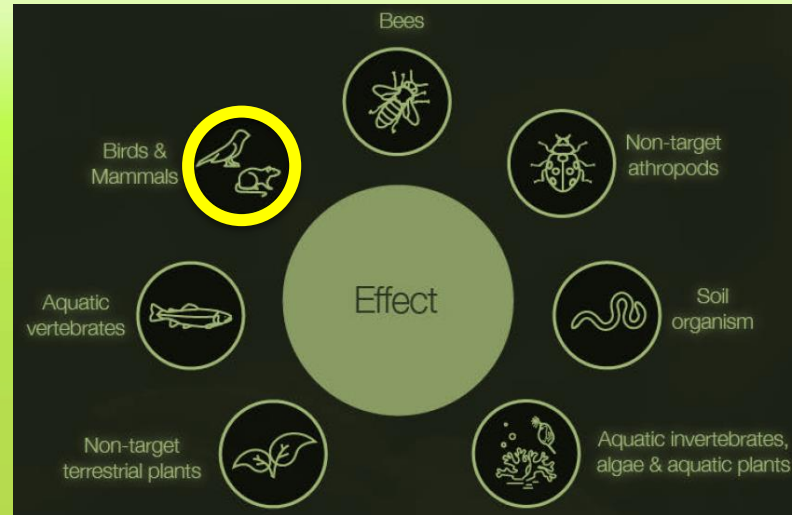


# Risk assessment on birds & mammals in the EU



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Realisation:  
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Leverkusen

# Overview



- Regulations & data requirements (EU)
- Guidance document
- Study types, guidelines & related endpoints
- Virtual Standard Risk Assessment Example
- Potential refinement options

# Regulations (European Union)

Regulation (EC) No. 1107/2009 concerning the placing of plant protection products on the market

& corresponding regulations:

- Regulation (EU) No. 283/2013  
= data requirements for active substances
- Regulation (EU) No. 284/2013  
= data requirements for plant protection products
- Regulation (EU) No. 546/2011  
= Uniform Principles

# Terms & Abbreviations

Term	Explanation
a.s.	Active substance (synonymous to active ingredient)
DDD	Daily Dietary Dose
Effect measurements	In the context of terrestrial vertebrate studies effects are commonly measured for the following endpoints: survival, body weight, food consumption, reproductive parameters etc.
Effect value	Dependent from study design & underlying guideline, effect values (often also referred to as 'endpoints') have different names (abbreviations) as they signify different effect levels that have been measured or calculated. Examples: LD <sub>50</sub> , NOEC etc.
f <sub>TWA</sub>	Time-weighted average factor
LD <sub>50</sub>	Lethal rate at which 50% of the tested species is dead
MAF	Multiple Application Factor
NO(A)EC	No Observed (Adverse) Effect Concentration
NOEL	No Observed Effect Level
ppm	Parts per million (synonymous to ,mg/kg diet')
prod.	Product, i.e. formulated product
TER	Toxicity to Exposure Ratio (= calculated for risk assessment)

# Guidance document

Guidance Document on Risk Assessment  
for Birds & Mammals on request from EFSA.  
EFSA Journal 2009; 7(12):1438 (short: 'EFSA GD, 2009')

Available online:

<http://www.efsa.europa.eu/en/efsajournal/pub/1438>

- New guidance document in preparation by EFSA

## Risk Assessment for Birds and Mammals



On request from EFSA, Question No EFSA-Q-2009-00223  
First published on 17 December 2009

# Acute toxicity test - Birds

## OECD TG 223 (US: OCSP 850.2100)

Test species:

- Bobwhite quail / Japanese quail preferred
- also other species testing possible (e.g. Mallard, pigeon, zebra finch, canary)

Single oral dose (limit test or dose response)

Observation period: 14 days

Parameters: mortality, symptoms, body weight, food consumption, pathology

**Endpoint: LD<sub>50</sub> [mg/kg bw]**

# Short term toxicity test - Birds

OECD TG 205 (US: OCSP 850.2200)

Test species:

- Bobwhite quail
- Mallard duck

No longer required  
in the EU

Feeding study: 5 test concentrations, 10 chicks per test group

Observation period: 5 day food with test item + 3 day untreated food

Parameters: mortality, symptoms, body weight, food consumption, pathology

**Endpoint: LC<sub>50</sub> [mg/kg diet]**

# Chronic toxicity test - Birds

## OECD TG 206 (US: OCSPP 850.2300)

Test species:

- Bobwhite quail or Japanese quail
- Mallard duck

Reproduction study (20 weeks):

Test item mixed into food 10 weeks before start of egg laying, thereafter 10 weeks reproduction

Parameters:

- Adults: mortality, symptoms, body weight, food consumption, pathology
- Eggs: number, eggshell, fertility, viability
- Chicks: hatch success, survival, body weight

**Endpoint: NOAEC** [mg/kg diet] = No Observed Adverse Effect Concentration  
converted to dose [mg/kg bw/d] for risk assessment

# Acute toxicity tests - Mammals

Test species:

→ see dossier Section Toxicology

- Rat , Mouse

Single oral dose (limit test or dose response)

- OECD TG 420: fixed dose procedure
- OECD TG 423: acute toxic class method
- OECD TG 425: up-and-down procedure

Observation period: 14 days

Parameters: mortality, symptoms, body weight, food consumption, pathology

**Endpoint: LD<sub>50</sub> [mg/kg bw]**

# Long-term toxicity tests - Mammals

Information from mammalian toxicology section is collected to identify the ecotoxicologically relevant reproductive endpoint for mammal long-term risk assessment.

Table copied from EFSA 2015, App. A\*

\* EFSA (European Food Safety Authority), 2015.

Technical report on the outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology.  
EFSA supporting publication 2015:EN-924. 62 pp.

## Appendix A – Template for collecting information from the mammalian toxicology section, relevant to identify the ecotoxicologically relevant reproductive endpoint of mammals

Endpoint	Studies to check
Body weight change <sup>1</sup> , behavioural effects and systemic toxicity <sup>2</sup>	28-day oral toxicity study (OECD 407)  Sub-chronic oral toxicity study (OECD 408)  Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Indices of gestation, litter size, pup and litter weight <sup>3</sup>	Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Indices of viability, pre- and post-implantation loss	Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Embryo/foetal toxicity including teratological effects	Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Number aborting and number delivering early	Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Systemic toxicity and effects on adult body weight	Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Indices of post-natal growth <sup>4</sup> , indices of lactation and data on physical landmarks	Multi-generation study (OECD 416)  Developmental studies (OECD 414)
Survival and general toxicity up to sexual maturity	Multi-generation study (OECD 416)  Developmental studies (OECD 414)

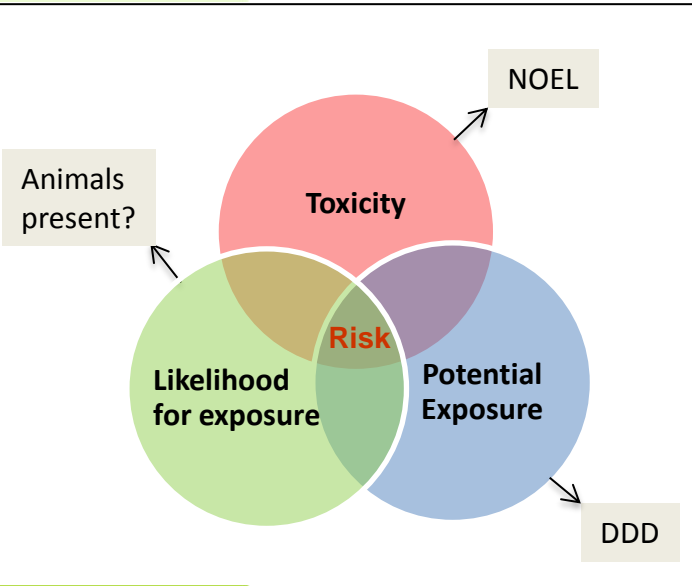
<sup>1</sup> Included as an indicator for parental effects which may disrupt reproduction.

<sup>2</sup> Effects derived from absorption of the substance that causes modification of an organ or an apparatus (biochemical, physiological and/or morphological). Examples include behavioural or physiological impairment (e.g. reduced locomotive activity, altered reflexes).

<sup>3</sup> Any effects in foetal body weight should be evaluated in the context of all pertinent data including other developmental effects as well as maternal toxicity.

<sup>4</sup> For example body weight gain, ear and eye opening, tooth eruption, hair growth and effects on sexual maturation such as age and body-weight at vaginal opening or balano-preputial separation.

# General principles



$$\text{TER} = \text{Toxicity to Exposure Ratio}$$

where

Toxicity → Endpoint value from a study (i.e. LD<sub>50</sub>, NOEL)

Exposure → Daily Dietary Dose (DDD)

→ Low risk to terrestrial vertebrates is indicated if  $\text{TER} \geq 5$   
(see Uniform Principles as laid down in Reg. (EU) No. 546/2011)

# Risk assessment – Basic equation

TER = Toxicity to Exposure Ratio

The diagram illustrates the relationship between the general Toxicity to Exposure Ratio (TER) and its specific applications. A central box contains the general formula: 
$$\text{TER} = \frac{\text{toxicity value}}{\text{exposure}}$$
 Two arrows originate from this box. The upper arrow points to the acute TER formula: 
$$\text{TER}_{\text{acute}} = \frac{\text{LD}_{50}}{\text{DDD}_a}$$
 The lower arrow points to the long-term TER formula: 
$$\text{TER}_{\text{longterm}} = \frac{\text{NOEL}}{\text{DDD}_{\text{lt}}}$$
 To the right of these formulas, the trigger values are specified: 
$$\frac{\text{Trigger}^*}{\text{TER} \geq 10}$$
 for the acute formula and 
$$\text{TER} \geq 5$$
 for the long-term formula.

$$\text{TER} = \frac{\text{toxicity value}}{\text{exposure}}$$

$$\text{TER}_{\text{acute}} = \frac{\text{LD}_{50}}{\text{DDD}_a}$$

$$\text{TER}_{\text{longterm}} = \frac{\text{NOEL}}{\text{DDD}_{\text{lt}}}$$

Trigger\*:  
$$\text{TER} \geq 10$$

$$\text{TER} \geq 5$$

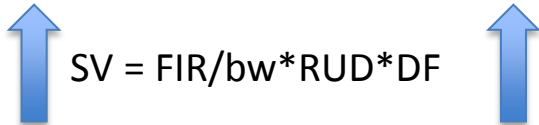
\* Trigger = Assessment Factor (= Safety Factor)

Safety factors are laid down in the Uniform principles (Reg. (EU) No. 546/2011) for each type of risk assessment.

# Daily Dietary Dose - acute

Simplified exposure:

$$\text{DDD}_{\text{acute}} = \text{SV}_{90} * \text{MAF}_{90} * \text{single appl. rate}$$



$$\text{SV} = \text{FIR}/\text{bw} * \text{RUD} * \text{DF} \quad \text{PT; PD = set to 1}$$
$$\text{DDD} = (\text{FIR}/\text{b.w.}) * \text{RUD} * \text{DF} * \text{MAF} * \text{PT} * \text{PD} * \text{single appl. rate}$$

where

SV = Shortcut Value (→ see Appendix A of EFSA GD 2009)

FIR/bw = Food intake rate / body weight (→ see Appendix G/L of EFSA GD 2009)

RUD = Residue Unit Dose

MAF = Multiple Application Factor (→ see also Appendix H of EFSA GD 2009)

DF = Deposition Factor (→ see Appendix E of EFSA GD 2009)

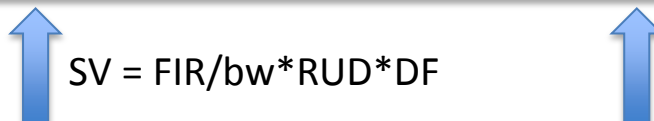
PD = Portion of Diet (→ see Appendix Q of EFSA GD 2009)

PT = Portion of Time (→ see Appendix P of EFSA GD 2009)

# Daily Dietary Dose – long-term

Simplified exposure:

$$\text{DDD}_{\text{longterm}} = \text{SV}_{\text{mean}} * \text{MAF}_{\text{mean}} * f_{\text{twa}} * \text{single appl. rate}$$



$$\text{DDD} = (\text{FIR}/\text{b.w.}) * \text{RUD} * \text{DF} * \text{MAF} * f_{\text{twa}} * \text{PT} * \text{PD} * \text{single appl. rate}$$

where

SV = Shortcut Value (→ see Appendix A of EFSA GD 2009)

FIR/bw = Food intake rate / body weight (→ see Appendix G/L of EFSA GD 2009)

RUD = Residue Unit Dose (see EFSA GD 2009, Note 6.; page 53)

MAF = Multiple Application Factor (→ see also Appendix H of EFSA GD 2009)

$f_{\text{twa}}$  = time weighted average factor (default value: 0.53)

DF = Deposition Factor (→ see Appendix E of EFSA GD 2009)

PD = Portion of Diet (→ see Appendix Q of EFSA GD 2009)

PT = Portion of Time (→ see Appendix P of EFSA GD 2009)

# Generic focal species & Shortcut Values

## Annexes

### Annex I Shortcut values for generic focal species

**Table I. 1.** Shortcut values for avian generic focal species. The shortcut value based on mean RUDs should be used for reproductive assessments, and the shortcut value based on 90<sup>th</sup> percentile RUDs should be used for acute assessments.

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90 <sup>th</sup> percentile RUDs
Bare soils	BBCH < 10	Small granivorous bird "finch"	Linnet ( <i>Carduelis cannabina</i> )	11.4	24.7
Bare soils	BBCH < 10	Small omnivorous bird "lark"	Woodlark ( <i>Lullula arborea</i> )	8.2	17.4
Bare soils	BBCH < 10	Small insectivorous bird "wagtail"	Yellow wagtail ( <i>Motacilla flava</i> )	5.9	10.9
Bulbs & onion like crops	BBCH 10 - 39	Small granivorous bird "finch"	Linnet ( <i>Carduelis cannabina</i> )	11.4	24.7
Bulbs & onion like crops	BBCH ≥ 40	Small granivorous bird "finch"	Linnet ( <i>Carduelis cannabina</i> )	6.9	14.8
Bulbs & onion like crops	BBCH 10 - 39	Small omnivorous bird "lark"	Woodlark ( <i>Lullula arborea</i> )	10.9	24.0
Bulbs & onion like crops	BBCH ≥ 40	Small omnivorous bird "lark"	Woodlark ( <i>Lullula arborea</i> )	6.5	14.4
Bulbs & onion like crops	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail ( <i>Motacilla flava</i> )	11.3	26.8
Bulbs & onion like crops	BBCH ≥ 20	Small insectivorous bird "wagtail"	Yellow wagtail ( <i>Motacilla flava</i> )	9.7	25.2
Bush & cane fruit	Fruit stage BBCH 71-79 currants	Frugivorous bird "blackcap"	Blackcap ( <i>Sylvia atricapilla</i> )	23.0	46.3
Bush & cane fruit	Whole season BBCH 00-79 Currants	Small insectivorous bird "warbler"	Willow warbler ( <i>Phylloscopus trochilus</i> )	20.3	52.2
Cereals	Late post-emergence (May-June) BBCH 71-89	Small insectivorous bird "passerine"	Fan tailed warbler	22.4	57.6
Cereals	Early (shoots) autumn-winter BBCH 10-39	Large herbivorous bird "goose"	Pink-foot goose ( <i>Anser brachyrhynchus</i> )	16.2	30.5
Cereals	BBCH 10 - 29	Small omnivorous bird "lark"	Woodlark ( <i>Lullula arborea</i> )	10.9	24.0
Cereals	BBCH 30 - 39	Small omnivorous bird "lark"	Woodlark ( <i>Lullula arborea</i> )	5.4	12.0
Cereals	BBCH ≥ 40	Small omnivorous bird "lark"	Woodlark ( <i>Lullula arborea</i> )	3.3	7.2
Cereals	Late season-5 eed heads	Small granivorous/ insectivorous bird "bunting"	Yellowhammer ( <i>Emberiza citrinella</i> )	12.5	27.0
Cotton	BBCH 10 - 19	Medium insectivorous bird "pratincole"	Collared Pratincoles <i>Glaucopis pratincola</i>	2.3	4.2
Cotton	BBCH ≥ 20	Medium insectivorous bird "pratincole"	Collared Pratincoles <i>Glaucopis pratincola</i>	1.1	3.0
Cotton	BBCH 10 - 49	Small omnivorous bird "sparrow"	House sparrow ( <i>Passer domesticus</i> )	11.2	17.7
Cotton	BBCH ≥ 50	Small omnivorous bird "sparrow"	House sparrow ( <i>Passer domesticus</i> )	2.8	4.4

**Indicator species** (screening step)

as well as

**Generic focal species** (Tier 1 risk assessment)

listed in EFSA Guidance 2009

- **Shortcut Values (SV-)** values per crop & growth stage →

A calculation tool (spreadsheet) has been made available together with the guidance document by EFSA.

Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)

# Screening versus Tier 1

“All pesticides should be subjected to Tier 1 assessment, unless they are shown by a screening assessment to pose a low risk. Tier 1 uses the same general approach as the screening assessment, but requires more detailed consideration of the relevance of toxicity endpoints and more specific exposure scenarios.” (EFSA GD 2009, page 35)

## Comparison of screening assessment versus Tier 1 risk assessment:

Screening step	Tier 1 risk assessment
Indicator species	Generic focal species (GFS)
<ul style="list-style-type: none"><li>- 1 indicator species for several crops</li><li>- Timing <u>not</u> considered</li></ul>	<ul style="list-style-type: none"><li>- crop-specific (several GFS per crop)</li><li>- Timing considered (BBCH)</li></ul>
MAF and $f_{TWA}$	MAF and $f_{TWA}$

# Risk Assessment - Example

The following example is based on a virtual product containing two virtual active substances (A and B) and a virtual intended use pattern.

<b>Formulated product</b>	<b>A+B SC 300</b> (200 g A/L + 100 g B/L)
<b>Intended use pattern</b>	2 x 1.0 L prod./ha, cereals (BBCH 30-69), 14 days interval between the 2 applications
<b>Application rate (active substance A)</b>	2 x 200 g a.s./ha
<b>Application rate (active substance B)</b>	2 x 100 g a.s./ha

# Virtual endpoints - Birds

## Endpoints of active substance A and active substance B for birds

Species	Substance	Exposure System	Ecotoxicological endpoint	Reference
Bobwhite quail	A	Oral, acute, 14 days	LD <sub>50</sub> > 2000 mg a.s./kg bw	SANCO/0815/99-Final (2003)
Bobwhite quail	A	Dietary, short-term	LC <sub>50</sub> > 5000 ppm	Not required according to EFSA GD 2009
Bobwhite quail	A	Dietary, reproductive toxicity, 21 weeks	NOEL 120 mg a.s./kg bw/d	SANCO/0815/99-Final (2003)
Mallard duck	B	Oral, acute, 14 days	LD <sub>50</sub> 1000 mg a.s./kg bw	EFSA Scientific Report 1001 (2009)
Mallard duck	B	Dietary, reproductive toxicity, 21 weeks	NOEL 50 mg a.s./kg bw/d	EFSA Scientific Report 1001 (2009)

a.s. = active substance; bw = body weight; ppm = parts per million (synonymous to mg/kg diet)

Remark: All values (i.e. endpoints and references) are virtual



## **Risk assessment example – Birds acute and long-term**

<b>Intended use</b>	Cereals, BBCH 30-69, 14 d interval				
<b>Active substance</b>	A (virtual a.s.)				
<b>Application rate (g/ha)</b>	2 × 200				
<b>Acute toxicity (mg/kg bw)</b>	> 2000				
<b>TER criterion</b>	10				
<b>Crop scenario</b>	<b>Generic focal species</b>	<b>SV<sub>90</sub></b>	<b>MAF<sub>90</sub></b>	<b>DDD<sub>90</sub> (mg/kg bw/d)</b>	<b>TER<sub>a</sub></b>
<b>Growth stage</b>					
Cereals BBCH 30-39	Small omnivorous bird "lark"	12.0	1.2	2.9	690
Cereals BBCH ≥ 40	Small omnivorous bird "lark"	7.2	1.2	1.7	1176
<b>Reprod. toxicity (mg/kg bw/d)</b>	120				
<b>TER criterion</b>	5				
<b>Crop scenario</b>	<b>Generic focal species</b>	<b>SV<sub>m</sub></b>	<b>MAF<sub>m</sub> × f<sub>TWA</sub></b>	<b>DDD<sub>m</sub> (mg/kg bw/d)</b>	<b>TER<sub>lt</sub></b>
<b>Growth stage</b>					
Cereals BBCH 30-39	Small omnivorous bird "lark"	5.4	1.4 × 0.53	0.80	150
Cereals BBCH ≥ 40	Small omnivorous bird "lark"	3.3	1.4 × 0.53	0.49	245

Note that according to the template the application rate is stated in g a.s./ha, but **kg a.s/ha** is used for TER calculations

default MAF values → EFSA GD 2009

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

<b>Intended use</b>	Cereals, BBCH 30-69, 14 d interval				
<b>Active substance</b>	A (virtual a.s.)				
<b>Application rate (g/ha)</b>	2 × 200				
<b>Acute toxicity (mg/kg bw)</b>	> 2000				
<b>TER criterion</b>	10				
<b>Crop scenario</b>	<b>Generic focal species</b>	<b>SV<sub>90</sub></b>	<b>MAF<sub>90</sub></b>	<b>DDD<sub>90</sub> (mg/kg bw)</b>	<b>TER<sub>a</sub></b>
<b>Growth stage</b>					
Cereals BBCH 30-39	Small omnivorous bird "lark"	12.0	1.2	2.88	694
Cereals BBCH ≥ 40	Small omnivorous bird "lark"	7.2	1.2	1.73	1157
<b>Reprod. toxicity (mg/kg bw/d)</b>	120				
<b>TER criterion</b>	5				
<b>Crop scenario</b>	<b>Generic focal species</b>	<b>SV<sub>m</sub></b>	<b>MAF<sub>m</sub> × TWA</b>	<b>DDD<sub>m</sub> (mg/kg bw/d)</b>	<b>TER<sub>lt</sub></b>
<b>Growth stage</b>					
Cereals BBCH 30-39	Small omnivorous bird "lark"	5.4	1.4 × 0.53	0.80	150
Cereals BBCH ≥ 40	Small omnivorous bird "lark"	3.3	1.4 × 0.53	0.49	245

Same Generic Focal Species - lower SV value is covered by higher SV value

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

<b>Intended use</b>	Cereals, BBCH 30-69, 14 d interval				
<b>Active substance</b>	B (virtual a.s.)				
<b>Application rate (g/ha)</b>	2 × 100				
<b>Acute toxicity (mg/kg bw)</b>	1000				
<b>TER criterion</b>	10				
<b>Crop scenario</b> <b>Growth stage</b>	<b>Generic focal species</b>	<b>SV<sub>90</sub></b>	<b>MAF<sub>90</sub></b>	<b>DDD<sub>90</sub></b> <b>(mg/kg bw)</b>	<b>TER<sub>a</sub></b>
Cereals BBCH 30-39	Small omnivorous bird “lark”	12.0	1.2	1.44	694
Cereals BBCH ≥ 40	Small omnivorous bird “lark”	7.2	1.2	0.86	1157
<b>Reprod. toxicity</b> <b>(mg/kg bw/d)</b>	50				
<b>TER criterion</b>	5				
<b>Crop scenario</b> <b>Growth stage</b>	<b>Generic focal species</b>	<b>SV<sub>m</sub></b>	<b>MAF<sub>m</sub> × TWA</b>	<b>DDD<sub>m</sub></b> <b>(mg/kg bw/d)</b>	<b>TER<sub>lt</sub></b>
Cereals BBCH 30-39	Small omnivorous bird “lark”	5.4	1.4 × 0.53	0.40	125
Cereals BBCH ≥ 40	Small omnivorous bird “lark”	3.3	1.4 × 0.53	0.24	204

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

# Virtual endpoints - Mammals

Endpoints of active substance A and active substance B for mammals

Species	Substance	Exposure System	Ecotoxicological endpoint	Reference
Rat	A	Oral, acute, 14 days	LD <sub>50</sub> > 1500 mg a.s./kg bw	SANCO/0815/99-Final (2003)
Rat	A	Dietary, reproductive toxicity, 21 weeks	NOED 250 mg a.s./kg bw/d	SANCO/0815/99-Final (2003)
Rat	B	Oral, acute, 14 days	LD <sub>50</sub> 500 mg a.s./kg bw	EFSA Scientific Report 1001 (2009)
Rat	B	Dietary, reproductive toxicity, 21 weeks	NOED 75 mg a.s./kg bw/d	EFSA Scientific Report 1001 (2009)

a.s. = active substance; bw = body weight

Remark: All values (i.e. endpoints and references) are virtual





## **Risk assessment example – Mammals acute**

# Risk assessment example – Mammals acute



Intended use	Cereals, BBCH 30-69, 14 d interval				
Active substance	A (virtual a.s.)				
Application rate (g/ha)	2 × 200				
Acute toxicity (mg/kg bw)	> 1500				
TER criterion	10				
Crop scenario Growth stage	Generic focal species	SV <sub>90</sub>	MAF <sub>90</sub>	DDD <sub>90</sub> (mg/kg bw)	TER <sub>a</sub>
Cereals BBCH ≥ 20	Small insectivorous mammal "shrew"	5.4	1.2	1.30	> 1157
Cereals BBCH ≥ 40	Small herbivorous mammal "vole"	40.9	1.2	9.82	> 153
Cereals BBCH 30-39	Small omnivorous mammal "mouse"	8.6	1.2	2.06	> 727
Cereals BBCH ≥ 40	Small omnivorous mammal "mouse"	5.2	1.2	1.25	> 1202

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Same Generic Focal Species (GFS), lower SV value is covered by higher SV value

# Risk assessment example – Mammals acute



Intended use	Cereals, BBCH 30-69, 14 d interval				
Active substance	B (virtual a.s.)				
Application rate (g/ha)	2 × 100				
Acute toxicity (mg/kg bw)	500				
TER criterion	10				
Crop scenario Growth stage	Generic focal species	SV <sub>90</sub>	MAF <sub>90</sub>	DDD <sub>90</sub> (mg/kg bw/d)	TER <sub>a</sub>
Cereals BBCH ≥ 20	Small insectivorous mammal "shrew"	5.4	1.2	0.65	771
Cereals BBCH ≥ 40	Small herbivorous mammal "vole"	40.9	1.2	4.91	102
Cereals BBCH 30-39	Small omnivorous mammal "mouse"	8.6	1.2	1.03	484
Cereals BBCH ≥ 40	Small omnivorous mammal "mouse"	5.2	1.2	0.62	801

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Same GFS, lower SV value = covered by higher SV value



## **Risk assessment example – Mammals long-term**

# Risk assessment example – Mammals long-term

Intended use	Cereals, BBCH 30-69, 14 d interval				
Active substance	A (virtual a.s.)				
Application rate (g/ha)	2 × 200				
Reprod. toxicity (mg/kg bw/d)	250				
TER criterion	5				
Crop scenario Growth stage	Generic focal species	SV <sub>m</sub>	MAF <sub>m</sub> × TWA	DDD <sub>m</sub> (mg/kg bw/d)	TER <sub>It</sub>
Cereals BBCH ≥ 20	Small insectivorous mammal "shrew"	1.9	1.4 × 0.53	0.28	887
Cereals BBCH ≥ 40	Small herbivorous mammal "vole"	21.7	1.4 × 0.53	3.22	78
Cereals BBCH 30-39	Small omnivorous mammal "mouse"	3.9	1.4 × 0.53	0.58	432
Cereals BBCH ≥ 40	Small omnivorous mammal "mouse"	2.3	1.4 × 0.53	0.34	732

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Same GFS, lower SV value = covered by higher SV value

# Risk assessment example – Mammals long-term

Intended use	Cereals, BBCH 30-69, 14 d interval				
Active substance	B (virtual a.s.)				
Application rate (g/ha)	2 × 100				
Reprod. toxicity (mg/kg bw/d)	75				
TER criterion	5				
Crop scenario Growth stage	Generic focal species	SV <sub>m</sub>	MAF <sub>m</sub> × TWA	DDD <sub>m</sub> (mg/kg bw/d)	TER <sub>It</sub>
Cereals BBCH ≥ 20	Small insectivorous mammal "shrew"	1.9	1.4 × 0.53	0.14	532
Cereals BBCH ≥ 40	Small herbivorous mammal "vole"	21.7	1.4 × 0.53	1.61	47
Cereals BBCH 30-39	Small omnivorous mammal "mouse"	3.9	1.4 × 0.53	0.29	259
Cereals BBCH ≥ 40	Small omnivorous mammal "mouse"	2.3	1.4 × 0.53	0.17	439

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Same GFS, lower SV value = covered by higher SV value

# Drinking water assessment

The assessment of the risk for birds (mammals) due to uptake of potentially contaminated drinking water is conducted for two (one) scenario(s):

a) **Leaf scenario**

Birds taking water that is collected in leaf whorls after application of a pesticide to a crop and subsequent rainfall or irrigation

→ only for leafy vegetables forming heads at BBCH  $\geq 40$

b) **Puddle scenario**

Birds and mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil.

# Secondary Poisoning

Calculated for lipophilic compounds ( $\log P_{ow} > 3^*$ ) which are expected to accumulate in tissue

## Earthworm-eating bird/mammal



<https://pixabay.com/de/amsel-vogel-gartenvogel-singvogel-2394788/>

Representative species: blackbird/shrew

- calculation of residues in earthworms ( $**PEC_{worm}$ )
- recalculated to DDD
- compared to long-term endpoint

## Fish-eating bird/mammal



<https://pixabay.com/de/fischreiher-graureiher-reiher-tier-1779348/>

Representative species: heron/otter

- calculation of residues in fish ( $**PEC_{fish}$ )
- recalculated to DDD
- compared to long-term endpoint

**TER  $\geq 5$  = acceptable risk**

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\* $P_{ow}$  = Octanol-Water partitioning coefficient (= material property of a.s.; see Phys.-Chem. chapter)

\*\*PEC = Predicted Environmental Concentration

# Higher tier - Refinement options

- If the Tier 1 risk assessment fails (i.e.  $TER < \text{Assessment Factor}$ ), refinement is required:

## Potential refinement options (case by case):

- ✓ Deposition Factor (DF)
- ✓ Focal species
- ✓ Initial residue values (RUD)
- ✓ FIR/bw
- ✓ Proportion of diet (PD)
- ✓ Proportion of time (PT) – only reproductive risk
- ✓ Residue decline ( $DT_{50}$  refinement)
- ✓ Field effect studies
- ✓ Dehusking
- ✓ Avoidance
- ✓ Geomean - only acute risk
- ✓ Merging studies / refining endpoint - only reproductive risk
- ✓ Extrapolating endpoints – birds only
- ✓ Monitoring/Observation for certain Focal Species

# Field studies (generic & effect)

## Mammals

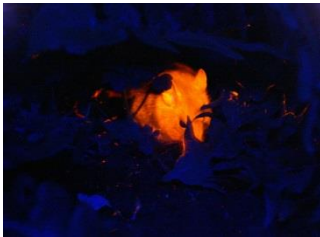


### Purpose:

- Determine PT or PD values for use in refinements
- Determine home ranges and further parameters
- Monitoring of population development
- Evaluate potential adverse effects of PPP on mammals

### Methods:

- Capture-mark-recapture (CMR), individual markage
- Infrared cameras
- Telemetry (radio-tracking)
- Collection of faeces + analysis of food composition
- Population monitoring
- Carcass search
- Residue analysis in dead animals



# Field studies (generic & effect)

## Birds

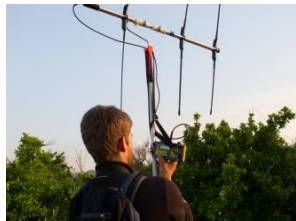


### Purpose:

- Determine PT or PD values for use in refinements
- Determine home ranges and further parameters
- Monitoring of population development
- Evaluate potential adverse effects of PPP on birds

### Methods:

- Transect counts
- Scan sampling
- Bird catch - and ringing
- Telemetry (radio-tracking)
- Monitoring of reproduction success
- Carcass search
- Residue analysis in dead animals



# Residue degradation studies



## Purpose:

Residue decline studies are conducted to derive a 21d-TWA or to refine the default  $DT_{50}$  of 10 days.

## Matrices:

- Arthropods (soil- or foliage dwellers) after spray application
- Plant material (seeds, seedlings, weeds) after spray application or seed treatment

## Principles of the study:

Residues are measured at certain time intervals (i.e. 0, 1, 2, 3, 5, 7, 10, 14, 21 days) after application

## Based on the study results

- 21 day time-weighted average (21d TWA) can be calculated or
- Single First Order (SFO)  $DT_{50}$  (<10 days) and corresponding (refined)  $f_{TWA}$

→ These values can be used for refinement of the risk assessment



# Conditions for product submission and approval

- The applicant only submits a dossier for registration of a plant protection product, when Environmental Risk Assessment (ERA) showed acceptable risk for all assessment areas
  - Authorities review the submitted dossier (containing study reports, evaluation and risk assessments + any further required data)
  - Authorities grant registration/approval only if they agree on an acceptable risk for all assessment areas
- Special mandatory conditions for use might apply (i.e. risk mitigation measures) which are printed on the label of the plant protection product