander exposure potential. This would include consideration of application method and rate, and appropriate physical-chemical properties. For those substances with significant exposure potential and/or those substances with toxicological concerns, additional exposure data would be required.

C. Data for Assessment of Environmental Risks

Sufficient information is required to assess the hazard potential of pheromones and other semiochemical pest control agents to terrestrial wildlife, aquatic animals, plants, and beneficial insects. The European Commission also requires that the environmental fate of a semiochemical (*e.g.* stability in air and water) be assessed, based on available information. Test data on a compound will only be required if its use will result in environmental contamination exceeding natural background levels. Application rates of up to 375 g SCLP/ha/yr are generally understood to result in exposure levels which are comparable to natural emissions and safe for non-target species (Maloney 1999). This threshold may or may not be applicable for other kinds of semiochemicals; applicants are invited to request waivers of environmental testing, based on information that indicates application rates are comparable to natural emissions.

Compared to conventional pesticides, fewer tests are required for semiochemicals and the number of organisms per test are reduced due to the non-toxic mode of action of semiochemicals and limited exposure of non-target organisms. Experience to date indicates that SCLPs are not acutely toxic to birds; LC_{50} and LD_{50} values greater than 5000 mg/kg or 2000 mg/kg, respectively, have been reported on quail and mallard duck for products submitted for registration (Touhey 1990). Avian dietary toxicity is only of concern for formulations that might be ingested, *e.g.* granules. Toxicity data for human safety are generally sufficient to assess potential effects on wild mammals, so no wild mammal testing is required. Non-target terrestrial plant studies (seedling emergence, vegetative vigour) would only be required of a semiochemical if there were reason to suspect possible effects.

Pheromones and other semiochemicals have been characterised as toxic to aquatic invertebrates (*Daphnia*) and fish (Federal Register v.59, July 1994; Inscoe and Ridgway 1992), although these results may reflect a suffocating effect of the oily surface film formed by high test concentrations of many SCLPs (Touhey 1990). Aquatic invertebrate and fish toxicity data are required for direct application to aquatic sites for all semiochemicals. One species of fish (rainbow trout), an aquatic invertebrate (*Daphnia magna*), and (in Europe) an algal species should be tested. Aquatic testing is not required for fixed point dispensers applied over land.

For potential effects on non-target insects, a discussion of available information may be sufficient. There are no widely accepted, simple tests for evaluating effects on non-target insects because the behavioural effects of semiochemicals are likely to influence reproduction or growth, which require longer-term testing and are more difficult to quantify than mortality. Generally, literature is provided by registrants on specificity to target insects. The registrant should also report any adverse effects on non-target insects noted during efficacy testing, particularly effects on insect predators or parasites of the target organism, species closely related to the target pest, and pollinators. The range of invertebrates likely to be affected by a semiochemical can be established by comparing baited and unbaited traps in environments similar to those of intended use. If no such effects are noted during efficacy testing, and in the absence of any other data indicating potential for adverse effects, no non-target testing will be indicated.

Environmental Fate

Data on the persistence of a semiochemical and its transport from the site of application to another site or medium may be required if ecotoxicity data or public literature indicate a hazard to biota. If the data indicate that significant persistence and transport of these agents in any part of the environment occur, such that significant exposure to non-target organisms could be expected, additional environmental testing will be necessary.

Environmental fate data are used to determine the estimated environmental concentration (EEC) by performing a simple mass-balance analysis of the pesticide, taking into consideration the pesticide application parameters (*i.e.* rate, frequency, and site of application) following initial tests that measure transport properties (volatility, dispenser-water leaching, vapour pressure and water solubility). Where persistence testing is required (hydrolysis, aerobic soil metabolism, aerobic aquatic metabolism, soil photolysis, aquatic photolysis, adsorption/desorption, and octanol/water partition coefficient), each of the transformation processes should be expressed as a half-life for the particular environment or as a rate constant for the environmental process depending on the test. Estimated environmental concentrations can then be calculated for different times using these data and the field application rate of the pesticide. Aquatic use patterns and non-dispenser pesticides will require mass balance analysis following persistence tests.

D. Data for Assessment of Efficacy

The mode of action of a semiochemical product should be explained in terms of its function in modifying the behaviour of the target pest, and information should be provided to support the claim that the active ingredient is a naturally occurring arthropod semiochemical.

In the European Union and Canada, data from scientifically conducted efficacy trials are required to support pest control claims on the product label, and to demonstrate how the product may be most

effectively used. Studies should be conducted with the end-use product proposed for registration, applied in a manner consistent with label instructions regarding timing, rate, method and site of application. The experimental design should include untreated plots as an indication of population pressure and, if possible, plots receiving a commercial standard treatment with conventional pesticides of known efficacy as a basis for comparison with the semiochemical treatment.

Pre-submission consultation is strongly recommended to discuss the adequacy of available information, the need for additional trials, and the performance standard for registration. Sufficient efficacy data are required to confirm the performance. At least one study should evaluate a range of rates to demonstrate the lowest effective rate of application. For products which act through mating disruption and which are to be used within an Integrated Pest Management (IPM) strategy, demonstration that mating success has been reduced (*e.g.* using caged or tethered female moths) may be sufficient to support registration. Alternatively, data from trap catches, together with assessment on reductions in pest numbers and/or damage, are required.

In conjunction with the efficacy trials, information on any adverse effects on the crop or site should be reported, including phytotoxicity and effects on non-target arthropods.

Qualitative information is required on the pest species life cycle, and on the nature and extent of damage it causes. Other useful information includes the compatibility of semiochemicals with Integrated Pest Management programmes and their contribution to risk reduction.

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APPENDIX 1

Guidance for Registration Requirements for Pheromones and Other Semiochemicals used for Arthropod Pest Control

The requirements for data or information are listed in the left column of the following table. Each requirement has been assigned a status of "R" or "CR".

- **R** means that information is required; the requirement may be satisfied:
  1. by data on the test substance;
  2. by published information;
  3. by surrogate information or bridging data to another substance, if both substances belong to a well-known group of substances, *e.g.* Straight-Chained Lepidopteran Pheromones (SCLPs); or
  4. by a rationale to waive the requirement because it is unnecessary or impractical.

- **CR** means that the information is only required under the conditions in the right column. Many of the data points marked CR represent types of information that are only required for high exposure scenarios, or if hazards are noted from other data points.

- **CR/R** means that the information is only required under the conditions in the right column for Canada, the US and Switzerland; and that the data point must be addressed in all submissions to European Union Member States, with the understanding that there is an appropriate basis for waiver rationale (see the right column).

Information in the right column further details the requirements, or specifies particular cases, for requesting a waiver.

The types of information that are underlined indicate where requirements are different among OECD countries.

Data requirements defined under European Union Plant Protection legislation are without prejudice to requirements to fulfil classification, packaging and labelling rules.

STATUS OF DATA REQUIREMENTS R Require data, surrogate data or a rationale to waive data CR only required in conditions under right-hand column		CONDITIONS AND COMMENTS
Mode of action	R	
FUNCTION, HANDLING and LABEL INFORMATION		
Information on Function & Handling: function of product, directions for use, formulation, field of use and use sites, pest(s) controlled, application rate and timing, pre-harvest interval, application method, precautionary and emergency measures, procedures to clean equipment and spills, disposal of unused product.	R	
Labeling requirements regarding hazard classification and risk identification	R	Required by EU, according to Directives 67/548/EEC and 99/45/EC.
CHEMISTRY		
TECHNICAL GRADE OF ACTIVE INGREDIENT (TGAI)		
Composition: - g/kg or g/L of TGAI - g/kg or g/L of all ingredients exceeding 1g/kg	R	For US and Canada, also provides figures in %w/w (to convert g/kg or g/L expressions to %w/w: divide by the density expressed in terms of g/kg or g/L, and multiply by 100) Where the manufacturing process is such that impurities and by-products which are particularly undesirable could be present in the TGAI, the content of each such compound must be determined and reported even if below 1 g/kg (0.1%w/w)
Identity by spectral confirmation, including one or more of UV/IR/NMR/MS.	R	To extent necessary to identify components.
Description of starting materials, production process and potential impurities	R	
Analytical data and methodology (including spectral confirmation of identity)	R	EU requires 5 batch data if feasible; Switzerland, US, Canada 3 production batches if feasible.
Analytical methodology and data for impurities of toxicological concern.	CR	Only required if manufacturing methods and materials indicate potential for presence of a toxic impurity.
Analytical method for residues.	CR	Relevant if residue data is required.
Colour, odour, physical state, relative density or specific gravity, stability (temperature, metals).	R	
For each known Active Ingredient Component (AIC) of the TGAI (i.e. pure active components which are separately synthesised)		
Description of starting materials and manufacturing process.	R	Required if AIC is made by or specifically for the TGAI manufacturer. If an AIC is purchased commercially, the name and address of its manufacturer and specifications describing its composition are required.

STATUS OF DATA REQUIREMENTS R Require data, surrogate data or a rationale to waive data CR only required in conditions under right-hand column		CONDITIONS AND COMMENTS
Physical properties: melting point, boiling point, solubility in water and other solvents, colour, odour.	R	
UV/visible absorption.	R	EU: required to estimate environmental fate. US/Canada/Switzerland: conditionally required for SCLPs, if toxicity tests demonstrate hazard to biota.
Vapour Pressure	R	
Volatility (Henry's law constant)	R	calculated from vapour pressure and water solubility
Dissociation constants (when component contains an acid or base functionality)	R	
Octanol/water partition coefficient.	R	May be waived if component hydrolyses in water or is soluble in water in all proportions.
Submission of analytical standards (samples).	R	
END-USE PRODUCT (EP)		
Formulation process and starting materials.	R	Required by US, Canada, Switzerland
Composition: - g/kg or g/L of TGAI - g/kg or g/L of all ingredients exceeding 1g/kg	R	For US and Canada, also provides figures in %w/w (to convert g/kg or g/L expressions to %w/w: divide by the EP density expressed in terms of g/kg or g/L, and multiply by 100) Where the manufacturing process is such that impurities and by-products which are particularly undesirable could be present in the TGAI, the content of each such compound must be determined and reported even if below 1 g/kg (0.1%w/w)
Analytical methodology (AI) for post-registration monitoring.	R	
Physical properties: colour, odour, physical state, specific gravity, pH, formulation type, container type, explosivity, viscosity, technical characteristics	R	To be addressed where applicable
Corrosion characteristics and stability of formulation during storage.	R	Stability of formulation during storage not required by US.
DATA FOR ASSESSMENT OF HEALTH RISK		
Summary	R	
TOXICOLOGY		
Acute oral toxicity: TGAI and EP	R	Data may be waived: - for TGAI, if substance is a member of a well characterised group e.g. SCLPs, and the acute toxicity of that group is described. - for EP, if toxic potential of formulant(s) are well known.

STATUS OF DATA REQUIREMENTS R Require data, surrogate data or a rationale to waive data CR only required in conditions under right-hand column		CONDITIONS AND COMMENTS
Acute dermal toxicity: TGAI and EP	R	Data may be waived: - for TGAI, if substance is a member of a well characterised group e.g. SCLPs, and the acute toxicity of that group is described. - for EP, if toxic potential of formulant(s) are well known.
Acute inhalation toxicity: TGAI and EP	R	
Primary eye irritation: TGAI and EP	R	
Primary dermal irritation: TGAI and EP	R	
Dermal sensitisation/reporting of hypersensitivity incidents : TGAI and EP	R	Data may be waived: as above (Canada, EU). US requires reporting of any hypersensitivity incidents, instead of test data.
Mutagenicity (gene mutation in microbes and mammalian cell systems, and chromosome aberration): TGAI	R	Data may be waived if substance is a member of a well characterised group e.g. SCLPs and the mutagenicity of that group is described.
Medical data, available information: TGAI and EP	R	
Short -term study by appropriate route: TGAI	CR/R	Required if there is a significant exposure potential, e.g. above background levels, or if a tolerance/MRL will be set. Data may be waived if the substance is a member of a well characterised group e.g. SCLPs and the repeated dose toxicity of that group is described.
Teratogenicity/ developmental toxicity/ 1 species: TGAI	CR/R	Required if there is a significant exposure potential, e.g. above background levels, or if a tolerance/MRL will be set. Data may be waived if the substance is a member of a well-known group of substances for which the teratogenicity/developmental toxicity is described.
Long term toxicity (chronic) and carcinogenicity.	CR	Trigger: adverse effects in mutagenicity or short-term studies; waived if long term exposure above background can be excluded.
Multigeneration reproduction, teratogenicity (in second sp.), animal metabolism, neurotoxicity, immunotoxicity	CR	Trigger: adverse effects or toxicity concerns arising from other data points for Health Risk.
OCCUPATIONAL OR BYSTANDER EXPOSURE (Using the End Use Product)		
Use Description/Scenario (Application & Post Application)	R	Estimation of exposure based on available information (application method, rate, physical chemical properties)
Passive dosimetry (mixer/loader/applicator and/or post-application) or biological monitoring	CR	Required if the use description information demonstrates significant exposure potential and/or if toxicity tests or published data indicate a concern. Solid-matrix dispensers are unlikely to present significant exposure potential, but some sprayed applications might.
Dislodgeable residues	CR	
Ambient air samples	CR	

STATUS OF DATA REQUIREMENTS R Require data, surrogate data or a rationale to waive data CR only required in conditions under right-hand column		CONDITIONS AND COMMENTS
Biological monitoring	CR	
Dermal absorption	CR	
Clothing penetration, epidemiology, package integrity.	CR	
METABOLISM STUDIES and RESIDUE ANALYSIS of FOOD, FEED AND TOBACCO		
Metabolism/toxicokinetics study on animals and plants which may be directly exposed to SC through use.	CR	Trigger: required if a tolerance /MRL is required, i.e. if semiochemical is for use on food/feed crops and if a toxicity concern is raised by toxicity data.
Analytical residue methodology for food crops	CR	
Crop residue data	CR	
Meat, milk, poultry, and egg residue data.	CR	
Freezer storage stability, produce quality	CR	
DATA FOR ASSESSMENT OF ENVIRONMENTAL RISK (using end use product EP unless otherwise specified)		
Summary	R	
EFFECTS ON NON-TARGET ORGANISMS		
Birds dietary toxicity	CR	Required if an EP could be ingested by birds, e.g. a granular EP
Bees : prefer EP	CR/R	Information/discussion, to address whether behaviour or reproduction would be affected, is required if exposure is likely to exceed natural background levels, e.g. >375 g ai/ha/yr for SCLPs.
Other terrestrial arthropods (crop-specific beneficials, related spp.): prefer EP	CR/R	
Freshwater invertebrate acute toxicity: prefer EP	CR/R	Required if applied by air, or directly to water, or at rate exceeding natural background levels, e.g. > 375 g ai/ha/yr for SCLPs. Not required for product in affixed dispensers on land. However, data may be required by EU for labeling (directive 67/565).
Freshwater fish acute toxicity: prefer EP	CR/R	
Algae: prefer EP	R	EU requirement: waived for EPs in affixed dispensers on land; may be waived if exposure is unlikely to exceed natural background levels (e.g. at > 375 g ai/ha/yr for SCLPs). Data may be required by EU for labeling (directive 67/565), although waivable based on structure-activity relationships.

STATUS OF DATA REQUIREMENTS R Require data, surrogate data or a rationale to waive data CR only required in conditions under right-hand column		CONDITIONS AND COMMENTS
Earthworms	R	EU requirement, if product is applied to soil and can accumulate in soil. Required if exposure exceeds natural background levels, (e.g. at > 375 g ai/ha/yr for SCLPs).
Soil microorganisms	R	
Long-term laboratory or field testing on: - aquatic animals - terrestrial animals - non-target plants - non-target insects	CR	Required on a case-by-case basis, when results of acute tests, observations from efficacy trials or literature indicate potential adverse effects and results of environmental fate tests indicate exposure of non-target organisms. Testing might include: bioaccumulation studies, chronic toxicology in freshwater invertebrates, long-term toxicology in freshwater fish.
ENVIRONMENTAL FATE		
Assessment based on available information : TGAI	R	EU requirement: may be waived if exposure is unlikely to exceed natural background levels, (e.g. at > 375 g ai/ha/yr for SCLPs.)
Experimental studies in compartments of possible concern: - Hydrolysis : TGAI - Phototransformation on soil and/or in water : TGAI - Stability in air, persistence of volatiles : TGAI - Biotransformation (aerobic soil and/or aerobic aquatic): TGAI - Adsorption-desorption : TGAI - Leaching of each AIC from dispenser by water : EP - Volatilisation from dispenser, release rate: EP	CR	Required on a case-by-case basis, e.g. if ecotoxicity data or public literature indicate a hazard to biota.
EFFICACY (for the end use product)		In US, submission of efficacy data is only required if product is to control a public health pest, e.g. fire ants
Efficacy Summary	R	
Description of pest problem and AI's mode of action	R	May be addressed by qualitative description.
Efficacy trials of product, used as directed on label, including reporting of adverse effects to site (e.g., phytotoxicity),	R	
Sustainability considerations (compatibility with integrated pest management; contribution to risk reduction)	R	May be addressed by qualitative description.