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Natural background exposure to pheromones:

Building confidence for risk management

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Contents

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Building confidence for risk management.

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ABSTRACT

Pheromones are made up of complex organic compounds that affect the behaviour of organisms of the same species as the emitter, released naturally into the environment at concentrations that vary with species, habitat, time of day and year, as well as local weather conditions at the time of measurement. Manufacturers of pheromone-based pesticides are required to demonstrate to regulators – as with any other pesticide – that they do not pose an unacceptable risk to humans and other non-target organisms and that they are effective as claimed on the label. OECD[3] recommends that regulators focus on the release rate per hectare per hour when evaluating authorisations of semiochemicals, including pheromones. Field measurements of concentration in the air compartment or total release rate of semiochemicals (e.g., due to severe outbreaks of the pest) are usually not available. The current EU guideline (GD)[4] provides a 3-step approach using a "fixed steady one-cell model" to calculate exposure of the product against the likely maximum natural background exposure. While the 3 examples in the GD (*Cydia pomonella, Pectinophora gossypiella, Spodoptera exigua*) show good agreement between the mathematical modelling and the measured results, some European regulators still require greater assurance on the scenario to be used with pheromone products for environmental risk assessment purposes. This paper will compare alternative approaches adopted by regulators in other regions, to the agreed framework in Europe.

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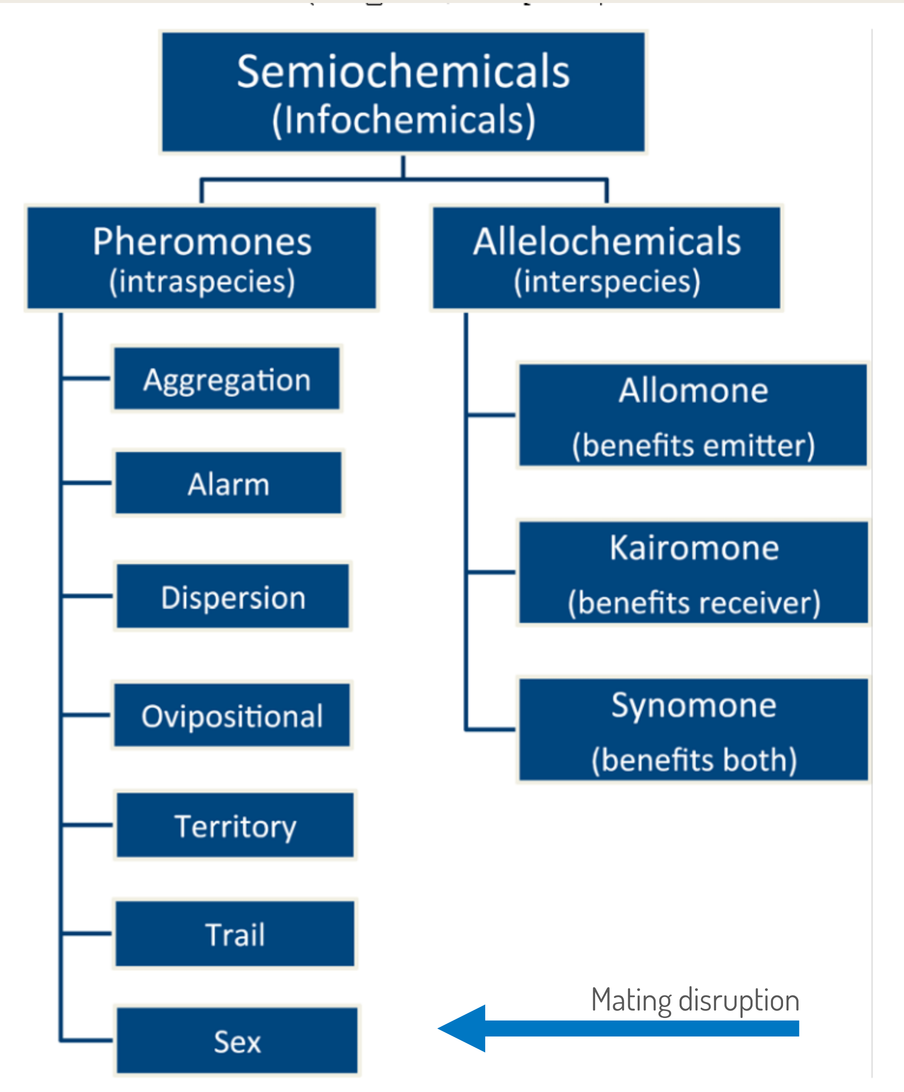
[3] OECD GUIDANCE DOCUMENT ON SEMIOCHEMICAL ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS, ENV/JM/MONO(2017)33, 10 Jan 2018 (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2017)33&doclanguage=en)
[4] GUIDANCE DOCUMENT ON SEMIOCHEMICAL ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS, SANTE/12815/2014 rev. 5.2, May 2016 (https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_app-proc_guide_doss_semiochemicals-201605.pdf)

Definitions

Semiochemical:

A semiochemical, from the Greek σημεῖον meaning "signal", is a chemical substance or mixture released by an organism that affects the behaviors of other individuals.*



*"Definition of Semiochemical". The Dictionary of Forestry. Bethesda, Maryland: The Society of American Foresters (SAF). 2008..

Definitions

Pheromone: A pheromone (from Greek phero "to bear" + hormone from Greek – "impetus") is a secreted or excreted chemical factor that triggers a social response in members of the **same** species*

German Biochemist Adolf Butenandt characterized the first such chemical, Bombykol (a chemically well-characterized pheromone released by the female silkworm to attract mates) * *

*Karlson, P.; Lüscher, M. (1959-01-03). "'Pheromones': a New Term for a Class of Biologically Active Substances". Nature. 183 (4653): 55–56. doi:10.1038/183055a0. PMID 13622694.
* *Butenandt, Adolf; Beckmann, Rüdiger; Hecker, Erich (2009). "Über den Sexuallockstoff des Seidenspinners, I. Der biologische Test und die Isolierung des reinen Sexuallockstoffes Bombykol". Hoppe-Seyler's Zeitschrift für Physiologische Chemie. 324 (Jahresband): 71–83. doi:10.1515/bchm2.1961.324.1.71. PMID 13689417.

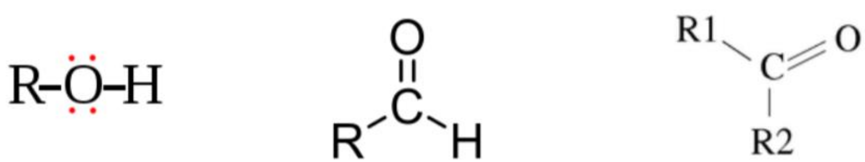
Definitions

- <u>Straight-chained lepidopteran pheromones</u> (SCLPs) are a group of pheromones consisting of unbranched aliphatics having a chain of nine to eighteen carbons, containing up to three double bonds and 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.

- unbranched aliphatic chain (between 9 and 18 carbons)

- ends in an alcohol, aldehyde or acetate functional group



- contains up to 3 double bonds

Definition: Natural background concentration

Natural exposure level is the level of exposure that might occur in the environment by a high population of emitting organisms independently from the use of plant protection products, thus humans and other non-target organisms are expected to be impacted by such exposure level (OECD, 2018)

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* OECD GUIDANCE DOCUMENT ON SEMIOCHEMICAL ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS, ENV/JM/MONO(2017)33, 10 Jan 2018 (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2017)33&doclanguage=en)

Lepidopteran pheromone biology Taxonomy

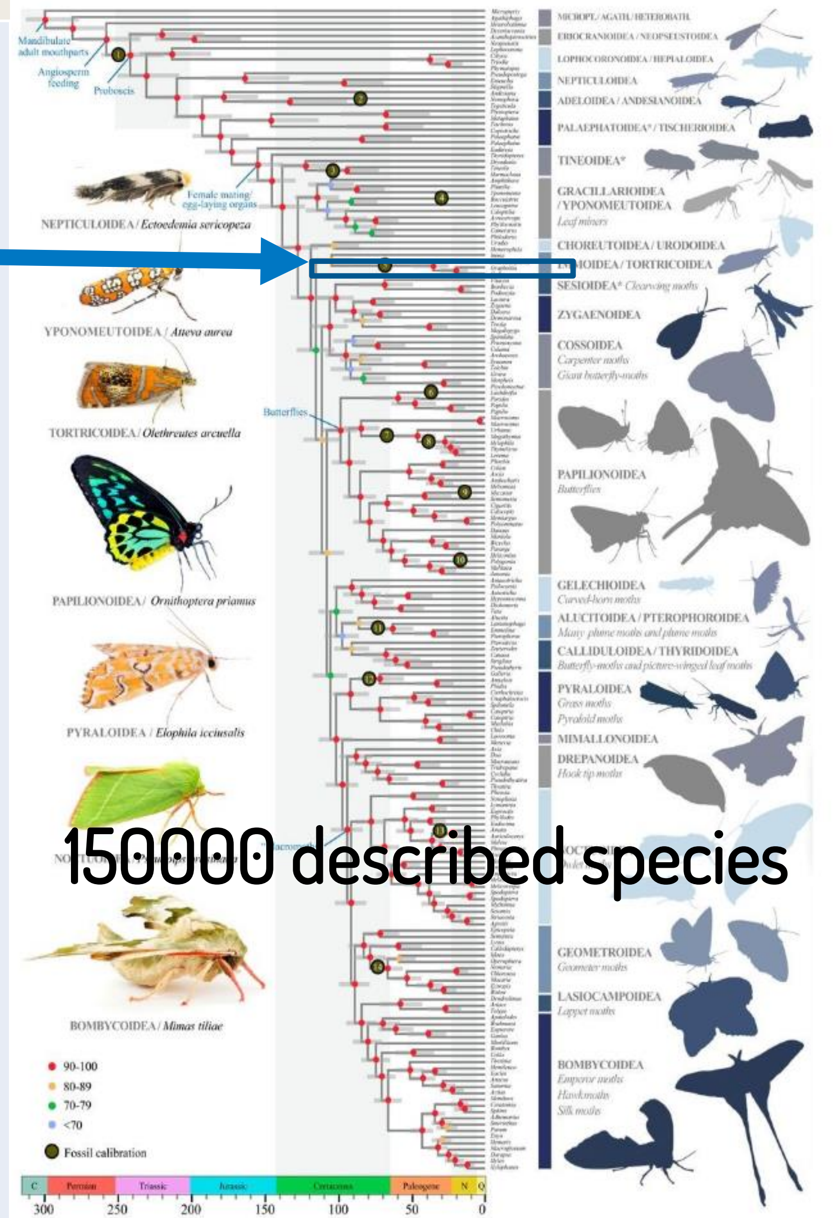
Targets in EU approved SCLP products:

- *Anarsia lineatella* (Peach twig borer)
- *Chilo suppressalis* (Asiatic rice borer)
- *Cydia pomonella*+ (Codling moth, Leaf roller)
- *Grapholita funebrana** (Plum fruit moth)
- *Grapholita molesta* (Oriental fruit moth)
- *Eupoecilia ambiguella* (Vine moth)
- *Lobesia botrana* (European grapevine moth)
- *Ostrinia nubilalis* (European corn borer)
- *Pectinophora gossypiella* (Pink bollworm)
- *Pseudococcidae ficus* (Vine mealybug)
- *Spodoptera littoralis* (Egyptian cotton leafworm)
- *Tuta absoluta* (Tomato leafminer)
- *Zeuzera pyrina* (Leopard moth)

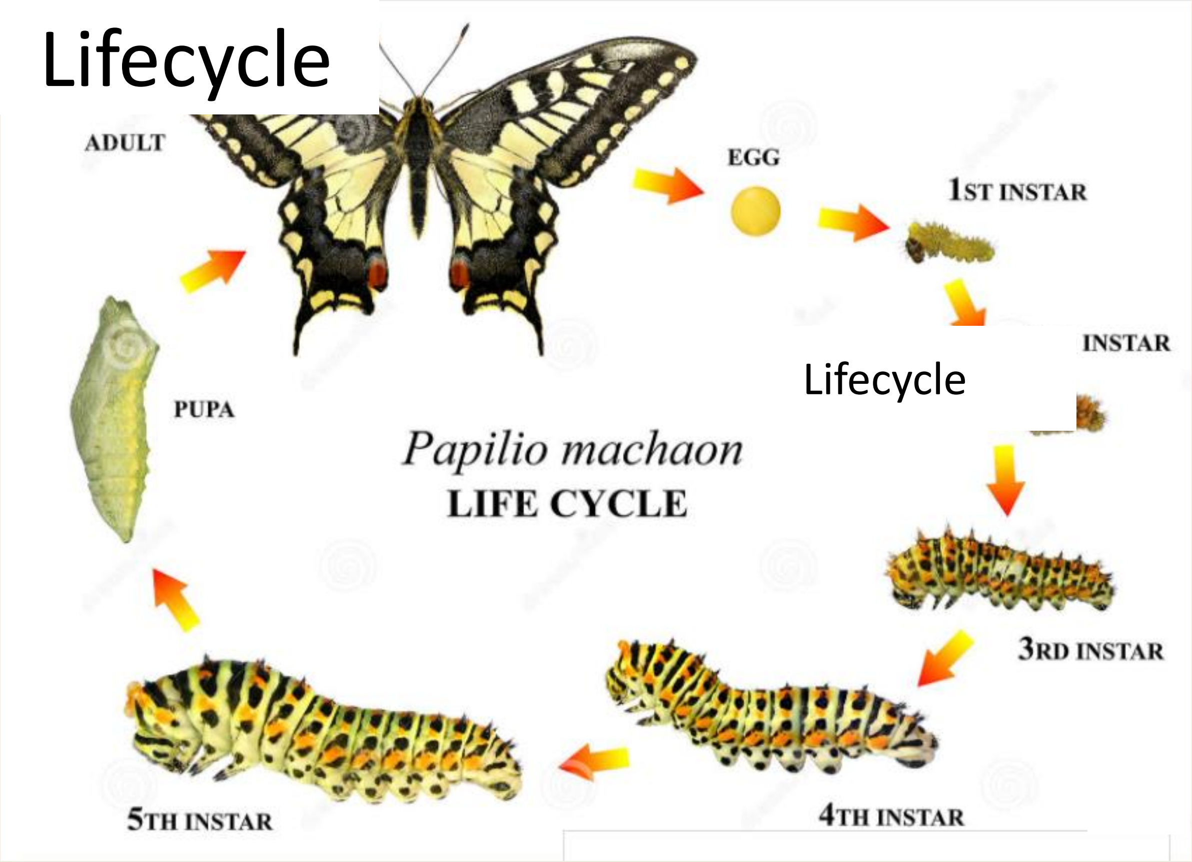
*obsolete latin name: *Cydia funebrana*

+*C. pomonella* larvae can easily be confused with *G. funebrana*

NB. Often targeted with other L. species by multiple pheromone tank-mixture products



Lifecycle



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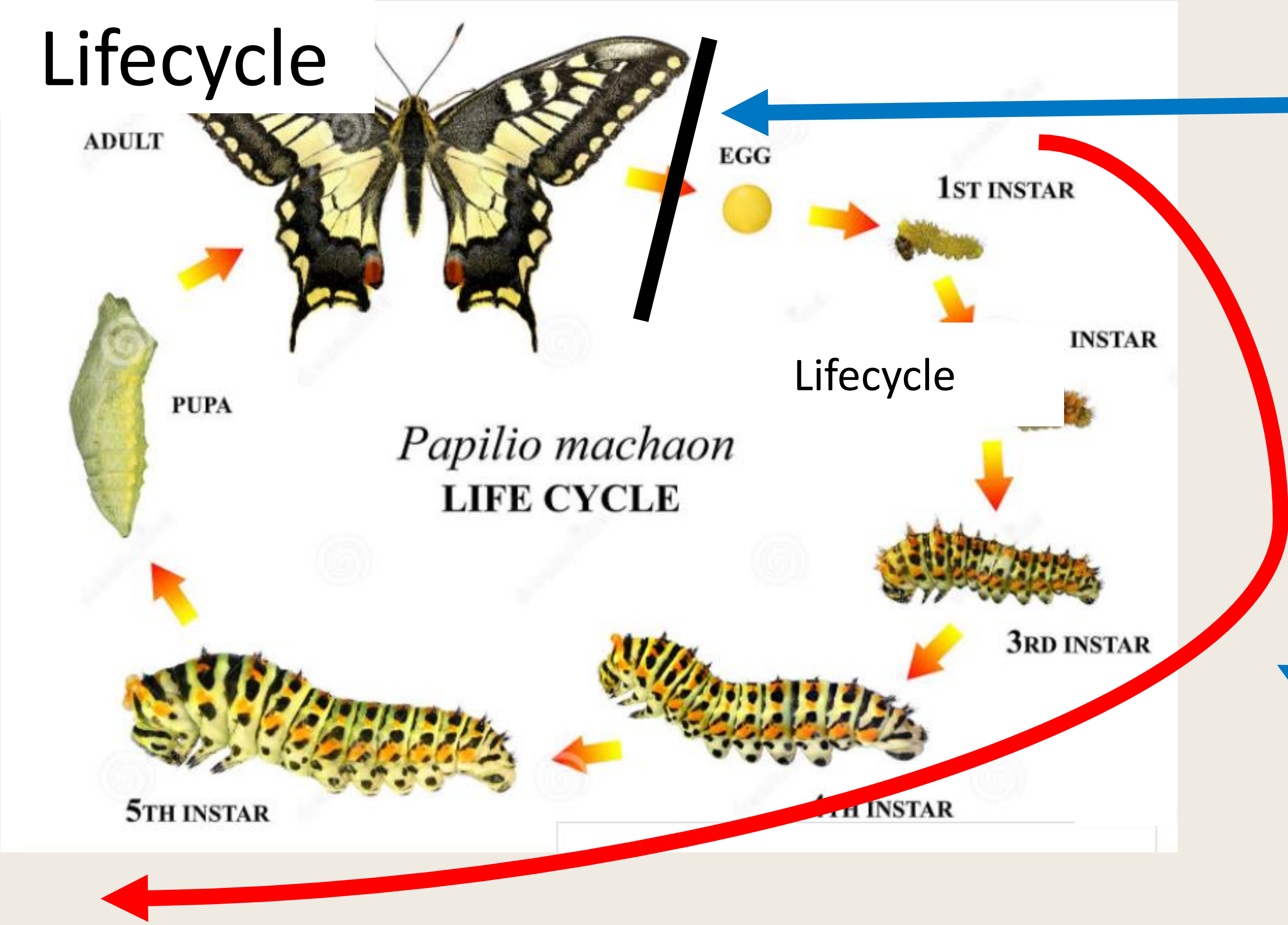

When control is targeted

When the damage is done...

Trad. chemistry (synthetic insecticides) treat when damage already underway.

EXAMPLES OF SEMIOCHEMICAL-BASED PLANT PROTECTION PRODUCTS

	Retrievable dispensers		Non-retrievable dispensers	
	Passive	Active	Capsule suspension	Dosable matrix
Typical unitary load (mass a.i.)	*ca.* 1-2%	*ca.* 10%	$< 0.1\%$	*ca.* 1-2%
Density of devices per surface (units per ha)	100-1,000	1-5	>>1,000,000	100-1,000
Exposure in deployment/app	Very low	None	Low	Low
Exposure in-use (residual)	Constant	Instantaneous	Constant	Constant
Chance of exposure (time)	Whole day	Night period	Whole day	Whole day

OECD GUIDANCE DOCUMENT ON SEMIOCHEMICAL ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS, ENV/JM/MONO(2017)33, 10 Jan 2018 (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2017)33&doclanguage=en)

Active Retrievable Dispensers

“Retrievable dispensers” only are currently proposed for renewal at the EU level for SCLPs

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SCLP products – safety profile

- No mammalian acute toxicty or mutagenicity
  - No subchronic tox
  - No developmental tox
  - Rapidly metabolized by enzyme systems
- Non-toxic/non-lethal mode of action
- Target pest specificity
- Effective at low rates at or below background levels
- No residues detected on food
- Dissipates rapidly in the environment
  - volatile
  - photo-oxidation degradation
  - typical ½-life in environment ~29-50 hrs

NATURAL EXPOSURE LEVELS IN RELATION TO APPLIED LEVELS

Step I: Estimate the **release of semiochemicals from a high population of the source organism** (natural exposure level).

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Step II: Compare **natural exposure level and exposure from the plant protection product**

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Step I: Estimate the **release of semiochemicals from a high population of the source organism** (natural exposure level).

Step II: Compare **natural exposure level and exposure from the plant protection product**

Step III: **Mathematical modelling to predict the final concentrations** derived from the application of semiochemical based plant protection products…

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Method to estimate the release of semiochemicals from a high population of the source organism (natural exposure level).

1. **"Natural exposure level":** This natural exposure should be compared with the exposure resulting from the intended use of the plant protection products. This approach applies when the exposure route is by the vapour phase only (retrievable dispensers and dosable matrix).

2. When use of the plant protection product results in similar exposure (within one order of magnitude by the same route) to the natural exposure level of the semiochemical (or a group of related semiochemicals, when justified), the risk characterisation is concluded.

   No further information is needed with the exception of identity, characterisation and analytical methods (see sections on Identity, physical and chemical properties and Analytical methods).

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Method to estimate the release of semiochemicals from a high population of the source organism (natural exposure level).

$$\boldsymbol{PRR = RIO \times NRO}$$

- **PRR** (Population Release Rate) is the release rate of the semiochemical from a justified high population of the source organism in nanograms per hectare and hour (ng/ha/h).

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Method to estimate the release of semiochemicals from a high population of the source organism (natural exposure level).

When the number of releasing organisms is not known:

$$\boldsymbol{NRO = YLD\ MPY \times \%INF\ 100 \times OCC}$$

- % INF (Infestation rate) is the **percentage of harvested units affected by the target organism** (%, dimensionless).

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- YLD (Yield) is the total yield of the crop in one cropping cycle (Kg/ha).
- MPY (Mass per yield unit) is the average mass of a standard unit (Kg) of the crop.
- OCC (Occupancy) is the number of releasing individuals per individual plant part (dimensionless).

gives

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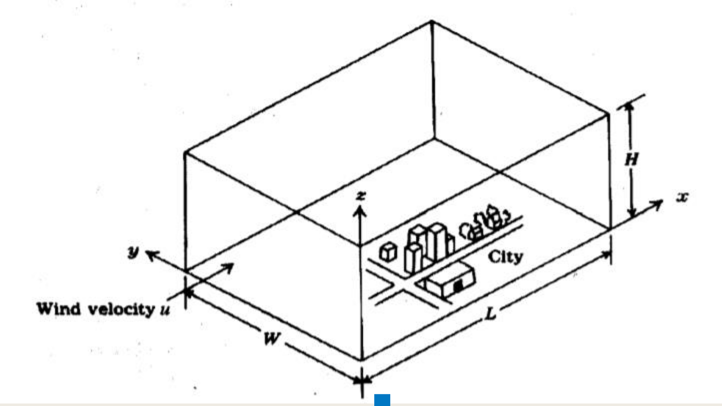
Fixed steady one-cell model

- One side (L) parallel to the wind direction.
- The atmospheric turbulence produces a complete blending of the pollutants homogeneous c concentration can be assumed inside the defined volume of air.
- The concentration of pollutants that enters the source area (x=0) from the
- exterior with the wind is constant and equal to b (background concentration).
- • The rate of emission of substances per unit area is q (e.g. in g/s·m2). This rate is constant and does not vary with the wind.
- • No contaminant enters or leaves through the sides of the box that are perpendicular neither to the wind direction nor from the upper side (blending height).



Worst-case concentration

*EU GUIDANCE DOCUMENT ON SEMIOCHEMICAL ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS SANTE/12815/2014 rev. 5.2, May 2016

Natural exposure vs. Dispenser release

Pest	Natural exposure level estimation (Av release rate, mg/ha/h)	Dispensers (Av release rate, mg/ha/h)	Magnitude of difference (regulated max is 1)	Mathematical prediction (ng/m3)
Codling Moth/ *Cydia*	3.1	12	0.4	
Pink bollworm/ *Pectinophora*	627	42	0.007	
Beet armyworm/ *Spodoptera*	4	0.4	0.1	

1.1 ng/m3 in a field where average release from the dispensers was 12 mg per hectare per hour (mg/ha/h). The mathematical model forecasts a value of 2.2 ng/m3 fo

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Example of Authority Questions, 2020

Applicant to provide an overview table with all the different SCLP, names, structures, target organism and estimated natural background values.

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Applicant to provide an overview table with all the different SCLP, names, structures, target organism and estimated natural background values.

1. There is limited information available on the individual SCLPs and their estimated natural background values.

2. For this reason, "the Commission is considering a horizontal mandate on the natural background levels of arthropod pheromones".

3. However, for risk assessment purposes according to OECD Guidance No. 12 (ENV/JM/MONO(2001)12)[5], an application threshold of up to 375g SCLPs/ha/year is considered appropriate to reflect the natural concentration levels of SCLPs.

4. EU Guidance document SANTE/12815/2014 specify what already indicated in OECD No. 12. According to SANTE/12815/2014, "*when the exposure route is by the vapour phase only and where the exposure caused by the use of the plant protection product is similar (within one order of magnitude) to natural exposure levels of the semiochemical, the ecotoxicological risk characterisation is concluded*".

Conclusions

- Natural background concentrations establish bench-mark exposure levels for risk assessment in pheromones (including SCLPs).

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- EU and OECD guidance models dispensers as fitting within the 1 order of magnitude difference from the considered natural background concentration (NBC).
- Although they tend to be species-specific for efficacy, for risk assessment, exposure to the entire SCLP group should be taken as the benchmark NBC.
- While there are expected variances in NBC by geography this difference **does not typically exceed 1 magnitude threshold**.
- A harmonized, predictable approach by regulators would facilitate the further development of semiochemicals including SCLPs as a means to control pest damage in place of older synthetic chemistry.

References

- https://en.wikipedia.org/wiki/Semiochemical#Pheromone
- OECD GUIDANCE DOCUMENT ON SEMIOCHEMICAL ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS, ENV/JM/MONO(2017)33, 10 Jan 2018 (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2017)33&doclanguage=en)
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