

GUIDANCE OF EFSA

Risk Assessment for Birds and Mammals¹

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ABSTRACT

The revised Guidance Document on Risk Assessment for Birds and Mammals on the basis of the Scientific Opinion of the PPR Panel on the Science behind the Guidance Document on Risk Assessment for Birds and Mammals (The EFSA Journal (2008) 734: 1-181) and its Appendices has been finalised based on the decisions of the Joint WG consisting of representatives from the European Commission, nominated Member States and technical experts from EFSA.

KEY WORDS

Birds, mammals, risk assessment, pesticide, plant protection product, active substance, refinement, level of protection.

SUMMARY

The European Food Safety Authority (EFSA) asked its Scientific Panel on Plant protection products and their Residues Unit (PPR Panel Unit) to prepare the revised the Guidance Document on Risk Assessment for Birds and Mammals on the basis of the Scientific Opinion of the PPR Panel on the Science behind the Guidance Document on Risk Assessment for Birds and Mammals (The EFSA Journal (2008) 734: 1-181) and its Appendices (EFSA, 2008).

This Guidance Document (GD) is further based on the decisions made by a Joint Working Group (WG) of nominated representatives from Member States, assisted by technical experts from EFSA and chaired by a representative of DG Health and Consumers. This Joint WG took necessary risk management decisions not within the remit of EFSA and decided on the options given in the Scientific Opinion. A record of their work and decisions is provided in the report of the Joint WG submitted to

1 On request from EFSA, Question No EFSA-Q-2009-00223, issued on 27 November 2009.

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the Standing Committee on the Food Chain and Animal Health (SCFCAH) meeting on 2 October 2009 (EC, 2009). An editorial team then implemented these decisions and rewrote the GD.

This GD addresses approaches to risk assessment for birds and mammals. In both cases, a tiered approach is used to assess the risk of mortality and reproductive effects.

A first-tier assessment procedure for a large range of scenarios including different crops and different types of pesticide uses (e.g. granules, seed treatment, and sprays) has been developed. Each scenario is a combination of the ecological characteristics of exposed species and other factors relevant to exposure, e.g. the type and structure of crop, and the type of formulation of the pesticide product. The best available data to define each scenario have been used. The Tier 1 assessment is supported by a calculation tool that has been developed during the revision of the GD.

The level of protection provided by each first-tier procedure, taking account of the conservatism of the assumptions used has been evaluated, uncertainties arising from factors omitted from the assessment (e.g. dermal exposure) and, where available, evidence on actual effects in field studies or from incident monitoring given.

Guidance on the range of options available for higher-tier risk assessment, e.g. refined dietary exposure assessments using realistic data on the ecology of relevant species; or field studies in order to get better residue data, better ecological data, or to measure effects are provided.

Further, guidance on how to combine different types of evidence from higher-tier risk assessment to form an overall judgement on the level of risk, giving appropriate weight to the strengths and uncertainties of each type of evidence, is presented.

More detailed guidance on specific aspects of higher risk assessment is given in a series of Appendices to this Guidance Document as well as to the opinion forming the basis of this GD (EFSA, 2008). Further Appendices provide detailed scientific background and underlying data for the first-tier assessment procedures. Worked examples for the reproductive risk assessment and comparisons of the outcome of the proposed new assessment procedures with the existing risk assessment scheme are available.

TABLE OF CONTENTS

Abstract	1
Summary	1
Table of contents	3
Background as provided by EFSA	5
Terms of reference as provided by EFSA	5
Implementation of the Guidance Document.....	6
Guidance.....	7
1. Introduction	7
1.1. The process	7
1.2. Scope of the Guidance Document.....	8
1.3. Risk assessment approach.....	8
2. Standard toxicity tests and the derivation of toxicity data for risk assessment	10
2.1. Acute toxicity to birds and mammals	10
2.1.1. Selection of acute endpoints	11
2.1.2. Extrapolated LD ₅₀ values from limit dose tests for birds	12
2.2. Short term toxicity to birds	12
2.3. Reproductive toxicity to birds and mammals.....	13
2.3.1. Determining toxicity endpoints from avian and mammalian reproductive toxicity studies.....	14
2.3.1.1. Conversion of endpoints from ppm to mg a.s./kg bw/d.....	16
2.4. Incorporation of additional toxicity information	17
2.4.1. How to deal with toxicity data from more than one species.....	17
2.4.2. How to deal with more than one acute study on the same species	19
2.4.3. How to deal with more than one reproduction study on the same species	19
2.5. Combined effects of simultaneous exposure to several active substances.....	20
3. Level of protection provided by the assessment procedures	21
4. Risk assessment modules for spray applications	21
4.1. Module 1: Acute dietary risk assessment for birds	23
4.2. Module 2: Acute dietary risk assessment for mammals.....	26
4.3. Module 3: Reproductive risk assessment for birds	29
4.4. Module 4: Reproductive risk assessment for mammals.....	34
5. Special topics.....	39
5.1. Risk assessment for granular formulations	39
5.1.1. Animals ingesting granules as source of food	40
5.1.2. Birds ingesting granules with/as grit	40
5.1.3. Birds ingesting granules when seeking seeds as food	42
5.1.4. Animals ingesting granules when eating soil-contaminated food	44
5.1.5. Animals consuming other food items with residues from granular applications.....	45
5.1.6. Explanatory notes to risk assessment for granules	46
5.1.7. Possible options for refinement	51
5.2. Risk assessment for treated seed.....	51
5.2.1. Selection of relevant risk assessment scenarios.....	51
5.2.2. First-tier RA and refinement options for birds and mammals feeding on treated seeds... ..	53
5.2.3. Refinement options.....	54
5.3. Risk assessment for substances with endocrine-disrupting properties in birds and mammals.....	61
5.4. Assessment of the risk from metabolites formed in potential food items	63
5.5. Risks for birds and mammals through drinking water	64
5.6. Bioaccumulation and food chain behaviour.....	68
6. Higher tier risk assessment – refinement steps	72
6.1. Refined modelling of dietary exposure and risk	77
6.1.1. Level of protection in refined dietary exposure assessment	77
6.1.2. Overview of refined dietary exposure assessment.....	78
6.1.3. Identification of focal species.....	82

6.1.3.1.	Identification of focal species using targeted observation data	83
6.1.3.2.	Extrapolation of study results from one MS or zone to another	83
6.1.3.3.	Identification of focal species using other sources of information	83
6.1.4.	Measured residues and residue dynamics.....	84
6.1.4.1.	Measured residues and residue dynamics in plant food items	84
6.1.4.2.	Measured residues and residue dynamics in arthropod food items.....	86
6.1.5.	Steps to refine the PT factor	87
6.1.5.1.	Criteria for performing radio tracking studies and evaluating observational data...	88
6.1.5.2.	Radio-tracking and inclusion of individuals in the estimate of PT	88
6.1.5.3.	Radio-tracking contact time as an estimate of foraging time.....	89
6.1.5.4.	How long should individuals be followed?	89
6.1.5.5.	How to use PT in deterministic case calculations.....	89
6.1.5.6.	Use of other sources of information in refining PT	89
6.1.6.	Steps to refine the information on composition of vertebrate diet (PD factor)	90
6.1.6.1.	Diet used in the screening step.....	90
6.1.6.2.	Diet used for the ‘generic focal species’	90
6.1.6.3.	Diet used for the ‘focal species’	91
6.1.7.	Dehusking.....	91
6.2.	Avoidance	93
6.3.	Metabolism & avoidance – application of body-burden models and dietary toxicity data...	95
6.4.	Field studies to detect or quantify mortality or reproductive effects	97
6.4.1.	Field study objectives	97
6.4.2.	Number of study sites: intensive versus extensive approach.....	97
6.4.3.	Methods for detecting effects in the field	98
6.4.4.	Interpretation of existing field studies	100
6.4.5.	Pen studies.....	100
6.4.6.	Conclusions and recommendations for use of field studies.....	100
6.5.	Use of wildlife incident data	101
6.6.	Phase-specific reproductive risk assessment.....	102
6.7.	Assessment of population-level effects.....	102
6.8.	Approaches for characterising uncertainty in higher-tier assessments	103
6.9.	Risk characterisation and weight-of evidence assessment.....	106
7.	Risk management and decision-making	109
7.1.	Risk management considerations.....	109
7.2.	Risk mitigation options.....	110
7.2.1.	Risk from seed treatments	110
7.2.2.	Risk from granules.....	111
7.2.3.	Risk from spray applications	111
	Recommendations	112
	Documentation provided to EFSA	112
	References	112
	Appendices	120
	Abbreviations	121
	List of Tables.....	123
	Annexes.....	124
Annex I	Shortcut values for generic focal species	124
Annex II	Review questionnaire on the ease of use of the Guidance Document.....	139

BACKGROUND AS PROVIDED BY EFSA

EFSA's Scientific Panel on Plant Protection Products and their Residues (PPR Panel) had completed a comprehensive scientific opinion (EFSA, 2008) for the revision of the Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC (SANCO/4145/2000 – final of 25 September 2002).

The scientific opinion contains various modules, some of which are alternative approaches for the same risk assessment area. The decision on which of these approaches to choose is a risk management decision and is therefore not within the remit of the EFSA PPR Panel, since EFSA is responsible for risk assessment and risk communication but not risk management.

As a result of the close cooperation and involvement of Member States (MS) and industry during the whole drafting process (two public consultations, the participation of representatives from MS and industry in the Core Working Group, a field-based consultation workshop in May 2007, a meeting with Member States in Dec 2007) together with the extensive comments received from the public consultations on the draft scientific opinion on the revised GD, it was understood that the users of the GD would prefer and need a GD that does not contain different options to choose from.

In a meeting on 31st Jan 2008, the EFSA Director on Risk Assessment decided to deal with risk management options by asking the PPR Panel to adopt a two-stage approach and to first prepare a scientific Opinion on the Science behind the GD on risk assessment for birds and mammals (*The EFSA Journal* (2008) 734: 1-181) using a modular approach. In a second stage, a Joint Working Group of nominated risk managers from Member States, assisted by technical experts from EFSA's PPR Panel, and chaired by a representative of the European Commission (DG Health and Consumers), was invited to consider the risk management issues and make respective decisions for the revised/new Guidance Document on risk assessment for birds and mammals to be finalised.⁴ The role of the PPR Panel members and EFSA staff in this WG was to assist in interpretation and understanding of the science in the Opinion, and not to participate in the risk management decisions.

Nominations had been received from the following Member States: Germany, Greece, Spain, Sweden, The Netherlands, and the United Kingdom.

TERMS OF REFERENCE AS PROVIDED BY EFSA

Based on the PPR Panel's scientific opinion on the science behind the proposed new GD on risk assessment for birds and mammals (*The EFSA Journal* (2008) 734: 1-181) the specific Working Group is tasked by EFSA to prepare a revised Guidance Document on Risk Assessment for Birds and Mammals which will be used for the risk assessment of pesticides under Council Directive 91/414/EEC.

The task of the group is to produce a clear Guidance Document, without the alternative options presented in the PPR Panel's scientific opinion, to address the risk management decisions required. The published scientific opinion has taken account of the extensive comments from the public consultation and the scientific principles have been agreed. The PPR Panel has written the opinion in such a way that each module is self-contained in order to help the choice for the revised Guidance Document to meet the risk management requirements.

⁴ The Working Group "Legislation" of the Standing Committee on the Food Chain and Animal Health (SCFCAH) was officially informed by the Head of the PPR Panel Unit about the situation during their meeting on 12th March 2008 and was asked to nominate risk managers from Member States for this new Working Group. This specific Working Group should consist of approximately ten people (at least one from the Commission, two members from the PPR Panel, one from the EFSA PPR Secretariat, and up to six risk managers from MS). In case of too many nominations from Member States, up to six with the most relevant experience were to be chosen. The Working Group ought to be chaired by either the Commission or a Member State representative.

IMPLEMENTATION OF THE GUIDANCE DOCUMENT

The Commission recommends that it is acceptable that an applicant applies already this current Guidance Document. For all dossiers submitted as of 1 July 2010 this current Guidance Document should be applied. This Guidance Document should be revised in 2012 taking into account experience from using it. Member States are encouraged to use a questionnaire that will be made available to provide feedback to EFSA.

GUIDANCE

1. Introduction

In 2006, the responsibility for producing new or for revising already-existing Guidance Documents (GDs) addressing risk assessment of pesticides was transferred from the European Commission to the European Food Safety Authority (EFSA). The Scientific Panel on Plant Protection Products and their Residues (PPR Panel) was asked by EFSA's Unit for the pesticide risk assessment peer-review (PRAPeR Unit) to start with the revision of the Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC (SANCO/4145/2000 – final of 25 September 2002), hereafter referred to as EC, 2002.

Use of term 'pesticide'

The term 'pesticides' is often used as a synonym for plant protection products, which are mainly used in agriculture to keep crops healthy and to prevent them from being destroyed as a consequence of disease and infestation. The active substances (a.s.) used in plant protection products are the chemicals or micro-organisms, including viruses, that are the essential component enabling the product to affect.⁵ To facilitate the reading of this document, the term 'pesticide' has been used throughout the text where possible.

1.1. The process

The revision process of the existing GD (EC, 2002) started off in summer 2006 with a public consultation on EFSA's website⁶. Based on these comments a Core Working Group (Core WG) and several sub WGs drafted a first document, taking into consideration input regarding scope and scale for the revision from risk managers received via a questionnaire. This document was discussed during a scientific workshop with Member States and other stakeholders in May 2007⁷ and further developed. In winter 2007 a second public consultation of the updated document⁸ took place and EFSA organised a meeting with Member States to exchange views on that document.

In the course of the revision, it became apparent that the task embraced several risk management issues which are not within EFSA's and the PPR Panel's remit. Therefore, the PPR Panel adopted a two-stage approach and first prepared a "Scientific Opinion on the Science behind the GD on risk assessment for birds and mammals", which was adopted in June 2008 (EFSA, 2008).

In the second stage, a Joint Working Group of representatives from Member States, chaired by the European Commission and assisted by EFSA technical experts considered the risk management issues and produced a report (EC, 2009)⁹ including all their decisions and recommendations on how to finalise the revision of the Guidance Document on risk assessment for birds and mammals. On the basis of this report, an editorial team¹⁰ produced the present Guidance Document.

⁵ See http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620925075.htm

⁶ See http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178660551795.htm

⁷ See http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178623592142.htm

⁸ At this time still named 'first draft of the revised GD'.

⁹ Available at:

http://ec.europa.eu/food/plant/protection/evaluation/guidance/report_birds_mammals_guidance_doc_sanco10997_2009_31_07_09.pdf

¹⁰ Christine Füll, Andy Hart, Robert Luttik.

1.2. Scope of the Guidance Document

Annex II and III of Directive 91/414/EEC¹¹ state that information should be provided to enable an assessment of the direct impact on birds and mammals likely to be exposed to the active substance, plant protection product and/or its metabolites. These impacts may result from either single long-term or repeated exposure and can be reversible or irreversible. In order to determine the risk, toxicity data are taken, along with an estimate of the likely exposure concentrations. This document provides a tiered approach to assessing both, direct acute and reproductive risk to birds and mammals.

Risk managers should be aware that two main issues have not been considered in the following risk assessment scheme: indirect effects and overspraying of eggs of ground nesting birds. Further work is required in this area to develop suitable schemes as well as risk mitigation measures.

Further, risk assessment for a rice scenario is not included in this document because it is envisaged that it will be addressed in a separate guidance document.

1.3. Risk assessment approach

The traditional acute and reproductive risk assessments schemes are based on a TER approach comprising three tiers. The first step in the process is a 'screening step'. It makes use of an 'indicator species'¹² along with worst-case assumptions regarding exposure. The aim of this step is to highlight those substances that do not require further consideration as their associated uses pose a low risk. Further, this step should identify, with sufficient certainty, false negatives (i.e. cases of undetected risks).

If a substance and its associated use do not pass the screening step, then the next step is the first-tier risk assessment. This uses more realistic exposure estimates along with a 'generic focal species'¹³. For the reproductive risk assessment, a variety of toxicity endpoints can be used. If this step is not successful, then further refined risk assessment is required. This involves a greater degree of realism and uses more realistic exposure estimates as well as a 'focal species'¹⁴ approach. Further details regarding each of these steps are provided in sections 4, 5 and 6 of this Guidance Document.

Indicator and generic focal species are representatives of real species occurring in a particular crop at a particular time. Data describing the feeding habits and other ecological needs have been collected by the PPR Panel from existing literature and compiled in Appendix A.¹⁵ The respective values for the

¹¹ On 24 Sep 2009, the Council adopted a new Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. This new legislation was published in the *Official Journal of the European Union* on 24 Nov 2009 and will become fully applicable as from 18 months following the date of publication (i.e. mid 2011). Annexes II and III have been incorporated into the new Regulation and are currently under revision.

¹² An 'indicator species' is not a real species but, by virtue of its size and feeding habits is considered to have higher exposure than (i.e. to be protective of) other species that occur in the particular crop at a particular time. It has a high food intake rate, and consumes one type of food which in turn has high residues on/in it.

¹³ A 'generic focal species' is not a real species, however it is considered to be representative of all those species potentially at risk, i.e. it is based on ecological knowledge of a range of species that could be at risk. It has a high food intake rate and may consume a mixed diet rather than just one as for the indicator species. The diet is not real but is considered to be representative of the species represented and hence a quartile approach has been used where only the 2, 3 or 4 largest food types have been extrapolated to either 25 % or 50 % of the total diet. The 'generic focal species' is also considered to be a representative of the types of birds or mammals that occur across Member States.

¹⁴ A 'focal species' is a real species that actually occurs in the crop when the pesticide is being used. The aim of using a 'focal species' is to add realism to the risk assessment insofar as the assessment is based on a real species that uses the crop. It is essential that the species actually occurs in the crop at a time when the pesticide is being applied. It is also essential that this species is considered to be representative of all other species that may occur in the crop at that time. As a 'focal species' needs to cover all species present in the crop, it is possible that there may be more than one 'focal species' per crop.

¹⁵ Appendices on the basis on EFSA (2008) that form part of this GD because they will be used on a day-to-day basis have been renamed to Appendix A, B, C etc. Some of them are updated, others remained unchanged. Letters "I" and "O" have been omitted in the naming.

indicator and generic focal species have been selected from these tables and compiled in the tables of Annex I to this GD and in section 4. They can be used directly in the exposure calculations and are called ‘shortcut values’.

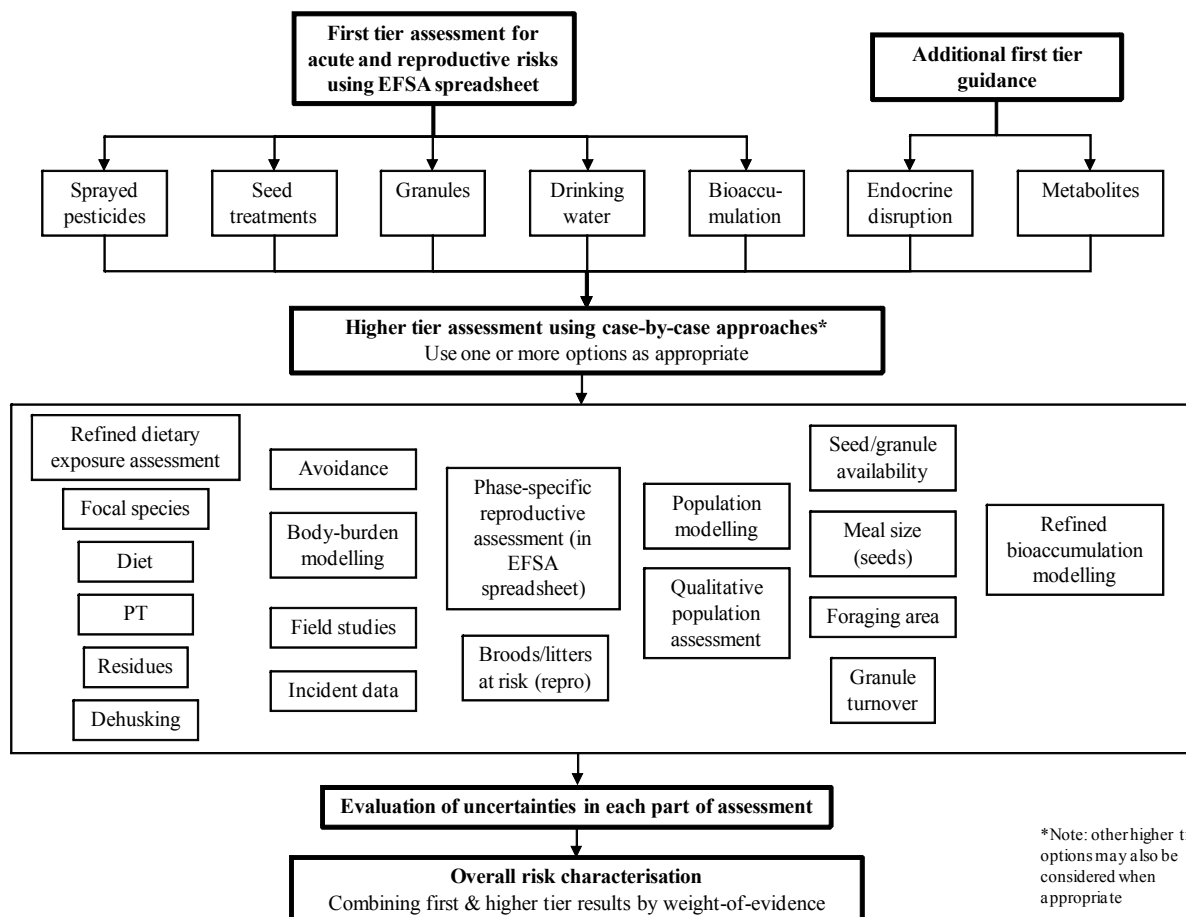


Figure 1. Flowchart for the risk assessment. Please note that for some types of assessment there is an optional screening step.

Please note that a calculation tool (spreadsheet) for Tier 1 risk assessment has been developed and is made available together with this Guidance Document.¹⁶

¹⁶ The calculation tool will appear on EFSA’s website in January 2010 after the finalisation of the quality check.

2. Standard toxicity tests and the derivation of toxicity data for risk assessment

In order to assess the risk of pesticides to birds and mammals, data on the acute and reproductive toxicity are required. Details regarding which avian studies should be provided are given in Annex II Section 8.1 and Annex III Section 10.1 of Directive 91/414/EEC. Details regarding which mammalian studies should be considered are provided in Annex II Section 5 and Annex III Section 7. Details of which studies are available and which key points need to be considered are outlined below.

The PPR Panel adopted and published 12 opinions related to data requirements of Annex II and III of Directive 91/414/EEC. In particular, the two opinions on ecotoxicological studies (EFSA, 2007, 2009a) provide recommendations concerning avian toxicity studies. These recommendations are currently considered by the European Commission in the revision process of Annexes II and III.

2.1. Acute toxicity to birds and mammals

Where possible, the test should provide for birds and mammals, the LD₅₀ values, the lethal threshold dose, time courses of response and recovery and the no observed effect level (NOEL) for lethality, and must include relevant gross pathological findings. Study design should be optimised for the achievement of an LD₅₀ rather than for any secondary endpoint.

Birds

According to Annex II of Directive 91/414/EEC, the acute oral toxicity of an active substance to a quail species (Japanese quail, *Coturnix coturnix japonica* or bobwhite quail, *Colinus virginianus*) or to mallard duck (*Anas platyrhynchos*) must be determined. The highest dose used in tests need not normally exceed 2000 mg/kg body weight. Due to issues of regurgitation it is recommended not to use the mallard duck (EFSA, 2007). Where regurgitation or emesis occurs at doses used for risk assessment, additional information is essential to complete the risk assessment. The amount of regurgitated material should be assessed for determination of the ingested dose. In the absence of this information, the lowest overall no observed effect level (NOEL) must be used for risk assessment purposes. Where more than one study has been submitted, the study/studies where no regurgitation has occurred should be used. If, however, mortalities appear in the study in which regurgitation has occurred (at dose levels at or around the LD₅₀ value for the non-regurgitation study), then it is proposed to use the NOEL (for regurgitation or mortality, whichever is lower) from the study where regurgitation has occurred.

Avian acute oral LD₅₀ studies generally are conducted with a minimum of 50 birds. A new draft guideline of the Organisation for Economic Cooperation and Development (OECD, 2002), which is currently under development, appears likely to deliver the same endpoints with similar precision using fewer birds (e.g. 12 – 24 individuals). In view of the policy goal of minimising animal testing, it is recommended that support be given to completing the development and evaluation of this guideline, and to ensuring that, when available, it can readily be assumed under Directive 91/414/EEC and Regulation (EC) 1107/2009, respectively.

The opinion of the PPR Panel on pirimicarb (EFSA, 2005a) showed that it would be useful to obtain additional information from acute oral toxicity studies, specifically, measurement of food consumption on the day of dosing, and the approximate times of onset and disappearance of overt clinical signs. This requires increased visual observations, e.g. every 1 - 2 hours on the day of dosing. Such information can be used for a refined assessment of the influence on risk of food avoidance responses and metabolism of the pesticide, as illustrated in EFSA (2005a). It was recommended that consideration should be given to requiring this information from acute oral studies (including OECD, 2002) as standard, in order to avoid the need to repeat studies in cases in which such an assessment becomes necessary.

Mammals

The following acute oral toxicity test methods with mammals are available (LD₅₀ mg/kg bw):

- OECD Test 420 (OECD, 2001a): Acute oral toxicity – fixed dose procedure
- OECD Test 423 (OECD, 2001b): Acute oral toxicity – acute toxic class method
- OECD Test 425 (OECD, 2006c): Acute oral toxicity – up-and-down procedure

The fine details of the above studies vary but the underlying principles are the same. Animals (normally rats, but data from studies with other mammals including mice and dogs are also relevant) are dosed once by oral gavage and observed for 14 days. Observations include body weight, clinical signs, death and necropsy findings. A limit dose of 2000 mg/kg bw or 5000 mg/kg bw (depending on study) should not be exceeded.

The fixed dose procedure and the acute toxic class method are range estimators and are useful for mammalian wildlife risk assessment only in cases where they can be used as a limit test (e.g. > 2000 mg/kg bw), or to provide a conservative surrogate for the LD₅₀ (i.e. lowest value of range).

An acute neurotoxicity study based on a US EPA procedure¹⁷ may also provide useful information. The basic design is that of the OECD Test 424, i.e. animals (normally rats; 5/sex/group) are dosed once, normally by oral gavage and observed for up to 14 days, but in addition, observations for neurological function (a functional observation battery) are taken pre-dosing and at the time of peak effect (up to 8 h post dose), day 7 and day 14. Other observations are body weight and specific histopathological investigation of nervous tissue.

If the result of the acute mammalian toxicity assessment does not pass the trigger value of Annex VI of Directive 91/414/EEC for Tier 1, the estimate of toxicity could be refined with a more precise test (e.g. up and down procedure of Test 425). Only in cases where there is a thoroughly justified need for more precision in estimating the acute mammalian LD₅₀ and slope, consideration could be given to performing studies using more animals (e.g. acute oral test, OPPTS¹⁸ 870-110).

2.1.1. Selection of acute endpoints

Occasionally, LD₅₀ values may be quoted for males and females separately. Some guidance on which endpoints to use is given below.

Birds

In the acute oral LD₅₀ study with birds, males and females normally are not tested separately; hence the endpoint is a combined one for both sexes. In the unlikely event that separate values for males and females are measured, it is proposed that the geometric mean be used unless there is a clear indication of a difference in sensitivity between the sexes (e.g. > 25 % in the LD₅₀; EPCO, 2005) – in which case the data from the more sensitive sex should be taken.

Mammals

The current OECD guideline 420 for acute mammalian oral toxicity states that only females should be tested except where there is evidence that males are likely to be more sensitive (OECD, 2001a). In cases where this guideline has been used, it is assumed that the more sensitive sex has been tested. However, it is likely that endpoints are derived from a range of guidelines and hence endpoints for males and females may be available. It is proposed that the geometric mean be used unless there is a

¹⁷ United States Environmental Protection Agency (870.6200 – Neurotoxicity screening battery):

http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/870_Health_Effects_Test_Guidelines/Series/870-6200.pdf

¹⁸ US EPA's Office of Pesticide Programs and Toxic Substances

clear indication of a difference in sensitivity between the sexes. In order to determine if one sex is more sensitive than the other, it is proposed to use the guidance in the EPCO manual (EPCO, 2005). One sex is considered more sensitive if the difference in the LD₅₀ value is >25 %. If this is the case then the lower LD₅₀ value should be used for risk assessment purposes.

2.1.2. Extrapolated LD₅₀ values from limit dose tests for birds

It is permissible to extrapolate an LD₅₀ value upwards in cases where there is no mortality or a single mortality at a limit dose in an acute avian toxicity study. The proposed extrapolation factors in Table 1 assume an average probit slope (5.43 – log dose against probit-transformed mortality) generated from a large sample of pesticides tested in the bobwhite quail and mallard duck (see EFSA 2008, Appendix 5). The extrapolation is carried out assuming a 50 % binomial probability bound that mortality could have occurred but had simply been missed by chance in the test. The extrapolation may therefore be underprotective, especially in the case of pesticides having steeper than average slopes of the dose-response-curve, and it is hence inadvisable to use this extrapolation where clear signs of toxicity are observed in the surviving individuals.

Table 1. Extrapolation factors based on the number of individuals tested at limit dose.

Number of animals tested at limit dose	Extrapolation factor for no mortality at a limit dose	Extrapolation factor for a single mortality at a limit dose
5	1.614	1.228
10	1.888	1.518
15	2.051	1.685
20	2.167	1.802

After choosing an extrapolation factor from Table 1, the extrapolated LD₅₀ value is calculated by multiplying the limit dose with the extrapolation factor:

$$LD_{50} = \text{limit dose} \times \text{extrapolation factor}$$

The method of calculating an extrapolated LD₅₀ from a limit dose could be equally applied to mammals. However, a requirement of this method is, being able to calculate an average probit slope from a sample of toxicity tests with a variety of substances. These data were available for birds but not for mammals. Hence, until the proper factors can be calculated for mammals, this method can only be applied to birds.

2.2. Short term toxicity to birds

The following short term dietary test method with birds is often available (LC₅₀ mg/kg food):

- OECD Test 205 (OECD, 1984): Avian dietary toxicity test

This risk assessment scheme does not routinely use output from this LC₅₀ study. In two opinions on the revision of Annexes II & III (EFSA, 2007, 2009a), the PPR Panel identified a number of scientific limitations and welfare issues concerning this study and therefore recommended that it should be conducted only for those pesticides where the mode of action and/or results from mammalian studies indicate a potential for the dietary LD₅₀ measured by the short term study to be lower than the LD₅₀ based on an acute oral study. This would apply, for instance, to many of the organochlorines compounds and anticoagulants. In such cases, where it is lower than the acute LD₅₀, the dietary LD₅₀ should be used in the acute risk assessment.

Although this test is no longer part of the core data packet, it is very often still available in the dossier. Information from the dietary toxicity test could be used on a case-by-case basis in higher-tier assessments when appropriate, e.g. in particular for body burden modelling (section 6.3). It can also provide an indication of whether avoidance is worth considering in higher tier assessment, but is not sufficient on its own to demonstrate that avoidance will prevent mortality. However, these types of information are also available from other studies, so in general new dietary LC₅₀ studies should not be conducted due to their scientific limitations and welfare issues (EFSA, 2007, 2009a).

2.3. Reproductive toxicity to birds and mammals

The following overview on toxicity studies available to assist in the reproductive risk assessment is based on Mineau (2005). If the substance being assessed is an endocrine-disrupting substance¹⁹, section 5.3 should be consulted.

Birds

A test for effects on reproduction in birds is currently requested if birds are likely to be exposed during the breeding season. There are two standard studies, OECD Test 206 (avian reproduction study; OECD, 1993) and the US EPA 71.4 study (US EPA, 1996). The US EPA protocol recommends that tests be carried out on first-time breeders of an upland game species, preferably the northern bobwhite quail (*Colinus virginianus*), and a wild waterfowl species, preferably the mallard duck (*Anas platyrhynchos*). The OECD version states that the Japanese quail (*Coturnix coturnix japonica*), preferably experienced breeders, is also acceptable. However, there are concerns regarding the appropriateness of this species due to its greater sensitivity and ability to attain breeding readiness under short daylight conditions.

Birds are acclimated to laboratory conditions. The substance to be tested is mixed into the diet. The birds are fed *ad libitum* for a recommended period of 10 weeks before they begin laying in response to a change in photoperiod. The egg-laying period should last 8 - 10 weeks. Eggs are removed from the adults the day they are laid, stored and then artificially incubated. Variables recorded during the study include:

- Adult body weight and food consumption;
- The number of eggs laid per hen;
- The mean eggshell thickness;
- The proportion of eggs set (placed in the incubator) that are fertile at 11 (bobwhite) or 14 days (mallard);
- The proportion of fertile eggs containing viable embryos one week later (i.e. days 18 and 21, respectively);
- The proportion of eggs that hatch and produce chicks;
- The survival of the chicks at 1 and 14 days of age;

Mammals

Outlined below is background information on the range of studies that may be considered in assessing the reproductive risk to mammals. Not all the studies are reproductive studies. This is due to the fact that some of these studies are used to address specific steps in the reproductive cycle in the phase-specific approach, which is one of the options for higher tier risk assessment (see section 6.6). Mammalian tests relevant for the reproductive risk assessment include the following:

¹⁹ Here: Materials that cause effects on bird and mammal reproduction through disruption of endocrine-mediated processes.

- OECD Test 416 (OECD, 2001c) – Two-generation reproduction toxicity study (adopted 22 January, 2001).

With this test, two or sometimes more generations can be assessed. It is specifically designed to address male and female reproductive performance including gonadal function, oestrous cycling, mating behaviour, conception, parturition, lactation and weaning. The results of such tests are the ones most often available for assessing long-term toxicity in mammals. The test uses rats or (less frequently) mice. Males are dosed during growth and, at least, during a complete spermatogenic cycle (56 days in mice, 70 days in rats). Females are dosed for two complete oestrous cycles. The animals are then mated. The pesticide is given throughout the study, typically in the diet. Sufficient pregnancies and offspring must be produced to enable assessment of maternal behaviour as well as of suckling, growth and development of the initial offspring generation (F1) right up to weaning. As the name implies, the two-generation test means that the F1 pups are kept on-dose and bred to produce a second generation, the F2 generation. The highest dose level should induce toxicity, but not mortality, in the parent animals. If necessitated by a decrease in food consumption, a pair-fed group could be added. Other than the functional endpoints such as fertility, litter size and survival, test endpoints include gross necropsy and pathology of the reproductive tract as well as histopathology where indicated (especially if reproductive organ histopathology was not performed on the shorter-term studies). The latest revisions to the test emphasized more detailed examinations of sperm parameters, sexual maturation and functional measurements of the reproductive output. The two-generation study allows an examination of the full growth, development and sexual maturation of the F1.

- OECD Test 414 (OECD, 2001d) – Prenatal developmental toxicity study (adopted 22 January, 2001).

This test doses pregnant female animals from the approximate day of implantation (ca. day 5 or 6 of gestation in rats and rabbits) to the day before delivery (ca. day 21 of gestation in rats). An earlier protocol used a shorter dosing period, restricted to the time of major organ and system differentiation. Doses are normally given by oral gavage. The study is designed to determine adverse effects on the dam such as reduced body weight, clinical signs and ability to maintain pregnancy. The study also identifies structural abnormalities in the foetus (e.g. thalidomide type effects). The foetuses are examined for viability, size, weight, sex ratio and specifically, for abnormalities of the skeleton and soft tissues/organs. The highest dose tested should produce some degree of maternal toxicity or be the limit dose of 1000 mg/kg bw/d. Foetal abnormalities are normally divided into severe cases (malformations), i.e. those ones that would compromise the ability to survive or function normally, and minor cases (variations/anomalies) that would have a minimal impact on the animal. For some endpoints it is also important weighing the maternal toxicity.

- OECD Test 407 (OECD, 1998a) – Repeated dose 28-day oral toxicity in rodents (adopted 27 July, 1995).
- OECD Test 408 (OECD, 1998b) – Subchronic oral toxicity – rodent 90 day study (adopted 21 September, 1998).

The above two tests are essentially the same except for the duration of the dosing period and among others the number of animals per group. They consist of repeated oral dosing of the test substance either by gavage or in the diet.

The use of gavage dosing can result in high systemic levels that induce adverse findings that cannot be produced when equivalent doses (in mg/kg bw/d) are given via the diet.

2.3.1. Determining toxicity endpoints from avian and mammalian reproductive toxicity studies

Future scientific developments may support changes to current practice in the ecotoxicological starting point for the risk assessment. It may be, for example, that benchmark doses or EC_x/ED_x

(concentration/dose where x % effect was observed/calculated) will come to be viewed as an alternative and often preferable reference point to the no-observed-effect concentration/level (NOEC/NOEL). Because a benchmark dose/concentration stands for a certain magnitude of effect, the replacement of the NOEC/NOEL/NOAEL by such benchmark value would have an impact on the level of protection which is achieved by the risk assessment scheme. This impact would have to be evaluated, and the scheme adjusted accordingly.

For the time being, this document refers to the no-observed-adverse-effect level (NOAEL) rather than either no-observed-effect concentration (NOEC) or no-observed-effect level (NOEL). This is due to the latter terms referring to levels or concentrations where there is no effect.²⁰

In determining a NOAEL there may not be a consideration of the effect or its biological relevance. Therefore, it is proposed to use endpoints that are based on a consideration of the biological and/or ecological relevance. This needs to be considered case-by-case, as illustrated by the following examples:

(a) Endpoint is statistically significantly different from the control but does not fit a dose/treatment response. In this case, the endpoint can be ignored. In the example below, the value 72 is considered to be statistically significantly different (*) from the control but there is no dose response and this endpoint can therefore be ignored.

Dose (mg a.s./kg bw/d)	0	10	30	100
Biological response	100	72*	98	95

(b) Endpoint is not statistically significantly different from the control but does fit a dose/treatment response. In this case, it may be appropriate to consider it as a NOAEL. In the example below, the effects in the top two doses are statistically significant (*) and dose/treatment related – while the response at 10 mg a.s./kg bw/d is not statistically significant from the control. However it would appear to be dose/treatment related and hence the NOAEL for this endpoint *could* be 5 mg a.s./kg bw/d. However, before deciding on this as the NOAEL, it is necessary to determine if the endpoint is biologically relevant (see below for details).

Dose (mg a.s./kg bw/d)	0	5	10	30	100
Biological response	100	98	75	55*	30*

(c) Endpoint is statistically significantly different from the control but may not be biologically relevant. In order to determine the biological relevance of an effect it should be considered whether the effect could lead to a functional deficit later on in the study, e.g. if a reduction in the weight of pups at birth leads to a decrease in level of survival. If not, then the effect may not be biologically relevant, however if there is a carry over of effects into the number of survivors, it can be considered biologically relevant.

It has been argued that a slight eggshell thinning should be ignored if there is no effect on hatchability. In a sample of 49 recent studies with mallard ducks, Mineau (2005) found that, 4 % of studies had a NOEC related to eggshell thickness but no evidence of increased breakage. Indeed, population effects in the wild tend to come about after thinning of 18 % or more (Blus, 2003).

²⁰ It may be possible to use a ‘bench mark dose’ rather than a NOAEL. Further details regarding ‘benchmark dose’ see EFSA (2005c).

However, before deciding that endpoints are not biologically relevant, the following must be taken into consideration:

- Because of high variability in inter-pair performance, the avian reproduction test is not a statistically robust test. The likelihood of false positives typically is not high.
- Interspecies differences mean that a mild effect in one of the two test species may be much more pronounced in a wild exposed species. Knowledge that a mechanism of toxicity exists should not be dismissed without consideration of this possible variation in sensitivity. An example of this variation is DDE-induced eggshell thinning, which is known to vary across bird orders by orders of magnitude (see Cooke, 1973 and Blus, 2003 for reviews).
- An effect may be higher in the field than in the laboratory. Again, with eggshell thickness, a shortage of readily available calcium in the wild would exacerbate toxic effects on eggshell thickness.

(d) Endpoint is statistically significantly different (*) from the concurrent control but is within the range of comparable historical control levels. It should be noted that the comparable controls must be from studies carried out following the same protocol/guideline and conducted within an appropriate timeframe (e.g. ± 2 years). In determining whether the effects can be discounted it is important to consider any effects in other test concentrations in the concurrent study. This is illustrated by the following:

Test 1

Dose (mg a.s./ kg)	0	5	10	30
Biological response	6	5	6	12*

Test 2

Dose (mg a.s./ kg)	0	5	10	30
Biological response	4	11	10	12*

Historical control ranges from 4 to 13.

Since the control, low dose and mid-dose are consistent, the findings at the top dose of Test 1 can be considered as relevant. In Test 2 the low and mid-dose findings do not appear to be dose or treatment related and hence the findings at the top dose is considered to be within normal variation and hence can be discounted.

2.3.1.1. Conversion of endpoints from ppm to mg a.s./kg bw/d

In the following risk assessment, it is necessary to have all toxicity endpoints in mg a.s./kg bw/d, i.e. in a daily dose format to be consistent with the units used in the exposure assessment. Endpoints from mammalian toxicity studies are usually presented in this way. However most avian reproduction studies and some mammalian reproduction/development studies tend to be reported in terms of parts per million (ppm) or mg a.s./kg diet and therefore their endpoints need to be converted into daily dose. For avian reproduction studies, a generic factor can be used. The results of nine studies were examined and the lowest conversion factor was calculated to be 0.1 (Appendix 6 of EFSA, 2008). On the basis of this work, as well as information from the French Food Safety Authority (AFSSA) and the Agritox database (discussed in Appendix 6 of EFSA, 2008), this figure is used in the first instance (e.g. in the screening step). For this conversion to be used, no food avoidance should have occurred in the study. If refinement is required, then food consumption data from the actual study should be applied. For this, the overall mean value for food consumption and body weight at the NOAEL must be used and this value be applied for conversion of the NOAEL to a daily dose.

Regarding mammalian toxicity studies, it is likely that for newer substances the endpoints tend to be presented as daily doses. However, daily food consumption can vary during a study and hence conversions can be based either on the average food consumption, or on the consumption specific to that phase. It is more appropriate to use the consumption relevant to the specific reproductive phase and therefore it is essential to discuss this with a toxicology specialist.

Table 2 presents a standard set of factors that can be used to provide internal consistency when converting concentrations in diet into mg/kg bw/d dose levels for mammals. This should be used only in the absence of specific information in a study report or summary (it can, however, be used to give a rough check of values cited in a study). Only routine study types, species and ages have been considered.

Table 2. Factors for converting endpoints from mammalian toxicity studies from ppm to mg a.s./kg bw/d. Endpoints reported as ppm should be multiplied by the relevant factor from the table to convert them to mg/kg bw/d.

Species	Age/study	Conversion factor from ppm to mg/kg bw/d
Rat	28 d and 90 d	0.1
Rat	Two-generation study first mating*	0.08
Rat	Two-generation study overall (females)*	0.12
Mouse	28 d and 90 d	0.20
Dog	adult/all	0.025

* The first mating value for a two-generation study should be used for assessment when effects (general or on reproduction) are seen to relate to the pre-mating phase of the first mating of a study, or effects seen only in male F0 parents at any time. For all other aspects of a two-generation study the overall conversion figure should be used.

2.4. Incorporation of additional toxicity information

According to Annex II (Directive 91/414/EEC), an acute toxicity study for one species of bird or mammal is required. The endpoint from this study is then applied in a risk assessment and the resulting TER is compared to the decision making criteria in Annex VI of Directive 91/414/EEC. If the TER is less than 10, then no authorization is permitted “unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact occurs after use of the plant protection product”. If the TER is greater than 10, then the acute risk to birds is considered to be “acceptable”. This implies that the acute toxicity data on one species together with an uncertainty factor of 10 gives a level of protection which is ‘acceptable’. Similarly, it can be assumed that as Annexes II stipulates reproductive data on one species of bird and mammal, then an appropriate level of protection is provided by applying an uncertainty factor or assessment factor of 5 to the appropriate toxicity endpoint for a single species.

2.4.1. How to deal with toxicity data from more than one species

If additional species are tested, it is necessary to consider which endpoint should be used in the risk assessment. In the past, it has been normal practice to take the lowest available endpoint. This means that, as more species are tested, the risk assessment is based on increasingly sensitive species. Consequently, the average level of protection exceeds the level implied by the provisions of Directive 91/414/EEC and Regulation (EC) 1107/2009, respectively.

In a previous opinion, the PPR Panel proposed an alternative approach of taking the geometric mean when more than one species is tested (Method 1 in EFSA, 2005b²¹). It was shown that this would ensure at least the same average level of protection as implied by the Directive, and avoid most of the increase in conservatism when additional species are tested. This was based on the assumption that toxicity data were normally distributed on a logarithmic scale.

As part of the work in preparing this Guidance Document, new research was undertaken to examine the sensitivity of the proposed approach to the assumption of normality. The analysis used the same measure of level of protection as the earlier opinion (the Mean Fraction Exceeded) and applied also an additional measure: the probability of the Fraction Exceeded being greater than a given percentile, e.g. the hazardous dose to 5 % of the species (HD₅). The details are reported in Appendix 7 of EFSA (2008). The results show that using the geometric mean of multiple species is conservative (achieves at least the same average level of protection as a single species). This is true for a wide range of distributions that are symmetric and unimodal (single peak) on a logarithmic scale, and also for asymmetric unimodal distributions where the long tail is to the left. It is also true for asymmetric distributions with long tails to the right²² and for some examples of bimodal distributions, provided that the standard uncertainty factor includes sufficient allowance for between-species variation in toxicity, which seems likely.

The Joint Working Group noted that in some cases, the LD₅₀ for most sensitive species might be lower than the geometric mean divided by the standard assessment factor of 10. As the standard factor of 10 is considered sufficient to provide appropriate allowance for between-species variation when only one species is tested, this implies that a small frequency of such cases is already taken into account, in which case the geometric mean approach is still appropriate. However, it was recognised that there could be concerns for situations where the variation between species was particularly wide. The Joint Working Group therefore decided on the following approaches:

- The geometric mean should be used for the acute assessment, except when the endpoint for the most sensitive species is more than a factor of 10 below the geometric mean of all the tested species. Where this is the case, the most sensitive species will be used for the risk assessment but generally without any assessment factor²³ (unless there are specific reasons to believe that this is not appropriate).

The new work also investigated how bias and measurement errors in toxicity data affect the use of the geometric mean when multiple species are tested. The results (see section 2.3.1 of EFSA, 2008) imply that using the geometric mean of multiple species will be conservative, however this depends on the measurement errors in NOECs following roughly a normal distribution, which requires further investigation. Therefore the Joint Working Group (EC, 2009) decided that, until further work is completed:

- For reproductive studies, the endpoint from the most sensitive tested species should be used.

²¹ Method 1 is appropriate for taxonomic groups where the minimum requirement is a single tested species, as is the case for birds and for mammals.

²² Distributions of acute toxicity data often have long tails to the right on the natural scale, but this is reduced or removed on the logarithmic scale, which is used for the geometric mean.

²³ No assessment factor is generally needed in such cases, because the most sensitive species is already more than a factor of 10 below the geometric mean, so the level of protection provided by using this endpoint should already be greater than that provided by the standard factor of 10. If there was specific reason to believe that between-species variation is greater for the substance under assessment than is allowed for by the standard factor of 10, then a suitable factor could be applied to the lowest endpoint. However, this factor should be less than 10, because taking the lowest endpoint already incorporates more protection than the standard factor. Note that the finding of a single endpoint more than a factor of 10 below the geometric mean is not in itself strong evidence that between-species variation is unusually large, because such cases are expected to occur occasionally.

The above highlights the possible application of endpoints if data on additional species are available. This refinement step should be used only if, for historical reasons, data on additional species are already available, i.e. data should **not routinely** be generated to specifically refine the endpoint. This is due to concerns with regard to animal welfare and to minimise the use of animals.

2.4.2. How to deal with more than one acute study on the same species

In cases where more than one acute study on the same species is available, it is proposed that the geometric mean of the endpoints for the same species should be taken (including only those studies that are considered suitable for use in risk assessment). This endpoint is then used in the overall geometric mean (see Table 3). The studies should be equivalent in terms of guideline and in particular the vehicle/solvent since, e.g. there may be a marked reduction in apparent toxicity of pyrethroids when using an aqueous rather than an oil based vehicle.

Table 3. LD₅₀ [mg/kg bw] for various bird species and their use in the calculation of the geometric mean.

Species	LD ₅₀ mg/kg bw	LD ₅₀ to be used in calculation of geometric mean
Mallard duck (study 1)	25	30
Mallard duck (study 2)	36	
Bobwhite quail	21	21
Japanese quail	36	36
Red winged blackbird	5	5
Overall geometric mean to be used in RA		18.3

2.4.3. How to deal with more than one reproduction study on the same species

Sometimes there may be more than one reproduction or developmental study on the same species available. In these cases it may be possible to merge the two datasets as if it were one study (JMPR, 2004)²⁴. However, in order to allow for the merger of the two studies, they should be conducted according to a similar protocol or guideline. It is also important to ensure that the key endpoints have been assessed in all studies and that the studies are similar, e.g. the two studies have similar dose-responses, the same species has been used, the same protocol followed, similar number of animals used, and same endpoints and same test conditions applied. It should also be checked whether the test substances are chemically equivalent (EC, 2005). It is not considered appropriate to use the output from the pilot study for this exercise nor to take the geometric means of the NOAEL.

This procedure is in line with how mammalian toxicologists deal with such data. An example of this is illustrated in Tables 4a, 4b and 4c.

²⁴ http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/2004_rep/report2004jmpr.pdf

Table 4a. Illustration of how to combine two studies on the same species (example a).

Study 1 Test concentration [mg/kg bw/d]	Effect	Study 2 Test concentration [mg/kg bw/d]	Effect
100	Yes	50	Yes
30	Yes	25	No
3	No	10	No
0	No	0	No
NOAEL	3		25

From the above example the NOAEL that could be used in the risk assessment would be 25 mg/kg bw/d. Presented below is another example of merging data sets. In this example, it is not possible to ignore the lower finding.

Table 4b. Illustration of how to combine two studies on the same species (example b).

Study 1 Test concentration [mg/kg bw/d]	Effect	Study 2 Test concentration [mg/kg bw/d]	Effect
100	Yes	50	Yes
30	Yes	35	No
3	No	10	No
0	No	0	No
NOAEL	3	NOAEL	35

Table 4c. Results following the combination of all these results as if it were one study.

Combined results from studies 1 and 2	
Test concentration mg/kg bw/d	Effect
100	Yes
50	Yes
35	No
30	Yes
10	No
3	No
0	No
NOAEL	10

As the NOAEL of 35 mg/kg bw /d from study 2 is higher than the LOAEL of 30 mg/kg bw/d from study 1, it is considered that the overall NOAEL from the above studies would be 10 mg/kg bw/d.

2.5. Combined effects of simultaneous exposure to several active substances

This assessment is not carried out for decisions on the inclusion of active substances in Annex I of Directive 91/414/EEC, but is important for national authorisation procedures for products that could contain more than one active substance. From the scientific point of view, combined action of several toxicants must be specifically considered in the risk assessment when it is obvious that such exposure situations will occur for animals. If an assessment is made for such a product in the context of national

authorisation, the simultaneous exposure of animals to residues of two or more potential toxicants should also be considered in the risk assessment. Further information is given in Appendix B.

3. Level of protection provided by the assessment procedures

Directive 91/414/EEC does not contain a precise definition nor detailed specifications of the level of protection that is required. Therefore, in developing this Guidance Document, careful consideration was given to how this should be addressed.

In summary, the procedures for **first-tier assessment** (described in sections 4 and 5) are designed to achieve a “*surrogate*” protection goal of making any mortality or reproductive effects unlikely. At **higher tiers**, assessments may be directed either at the surrogate protection goal or at the *actual protection goal of clearly establishing that there will be no visible mortality and no long-term repercussions for abundance and diversity*. If the actual protection goals are defined more precisely by risk managers or legislators in future, then the protection goals and assessment procedures should be reviewed and revised accordingly.

The level of protection provided at Tier 1 is determined by the standard assessment procedures set out in this document and therefore does not need to be reconsidered case by case. However, since there is no standardised approach for higher tier assessments, the level of protection needs to be evaluated case by case for every higher tier assessment. Guidance for this is given in section 6.8.

A full account of these issues is provided in Appendix C, together with evaluations of the levels of protection provided by the first-tier assessment procedures set out in this Guidance Document. These evaluations are provided both for reference and as a starting point for evaluating the level of protection in higher tier assessments.

In addition to the level of protection, the impact of the assessment procedures on the proportions of pesticides requiring higher-tier assessment may be a relevant consideration for risk managers. An analysis of this is presented in Appendix D.

4. Risk assessment modules for spray applications

There are four different risk assessment modules for dietary exposure due to the use of sprayed products:

Module 1	Acute risk assessment for birds
Module 2	Acute risk assessment for mammals
Module 3	Reproductive risk assessment for birds
Module 4	Reproductive risk assessment for mammals

All four modules must be completed.

In bird and mammal risk assessment three categories of species have been defined: the indicator species, the generic focal species and the focal species. The ‘**indicator species**’ is used in the first screening step and for eliminating all those substances that clearly pose a low risk to birds and mammals. This ‘indicator species’ is not a real species but, by virtue of its size and feeding habits is considered to have higher exposure than (i.e. to be protective of) other species that occur in a particular crop (see Table 5 below) at a particular time.

In the first-tier risk assessment, a ‘**generic focal species**’ will be used for further risk assessment. Again it is not a real species, however it is considered to be representative of all those species potentially at risk. Instead of the one single food item approach of the screening step in this assessment a mixed diet is applied when appropriate for the generic focal species. In addition, interception of the spray by the crop is taken into account by calculating the residue level on the several food types for the birds and the mammals (see Appendix E).

In refined risk assessment it is appropriate to use ‘**focal species**’, i.e. a real species that actually occurs in the crop when the pesticide is being used (see section 6.1.3 for identification of focal species.).

The approach used to select both, indicator and generic focal species, is described in Appendix 10 of EFSA (2008).

For the first-tier risk assessment it is not necessary that the generic focal species only eats part of the crop. Even when the crop is unpalatable it is assumed that weeds and weed seeds will be available as food for birds and mammals. Often these weeds and weed seeds will be covered by the crop and therefore crop interception has been taken into account. The degree of interception is defined by the growth stages (BBCH²⁵ stages) for each crop category (BBA, 2001).

Rice is not included in this document because it is envisaged that it will be addressed in a separate guidance document.

It should be noted that the screening steps are based on worst-case assumptions and should be used to identify those substances and associated uses that do not pose a risk to birds and mammals and for which no further acute risk assessment is therefore required. The screening steps are an option and the assessment may as well start at the first-tier assessment.

In the assessment for the potential risk of bird and mammals in the screening step and the first-tier, crop groups have been defined. Those groups consist of crop species that have similar growing patterns and therefore it is assumed that the exposure of the indicator species and generic focal species will be the same. This list (see Table 5) is not exhaustive, but covers most of the larger crops.

To facilitate the assessment process, shortcut values are provided to assist with the exposure calculations. These are data describing the feeding habits and other ecological needs for the indicator and generic focal species that can be used directly in the exposure calculations. Shortcut values based on mean residue unit doses (RUDs) are used for reproductive assessments. Shortcut values based on 90th percentile RUDs are used for acute assessments to take account of the likelihood that individual animals may feed in one field for all or most of a single day. Over the longer periods that are relevant for some reproductive endpoints, animals may feed on several fields and thus tend to average out variation in residues, although it is also possible that an individual may continue to feed in a single field with high (or low) residues over multiple days. Considering this together with other factors affecting the level of protection, it was deemed reasonable to use the 90th percentile RUD for the acute assessment and the mean RUD for the reproductive assessment (see Appendix C for detailed evaluation of the levels of protection).

²⁵ Biologische Bundesanstalt, Bundessortenamt und Chemische Industrie

Table 5. Crop groups and crop species

Crop group	Crop species
Bare soil	All arable crops (BBCH < 10)
Bulbs and onion like crops	Bulbs (like tulips etc.), onions, garlic, shallots, etc.
Bush and cane fruit	Blackberry, dewberry, loganberry, raspberry, gooseberry, red and blackcurrant, etc.
Cereals	Wheat, barley, oats, rye, rice, millet, sorghum, triticale, etc.
Cotton	Cotton
Fruiting vegetables	Tomatoes, peppers, chilli peppers, aubergines, cucumber, gherkins, courgettes, melons, squashes, watermelons, etc.
Grassland	Grass
Hops	Hops
Leafy vegetables	Broccoli, cauliflower, Brussels sprouts, cabbage, Chinese cabbage, kale, cress, lambs lettuce, lettuce, escarole, spinach, chicory, chervil, chives, parsley, artichokes, cardoons, rhubarb, asparagus, etc.
Legume forage	Alfalfa, clover, etc.
Maize	Maize, sweet corn, etc.
Oilseed rape	Oilseed rape, linseed, field (faba) beans, quinoa, poppy, mustard, sesame, etc.
Orchards	Grapefruit, lemon, lime, mandarins, oranges, pomelos, olives, almonds, chestnuts, hazelnuts, macademia, pecans, pine, pistachios, walnuts, apple, pear, quinces, apricots, cherries, peaches, nectarines, plums, avocado, date, kiwi, mango, pomegranate, fig, kumquat, litchi and passion fruit, etc.
Ornamentals/nursery	Flowers and plants for transplanting
Potato	Potato, sweet potatoes, etc.
Pulses	Peas, lentils, French beans, soybeans, buckwheat, etc.
Root and stem vegetables	Beetroot, carrot, celeriac, horseradish, Jerusalem artichoke, parsnips, parsley root, radishes, salsify, Swedes, turnips, celery, kohlrabi, fennel, etc.
Strawberries	Strawberry, bilberry, cranberry, etc.
Sugarbeet	Sugarbeet
Sunflower	Sunflower
Vineyards	Grape

4.1. Module 1: Acute dietary risk assessment for birds

The 'daily dietary dose' (DDD) is defined by the food intake rate of the species of concern (i.e. the indicator species, the generic focal species or the focal species), the body weight of the species of concern, the concentration of a substance in/on fresh diet (see Appendix F) and the fraction of diet obtained in the treated area.

The estimated food intake rates are based on the daily energy expenditure of the species of concern, the energy in the food, the 'energy' assimilation efficiency of the species of concern, and the moisture content of the food (see Appendix G).

The above information is combined into a single value for a specific species-crop-combination and termed a 'shortcut value' (SV).

Screening assessment

Step 1

Identify which of the indicator species listed in Table 6 is relevant to the crop

Table 6. Acute shortcut values (based on 90th percentile residues) for avian indicator species.

Crop	Indicator species	Shortcut value for acute assessment
Bare soils and hop	Small granivorous bird	24.7
Grassland	Large herbivorous bird	30.5
Bush and cane fruit	Small frugivorous bird	46.3
Orchards and ornamentals/nursery	Small insectivorous bird	46.8
Vineyard	Small omnivorous bird	95.3
Bulbs and onion like crops, cereals, fruiting vegetables, leafy vegetables, legume forage, maize, oilseed rape, potatoes, pulses, root and stem vegetables, strawberries, sugar beet, and sunflower	Small omnivorous bird	158.8
Cotton	Small omnivorous bird	160.3

Step 2

Calculate the daily dietary dose (DDD) for a single application by multiplying the shortcut value based on the 90th percentile residue (presented in Table 6) with the application rate in kg/ha.

$$DDD_{\text{single application}} = \text{application} \cdot \text{rate} \cdot [\text{kg} / \text{ha}] \cdot \text{shortcut} \cdot \text{value}$$

Step 3

Multiply the daily dietary dose for a single application with an appropriate multiple application factor for 90th percentile residue data (MAF_{90}) when the substance is applied two or more times (see Table 7). Or calculate a specific MAF_{90} according to Appendix H for non-standard application intervals.

$$DDD_{\text{multiple applications}} = DDD_{\text{single application}} \times MAF_{90}$$

MAF_{90} values for other application intervals can be calculated either using the formula in Appendix H with the input parameters for 'grass + cereals (adjusted)' or using the values for the next lower application interval. The limit value in the rightmost column should be used for higher number of applications with one of the tabulated intervals.

Table 7. Multiple application factors for 90th percentile residue data (MAF₉₀) for selected application intervals and $n = 1-8$ applications (considering a default DT₅₀ of 10 d on foliage).

Application interval (d)	MAF ₉₀ for 90 th percentile residue data for n applications								
	1	2	3	4	5	6	7	8	∞
7	1.0	1.4	1.6	1.8	1.9	1.9	1.9	1.9	2.0
10	1.0	1.3	1.5	1.5	1.6	1.6	1.6	1.6	1.6
14	1.0	1.2	1.3	1.3	1.4	1.4	1.4	1.4	1.4

Step 4

Take the appropriate LD₅₀ (mg/kg bw/d) for birds (see section 2).

Step 5

Calculate the toxicity-exposure-ratio

$$TER = \frac{LD_{50}}{DDD}$$

Step 6

Compare the TER to the respective trigger value.

TER ≥ 10

No refinement required

TER < 10

Go to first-tier risk assessment (Step 7)

Tier 1 risk assessment

All pesticides should be subjected to Tier 1 assessment, unless they are shown by a screening assessment (Steps 1-6) to pose a low risk. Tier 1 uses the same general approach as the screening assessment, but requires more specific exposure scenarios.

Step 7

Identify all of the generic focal species listed in Table I.1 (Annex I) that are relevant for the crop.

Step 8

Calculate the daily dietary dose (DDD) for a single application for each generic focal species by multiplying the shortcut value based on the 90th percentile residue (presented in Table I.1, Annex I) with the application rate in kg/ha.

$$DDD_{\text{single-application}} = \text{application} \cdot \text{rate} \cdot [\text{kg} / \text{ha}] \cdot \times \cdot \text{shortcut} \cdot \text{value}$$

Step 9

Multiply the DDD for a single application with an appropriate multiple application factor for 90th percentile residue data (MAF_{90}) when the substance is applied two or more times (see Table 7). Or calculate a specific MAF_{90} according to Appendix H for non-standard application intervals.

$$DDD_{\text{multiple-applications}} = DDD_{\text{single-application}} \times MAF_{90}$$

Step 10

Take the appropriate LD_{50} for birds (same as Step 4).

Step 11

Calculate the toxicity-exposure-ratio:

$$TER = \frac{LD_{50}}{DDD}$$

Step 12

Compare the TER to the respective trigger value.

All TERs ≥ 10

No refinement required

One or more of the TERs < 10

Higher tier risk assessment required

For higher tier options see section 6.

4.2. Module 2: Acute dietary risk assessment for mammals

The ‘daily dietary dose’ (DDD) is defined by the food intake rate of the species of concern (i.e. the indicator species, the generic focal species or the focal species), the body weight of the species of concern, the concentration of a substance in/on fresh diet (see Appendix F) and the fraction of diet obtained in the treated area.

The estimated food intake rates are based on the daily energy expenditure of the species of concern, the energy in the food, the ‘energy’ assimilation efficiency of the species of concern, and the moisture content of the food (see Appendix G).

The above information is combined into a single value for a specific species-crop-combination and termed a ‘shortcut value’ (SV).

Screening assessment

Step 1

Identify which of the indicator species listed in Table 8 is relevant to the crop.

Table 8. Acute shortcut values (based on 90th percentile residues) for mammalian indicator species.

Crop	Indicator species	Shortcut value for acute assessment
Bare soil	Small granivorous mammal	14.4
Bush and cane fruit	Small herbivorous mammal	81.9
Bulbs and onion like crops, cereals, oilseed rape, potatoes, root and stem vegetables, strawberries, sugar beet, and sunflower	Small herbivorous mammal	118.4
Cotton, fruiting vegetables, grassland, leafy vegetables, legume forage, maize, orchards, ornamentals/nursery, pulses, and vineyard	Small herbivorous mammal	136.4

Step 2

Calculate the daily dietary dose (DDD) for a single application by multiplying the shortcut value based on the 90th percentile residue (presented in Table 8) with the application rate in kg/ha.

$$DDD_{\text{single-application}} = \text{application} \cdot \text{rate} \cdot [\text{kg} / \text{ha}] \cdot \text{shortcut} \cdot \text{value}$$

Step 3

Multiply the DDD for a single application with an appropriate multiple application factor for 90th percentile residue data (MAF₉₀) when the substance is applied two or more times (see Table 9). Or calculate a specific MAF₉₀ according to Appendix H for non-standard application intervals.

$$DDD_{\text{multiple-applications}} = DDD_{\text{single-application}} \times MAF_{90}$$

Table 9. Multiple application factors for 90th percentile residue data (MAF₉₀) for selected application intervals and $n = 1 - 8$ applications (considering a default DT₅₀ of 10 d on foliage).

Application interval (d)	MAF ₉₀ for 90 th percentile residue data for n applications								
	1	2	3	4	5	6	7	8	∞
7	1.0	1.4	1.6	1.8	1.9	1.9	1.9	1.9	2.0
10	1.0	1.3	1.5	1.5	1.6	1.6	1.6	1.6	1.6
14	1.0	1.2	1.3	1.3	1.4	1.4	1.4	1.4	1.4

MAF₉₀ values for other application intervals can be either calculated using the formula in Appendix H with the input parameters for ‘grass + cereals (adjusted)’ or the values for the next lower application interval should be used. For higher number of applications with one of the tabulated intervals, the limit value in the rightmost column should be used.

Step 4

Take the appropriate LD₅₀ in mg/kg bw/d for mammals (see section 2).

Step 5

Calculate the toxicity-exposure-ratio.

$$TER = \frac{LD_{50}}{DDD}$$

Step 6

Compare the TER to the respective trigger value.

TER ≥ 10

No refinement required

TER < 10

Go to first-tier risk assessment (Step 7)

Tier 1 risk assessment

All pesticides should be subjected to Tier 1 assessment, unless they are shown by a screening assessment (Steps 1-6) to pose a low risk. Tier 1 uses the same general approach as the screening assessment, but requires more specific exposure scenarios.

Step 7

Identify which of the generic focal species listed in Table I.2 (Annex I) are relevant for the crop.

Step 8

Calculate the daily dietary dose (DDD) for a single application for each generic focal species by multiplying the shortcut value based on the 90th percentile residue (presented in Table I.2, Annex I) with the application rate in kg/ha.

$$DDD_{\text{single-application}} = \text{application} \cdot \text{rate}[\text{kg} / \text{ha}] \times \text{shortcut} \cdot \text{value}$$

Step 9

Multiply the DDD for a single application with an appropriate multiple application factor for 90th percentile residue data (MAF₉₀) when the substance is applied twice or more times (see Table 9). Alternatively, calculate a specific MAF₉₀ according to Appendix H for non-standard application intervals.

$$DDD_{\text{multiple-applications}} = DDD_{\text{single-application}} \times MAF_{90}$$

Step 10

Take the appropriate LD₅₀ for mammals (same as Step 4)

Step 11

Calculate the toxicity-exposure-ratio:

$$TER = \frac{LD_{50}}{DDD}$$

Step 12

Compare the TER to the respective trigger value.

All TERs ≥ 10

No refinement required

One or more of the TERs < 10

Higher tier risk assessment required

For higher tier options see section 6.

4.3. Module 3: Reproductive risk assessment for birds

An avian reproductive toxicity study and associated risk assessment should not be necessary if it can be demonstrated that exposure will not occur during the reproductive season for birds. This is based on the assumption that if a bird is not in a reproductive phase then exposure to pesticides is unlikely to cause an adverse effect on reproduction.

However, delayed effects on reproduction from exposure during the non-reproductive period may be unlikely but they are possible. Therefore, if the proposed use of the product under assessment is to be made outside the breeding season of birds, the mammalian toxicity data package should be examined to determine if the active substance has either antiandrogenic or antiestrogenic activity. If such activity is indicated then there is a need for a reproductive risk assessment even if exposure during the breeding season is unlikely (see section 5.3 on endocrine disruption).

Screening assessment

The screening assessment may be useful to identify quickly those substances that pose very low reproductive risk, for which more detailed assessment is unnecessary. If preferred, assessors may proceed directly to Tier 1 (Step 5).

Step 1

Determine if breeding birds could be exposed to either the active substance or the associated product. If not, no further assessment is required.

Step 2

If exposure is possible, determine the lowest NOAEL from the available avian reproduction study/studies. See section 2.3.1 for details on how to determine a NOAEL.

It should be noted that the endpoints from the current guidelines are presented as ppm diet or mg a.s./kg diet. Therefore, it is necessary to convert the endpoints to daily doses, i.e. mg a.s./kg bw/d. In the first instance a generic factor of 0.1 can be used and applied to the ppm or mg a.s./kg food endpoint (see section 2.3.1.1).

In addition, obtain the acute oral LD₅₀ value used in the acute avian assessment (either the LD₅₀ for a single species, or the geometric mean for multiple species) and divide it by 10 to obtain LD₅₀/10. The

LD₅₀/10 is used as an endpoint in the reproductive assessment to take account of the possibility of reproductive impairment due to sublethal effects on pair formation and breeding site selection, incubation, parental care of nestlings, and survival of fledgling birds (see Appendix J)²⁶.

For the screening assessment, take the lowest of the LD₅₀/10 and the lowest NOAEL from the avian reproduction study/studies.

Step 3

Identify the appropriate indicator species and shortcut value for the crop under assessment from Table 10. If multiple applications are to be made, then Table 11 should be consulted and the appropriate ‘multiple application factor’ (MAF_m) should be used. Calculate the daily dietary dose (DDD):

$$DDD = \text{application rate} \times \text{shortcut value} \times TWA \times MAF_m$$

The value to be used for the time-weighted average factor (TWA) depends on whether the toxicity endpoint from Step 2 could be caused by a short-term exposure (STE) or only by a long-term exposure (LTE)²⁷.

- If the toxic effect is considered to be caused by LTE, use TWA = 0.53 (estimates time-weighted exposure over 21 days, assuming a default DT₅₀ of 10 days).
- If the toxic effect is considered to be caused by STE, use TWA = 1 (one day exposure).

Table 10. Indicator species and shortcut values (based on mean residues) for the avian reproductive assessment.

Crop	Indicator species	Shortcut value for reproductive assessment
Bare soils and hop	Small granivorous bird	11.4
Grassland	Large herbivorous bird	16.2
Orchards and ornamentals/nursery	Small insectivorous bird	18.2
Bush and cane fruit	Small frugivorous bird	23.0
Vineyard	Small omnivorous bird	38.9
Bulbs and onion like crops, cereals, fruiting vegetables, leafy vegetables, legume forage, maize, oilseed rape, potatoes, pulses, root and stem vegetables, strawberries, sugar beet, and sunflower	Small omnivorous bird	64.8
Cotton	Small omnivorous bird	65.4

²⁶ Note that division of the LD₅₀ by 10 is for extrapolation from lethal to sublethal endpoints (see Appendix 11 of EFSA, 2008) and is not related to the normal assessment factor of 10 used in acute assessments. When LD₅₀/10 is used in the reproductive assessment, the resulting TER should be compared to the normal reproductive assessment factor of 5 (see Steps 4 and 8).

²⁷ It is intended to develop further guidance on criteria for determining which effects could be caused by short-term exposures. The Joint Working Group decided that, until such guidance is available, it should be assumed as a default that the effects are caused by LTE, unless there is specific evidence for the pesticide under assessment that the effect could be caused by STE.

Table 11. Multiple application factors assuming mean residues (MAF_m), for use in reproductive assessments.

MAF_m are shown for selected application intervals and $n = 1-8$ applications, assuming a default DT₅₀ of 10 d on foliage. MAF_m values for other application intervals can be either calculated either using the formula in Appendix H or using the values for the next lower application interval. The limit value in the rightmost column should be used for higher numbers of applications with one of the tabulated intervals. These MAF factors should be used for all food types (i.e. arthropods and vegetation). Further information on this issue is provided in Appendix H.

Application interval (d)	MAF _m for n applications								
	$n = 1$	2	3	4	5	6	7	8	Limit
7	1.0	1.6	2.0	2.2	2.4	2.5	2.5	2.5	2.6
10	1.0	1.5	1.8	1.9	1.9	2.0	2.0	2.0	2.0
14	1.0	1.4	1.5	1.6	1.6	1.6	1.6	1.6	1.6

Step 4

Calculate the toxicity-exposure-ratio and compare the TER to the respective trigger value.

$$TER = \frac{\text{lowest endpoint (Step 2)}}{\text{relevant DDD (Step 3)}}$$

TER ≥ 5

No further assessment required

TER < 5

Go to Tier 1 (Step 5)

Tier 1 risk assessment

All pesticides should be subjected to Tier 1 assessment, unless they are shown by a screening assessment (Steps 1-4) 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.

Step 5

Obtain the acute oral LD₅₀ value used in the acute avian assessment (either the LD₅₀ for a single species, or the geometric mean for multiple species) and divide it by 10 to obtain LD₅₀/10 (see Step 2 and Appendix J for more explanation of the relevance of LD₅₀/10 for reproductive assessments).

For each available reproduction study, identify the NOAEL for reproductive effects, ignoring purely parental effects (e.g. changes in parental body weight and food consumption²⁸).

²⁸ These endpoints are excluded because, for birds, LD₅₀/10 is considered a more appropriate indicator of the NOAEL for parental effects with potential to disrupt reproduction.

It is normal for toxicity endpoints to be determined statistically. In the vast majority of cases it is acceptable to use these endpoints. However, occasionally care needs to be exercised to ensure that the endpoint is appropriate. Further information on this issue is provided in section 2.1.1.

Endpoints that are presented as ppm diet or mg a.s./kg diet must be converted to daily doses, i.e. mg a.s./kg bw/d. At Tier 1, this should be done using the actual body weight and food consumption data from the study under consideration. In order to do this, take the mean value for food consumption over the whole study and average body weight over the duration of the study at the NOAEL and use these figures to convert the NOAEL to a daily dose.

After converting the lowest reproductive endpoint from each study or merged dataset to a daily dose, identify the lowest of the converted endpoints²⁹. If the LD₅₀/10 (from Step 5) is lower than the lowest reproductive endpoint, then use the LD₅₀/10 as the endpoint for the Tier 1 reproductive assessment. Otherwise, use the lowest reproductive endpoint. Proceed to Step 6.

Step 6

Identify the appropriate crop and **generic focal bird species** in Annex I. Where more than one generic focal species is relevant for the crop, the one that is relevant in terms of time of application or growth stage should be selected. Where there is more than one generic focal species in terms of timing etc. Tier 1 risk assessments (and refined assessments, if necessary) should be carried out for all the relevant generic focal species.

Step 7

For each relevant generic focal species, calculate the daily dietary dose (DDD):

$$DDD = \text{application rate} \times \text{shortcut value} \times TWA \times MAF_m$$

The relevant shortcut value (based on mean residues) for each generic focal species should be obtained from the tables in Annex I.

If multiple applications are to be made, then Table 11 (see Step 3 above) should be consulted and the appropriate ‘multiple application factor’ or MAF_m should be used.

The value to be used for the time-weighted average factor (TWA) depends on whether the toxicity endpoint from Step 2 could be caused by a short-term exposure (STE) or only by a long-term exposure (LTE)³⁰.

- If the toxic effect is considered to be caused by LTE, use TWA = 0.53 (estimates time-weighted exposure over 21 days, assuming a default DT50 of 10 days).
- If the toxic effect is considered to be caused by STE, use TWA = 1 (one day exposure).

²⁹ The geometric mean of LD₅₀s across species is used in the acute risk assessment. It is intended to investigate further whether the geometric mean is also suitable for use in reproductive risk assessment. Until further guidance is developed, the most sensitive species should be used in the reproductive assessment (see section 2.3.1).

³⁰ It is intended to develop further guidance on criteria for determining which effects could be caused by short-term exposures. Until such guidance is available, it should be assumed as a default that the effects are caused by LTE, unless there is specific evidence for the pesticide under assessment that the effect could be caused by STE.

Step 8

For each relevant generic focal species, calculate the toxicity-exposure-ratio and compare the TER to the respective trigger value.

$$TER = \frac{\text{lowest endpoint (Step 5)}}{\text{relevant DDD (Step 7)}}$$

TER ≥ 5 **No further assessment required for this generic focal species**

TER < 5 **Refined assessment required for this generic focal species – go to Step 9**

Step 9

Refinement options

Refined assessments should be carried out for all generic focal species that have a TER < 5 at Step 8.

Outlined below is a summary of selected options for refinement steps that can be used individually or combined together. Before considering any of the following refinement steps it is important to take account of the general principles for refinement steps in higher-tier risk assessment (section 6), and in particular to ensure that the likely level of protection resulting from a refined risk assessment reflects the expectations of the risk manager.

Re-assessment of the exposure period relevant to the toxicity endpoints. – The screening and Tier 1 assessments use time-weighted averages over 21 days, except where there is specific evidence that the effects could be caused by short-term exposures. The default periods of 21 days for long-term effects and 1 day for short-term effects are arbitrary choices without specific scientific justification. In refined assessments the evidence for the exposure period relevant to each endpoint should be reviewed in more detail. See Appendix J for more information.

Refine the residue element of the initial DDD calculation. – For this, data are required on either the initial residue values and/or the residue decline. Details regarding refining the risk using specific residue data are provided in Appendix J and the respective refinement section (6.1.4) of this Guidance Document.

Refine ecological parameters. – It is possible to refine the DDD by using more relevant data on the ecological components of the risk assessment, i.e. focal species (FS), proportion of an animal's daily diet obtained in habitat treated with pesticide (PT) and composition of diet obtained from treated area (PD) (see sections 6.1.3, 6.1.5 and 6.1.6).

Phase-specific risk assessment. – The screening and Tier 1 assessments do not distinguish between different phases of reproduction. In reality, different phases of reproduction may differ both in their exposure and their toxicological sensitivity to the pesticide. Furthermore, only a proportion of birds will be exposed and, for those that are exposed, the peak exposure may not occur during the most sensitive reproductive phase. These factors may be addressed by phase-specific risk assessment. To gain the full benefits of this approach requires detailed data that may not be available in some cases (e.g. time of application of the pesticide, time of breeding phases for focal species etc). However, the phase specific approach may be an effective approach if these data are available. For further information see Appendix J.

Field trials. – Theoretically, it is possible to carry out a field study to assess the potential effects on reproduction. However, from a practical point of view, this refinement step is not really viable for avian reproduction (see section 6.4).

Population modelling. – If, despite the above refinements, there is still concern regarding the risk to birds, then one option would be to assess the risk at the population level. Unfortunately there are no population models that can be readily used or adapted for use in pesticide risk assessment. This should not, however, preclude their use. Possible examples of population models are presented in Topping et al. (2005), Sibly et al. (2005), Roelofs et al. (2005) and Wang and Grimm (2007). It should be noted that the models included in these references are not endorsed but are provided as an indication of the types of studies that are available. Due to the complexity of this issue, it is envisaged that each assessment would be on a case-by-case basis. For further discussion of assessing population level effects, see section 6.7.

Modified toxicity studies. – If the substance under consideration ‘passes’ the assessment assuming that the effects are the result of long-term exposure, but ‘fails’ if it is assumed that effects are the result of short-term exposure, then it may be possible to carry out further toxicity studies to determine if effects are due to short or long-term exposure. It should be noted that due to animal welfare reasons, this refinement step should only be used if the above exposure orientated refinements have not provided sufficient information to identify an ‘acceptable’ TER.

4.4. Module 4: Reproductive risk assessment for mammals

A mammalian reproductive risk assessment is not necessary if it can be demonstrated that exposure will not occur during the breeding season. If exposure is possible then a risk assessment is required.

Screening assessment

The screening assessment may be useful to identify quickly those substances that pose very low reproductive risk, for which more detailed assessment is unnecessary. If preferred, assessors may proceed directly to Tier 1 (Step 5).

Step 1

Determine if breeding mammals could be exposed to either the active substance or the associated product. If not, no further assessment is required.

Step 2

If exposure is possible, then the same endpoint as in the human risk assessment should be used (without the assessment factor applied as part of the human risk assessment³¹). If the endpoint is in ppm or mg a.s./kg bw then Table 2 should be used to convert the endpoint to a daily dose, or mg a.s./kg bw/d.

Step 3

Identify the appropriate indicator species and shortcut value for the crop under assessment from Table 12. If multiple applications are to be made, then Table 13 should be consulted and the appropriate ‘multiple application factor’ or MAF_m should be used. Calculate the daily dietary dose (DDD):

$$DDD = \text{application rate} \times \text{shortcut value} \times TWA \times MAF_m$$

³¹ The standard Annex VI trigger value of 5 should be used for the non-target mammal assessment (see Step 4).

The value to be used for the time-weighted average factor (TWA) depends on whether the toxicity endpoint from Step 2 could be caused by a short-term exposure (STE) or only by a long-term exposure (LTE)³².

- If the toxic effect is considered to be caused by LTE, use TWA = 0.53 (estimates time-weighted exposure over 21 days, assuming a default DT₅₀ of 10 days).
- If the toxic effect is considered to be caused by STE, use TWA = 1 (one day exposure).

Table 12. Indicator species and shortcut values (based on mean residues) for the mammalian reproductive assessment.

Crop	Indicator species	Shortcut value for reproductive assessment
Bare soil	Small granivorous mammal	6.6
Bush and cane fruit	Small herbivorous mammal	43.4
Bulbs and onion like crops, cereals, oilseed rape, potatoes, root and stem vegetables, strawberries, sugar beet, and sunflower	Small herbivorous mammal	48.3
Cotton, fruiting vegetables, grassland, leafy vegetables, legume forage, maize, orchards, ornamentals/nursery, pulses, and vineyard	Small herbivorous mammal	72.3

Table 13. Multiple application factors assuming mean residues (MAF_m), for use in reproductive assessments.

MAF_m are shown for selected application intervals and $n = 1-8$ applications, assuming a default DT₅₀ of 10 d on foliage. MAF_m values for other application intervals can be either calculated either using the formula in Appendix H or using the values for the next lower application interval. The limit value in the rightmost column should be used for higher numbers of applications with one of the tabulated intervals. These MAF factors should be used for all food types (i.e. arthropods and vegetation). Further information on this issue is provided in Appendix H.

Application interval (d)	MAF _m for n applications								
	$n = 1$	2	3	4	5	6	7	8	Limit
7	1.0	1.6	2.0	2.2	2.4	2.5	2.5	2.5	2.6
10	1.0	1.5	1.8	1.9	1.9	2.0	2.0	2.0	2.0
14	1.0	1.4	1.5	1.6	1.6	1.6	1.6	1.6	1.6

³² It is intended to develop further guidance on criteria for determining which effects could be caused by short-term exposures. The Joint Working Group decided that, until such guidance is available, it should be assumed as a default that the effects are caused by LTE, unless there is specific evidence for the pesticide under assessment that the effect could be caused by STE.

Step 4

Calculate the toxicity-exposure-ratio and compare the TER to the respective trigger value.

$$TER = \frac{\text{lowest endpoint (Step 2)}}{\text{relevant } DDD \text{ (Step 3)}}$$

TER ≥ 5

No further assessment required

TER < 5

Go to Tier 1 (Step 5)

Tier 1 risk assessment

All pesticides should be subjected to Tier 1 assessment, unless they are shown by a screening assessment (Steps 1-4) 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.

Step 5

Identify the endpoint from the developmental study that is used in the human risk assessment. Check if the developmental study contained lower endpoints that were considered rodent-specific and, if so, take the lowest of these instead of the endpoint used for human risk assessment.

Identify the lowest NOAEL from the 2-generation rat study³³. If there is no 2-generation rat study, identify the lowest NOAEL from the extended 1-generation rat study.

Note that relevant rodent-specific endpoints should not be disregarded (as they are in human risk assessment).

Endpoints that are presented as ppm diet or mg a.s./kg diet must be converted to daily doses, i.e. mg a.s./kg bw/d. At Tier 1, this should be done using the actual body weight and food consumption data from the study under consideration. In order to do this, take the mean value for food consumption over the whole study and average body weight over the duration of the study at the NOAEL and use these figures to convert the NOAEL to a daily dose.

If the lowest relevant endpoint from the developmental study is lower than the lowest endpoint from the 2-generation rat study, then use the developmental study endpoint as the endpoint for the Tier 1 reproductive assessment. Otherwise, use the lowest relevant endpoint from the 2-generation rat study. Proceed to Step 6.

Step 6

Identify the appropriate crop and **generic focal mammal species** in Annex I. Where more than one generic focal species is relevant for the crop, the one that is relevant in terms of time of application or growth stage should be selected. Where there is more than one generic focal species in terms of timing etc., Tier 1 risk assessments (and refined assessments, if necessary) should be carried out for all the relevant generic focal species.

³³ The lowest endpoint is taken to avoid the need for detailed re-evaluation of the mammalian studies in Tier 1 of the ecotoxicological assessment. The relevance of the endpoints for wild mammals may be reconsidered as a refinement option (see Step 9).

study (or merged dataset, where it is appropriate to merge studies, see section 2.4.3) the endpoints that are considered relevant for reproductive performance, as listed below³⁵:

- NOAEL for body weight change³⁶, behavioural effects and systemic toxicity;³⁷
- NOAEL for indices of gestation, litter size, pup and litter weight;³⁸
- NOAEL for indices of viability, pre- and post-implantation loss;
- NOAEL for embryo/foetal toxicity including teratological effects;
- NOAEL for number aborting and number delivering early;
- NOAEL for systemic toxicity and effects on adult body weight;
- NOAEL for indices of post-natal growth³⁹, indices of lactation and data on physical landmarks;
- NOAEL for survival and general toxicity up to sexual maturity.

Effects on other endpoints are considered not relevant for reproductive performance and may be disregarded.

Note that slight delays, e.g. 1 day, in obtaining a particular endpoint or developmental milestone can be ignored. However, longer delays could be considered as adverse effect. This is based on the frequency of measuring and hence is a pragmatic approach. Note that a 1-d delay may be of importance for certain substances. It should be checked that this is not treatment related before discounting it. Further discussion of the ecological relevance of test endpoints for wild mammals may be found in Appendix J and EFSA (2006).

Examination of additional mammalian toxicity studies. – The Tier 1 assessment concentrates on endpoints from the 2-generation rat study and the developmental study. In refined assessments it is desirable also to examine other mammalian toxicity studies to check whether they contain lower NOAELs for relevant endpoints. The lowest relevant NOAEL should be used for assessment⁴⁰.

Re-assessment of the exposure period relevant to the toxicity endpoints. – The screening and Tier 1 assessments use time-weighted averages over 21 days, except where there is specific evidence that the effects could be caused by short-term exposures. The default periods of 21 days for long-term effects and 1 day for short-term effects are arbitrary choices without specific scientific justification. In refined assessments the evidence for the exposure period relevant to each endpoint should be reviewed in more detail, in consultation with a mammalian toxicologist. See Appendix J for more information.

Refine the residue element of the initial DDD calculation. – To do this, data are required on either the initial residue values or/and the residue decline. Details regarding refining the risk using specific residue data are provided in section 6.1.4.

³⁵ For information on why these endpoints are considered relevant, see Appendix J.

³⁶ This is included as an indicator of parental effects with potential to disrupt reproduction. It is considered in the reproductive assessment for mammals but not for birds, where LD₅₀/10 is used instead.

³⁷ 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).

³⁸ 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.

³⁹ 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.

⁴⁰ The geometric mean of LD₅₀s across species is used in the acute risk assessment. It is intended to investigate further whether the geometric mean is also suitable for use in reproductive risk assessment. Until further guidance is developed, the most sensitive species should be used in the reproductive assessment (see section 2.3.1).

Refine ecological parameters. – It is possible to refine the DDD by using more relevant data on the ecological components of the risk assessment, i.e. focal species (FS), proportion of an animal's daily diet obtained in habitat treated with pesticide (PT) and composition of diet obtained from treated area (PD) (see sections 6.1.3, 6.1.5 and 6.1.6).

Phase-specific risk assessment. – The screening and Tier 1 assessments do not distinguish between different phases of reproduction. In reality, different phases of reproduction may differ both in their exposure and their toxicological sensitivity to the pesticide. Furthermore, only a proportion of mammals will be exposed and, for those that are exposed, the peak exposure may not occur during the most sensitive reproductive phase. These factors may be addressed by phase-specific risk assessment. To gain the full benefits of this approach requires detailed data that may not be available in many cases (e.g. time of application of the pesticide, time of breeding phases for focal species etc.). However, the phase specific approach may be an effective approach if these data are available. For further information see Appendix J.

Field trials. – Effects on reproduction for small mammals may be studied by using capture-mark-release-recapture techniques to monitor population density and age structure (see section 6.4).

Population modelling. – If, despite the above refinements, there is still concern regarding the risk to mammals, then one option would be to assess the risk at the population level. Unfortunately, there are no population models that can be readily used or adapted for use in pesticide risk assessment. Existing possible examples of population models are presented in Topping et al. (2005), Sibly et al. (2005), Roelofs et al. (2005) and Wang and Grimm (2007). It should be noted that the models included in these references are not endorsed but are provided as an indication of the types of studies that are available. Due to the complexity of this issue, it is envisaged that each assessment would be on a case-by-case basis. For further discussion of assessing population-level effects, see section 6.7.

5. Special topics

5.1. Risk assessment for granular formulations

The following approach for assessing the risk for granular formulations is closely based on the method presented in EPPO/OEPP (2003) and the method presented in the fosthiazate opinion of the Scientific Committee on Plants (SCP, 2002).

It is possible that birds and mammals may be exposed to granules in different ways:

- a) Birds and mammals may ingest granules as a source of food.
- b) Birds may ingest granules as grit.
- c) Birds may mistake granules for small seed.
- d) Birds and mammals may ingest granules when they eat food contaminated with soil.
- e) Birds and mammals may consume food contaminated with residues resulting from granular applications.

Assessments for these are addressed in sections 5.1.1 - 5.1.5. It is important that all relevant routes are considered. In addition, route b) above should also be considered for pelleted seeds.

During the development of the granule risk assessment scheme it became apparent that birds, predominately dabbling ducks, may be at risk from dabbling in puddles⁴¹ that have formed on slow- or

⁴¹ Since at least the early 1970s, pesticide poisoning from granular insecticide formulations has been documented as an important cause of wildlife mortality in British Columbia, Canada. Incidents have occurred where it would appear that waterfowl, primarily dabbling ducks (family *Anatinae*), have foraged extensively in puddles that have formed in slow-draining agricultural fields during autumn and winter following the application of the pesticide to potatoes and other root

poorly drained fields recently treated with granules. This scenario is relatively rare, but has caused incidents in the past. Ideally this scenario should be assessed if conditions similar to those that caused previous incidents are likely to occur. It should be noted that this scenario is due to the correct use of substances and cannot be attributed to misuse. Unfortunately, due to a lack of information, it has not been possible to develop a risk assessment for this scenario.

An animal visiting a field treated with granules might be exposed via several routes in the same period of time, e.g. by ingesting granules and through drinking water. In principle, it would be logical to combine such exposures by adding them together (SCP, 2002). If this is done, account should be taken of the probability of each combination of routes occurring for the same individual. In practice, this will be very uncertain. A practical solution to this would be to estimate total exposure for each plausible combination of routes. If any combination raised a concern, then the risk assessor together with the risk manager could decide to require new data to confirm/refute the concern, or to accept the additional risk if the concern was not very high, and/or the probability of the combination was likely to be low (provided the individual routes were not of concern when considered separately).

Assessing the exposure of birds to granules presents special difficulties. Scientific knowledge in this area has continued to develop since the presentation of the first decision-making sub-scheme for the environmental risk assessment of plant protection products for terrestrial vertebrates by the OEPP/EPPO in 1994 (ECOFRAM, 1999; SCP, 2002; Luttik, 2003; OEPP/EPPO 2003; Luttik and de Snoo, 2004).

5.1.1. Animals ingesting granules as source of food

If there is a possibility that birds and mammals will mistake granules for food (e.g. in the case of granular products formulated on corncob carrier, carriers to which oil is added or carriers having some calorific value), it is appropriate to run the same procedure as for contaminated food (e.g. oversprayed). For this type of assessment it is necessary to know the caloric value of the granular material. With this value and the daily caloric demand of a bird or mammal of concern, the amount of granules and therefore the amount of active substance can be calculated to which the animal will be exposed. Species of concern, appropriate for the first-tier assessment are an omnivorous bird (e.g. house sparrow of 27.7 g) and an omnivorous mammal (e.g. wood mouse of 21.7 g).

5.1.2. Birds ingesting granules with/as grit

Grit consumption by farmland birds is an important constituent of dietary intake both for mineral content and mastication (Best and Gionfriddo, 1994). Significant differences exist between granivorous and non-granivorous species with respect to the size of grit ingested, with non-granivorous generally taking in grit indiscriminately with soil particles, while granivorous species pick up grit particles selectively (Luttik and de Snoo, 2004). Accordingly, the type of soil and its constituent composition can substantially influence the extent to which birds may be exposed to granular products. For seed-eating birds, e.g. finches, pigeons, partridges and pheasants that need grit

crops. In the wet highly acidic soils of the delta, granular formulations have been found to persist for several months beyond projected post application intervals (Wilson et al., 2002). A review of incident cases elsewhere, e.g. kills of waterfowl in US rice fields, suggests that these conditions may not be unique (Mineau, 1993). It is thought that waterfowl may be exposed through drinking from these puddles as well as when they are sifting through the saturated sediments for food. Granules appear to have the right size to be retained by the bill lamellae and they are ingested along with weed seeds, debris and grit. Raptors and other scavengers in turn are poisoned by the insecticides after scavenging on dead or dying waterfowl that have consumed the granules. The majority of raptors poisoned by anti-cholinesterase pesticides in the Fraser Delta have waterfowl remains in their ingesta. A few poisoned waterfowl carcasses can attract large numbers of scavengers (Peterson et al., 2001). All available information suggests that the poisonings are not the result of poor use, or misuse, and that a solution to the problem does not reside with a more careful use of the granular products but, rather, with choosing products of lower toxicity.

for mastication of their food, the method for assessing the potential risk for the ingestion of granules follows the method proposed in the OEPP/EPPO (2003).

Acute risk assessment

Step 1

Calculate the acute daily grit dose ($DGritD_{acute}$)⁴² for small and large granules.

$$DGritD_{acute} \text{ (small granules)}^{43} = 651 \times \frac{G_{density}}{(15200 + G_{density})} \times G_{loading}$$

$$DGritD_{acute} \text{ (large granules)}^{44} = 2453 \times \frac{G_{density}}{(71 + G_{density})} \times G_{loading}$$

With:

$G_{density}$ = number of granules on soil surface (this number should be based on real practice and not on theoretical incorporation efficiencies; see Appendix 21 of EFSA, 2008)

$G_{loading}$ = the amount of the active substance in one granule

Step 2

Take the appropriate LD_{50} value (see section 2).

Step 3

Calculate the toxicity-exposure ratio for the relevant granule size and compare the TER to the respective trigger value.

$$TER_{acute} = \frac{LD_{50}}{DGritD_{acute}}$$

$TER_{acute} > 10$

No refined acute risk assessment required

$TER_{acute} \leq 10$

Refined acute risk assessment required

Reproductive risk assessment

It is acknowledged that granules will only be present on a soil surface for a short time; however, reproductive RA is still required as there may be a long-term effect due to short-term exposure. The methodology outlined in section 4 should be followed. The initial exposure estimates should be based on the concentration in the granule. Where a TWA approach is required the degradation/dissipation of the active substance of the granule will be necessary.

⁴² See note 1 in section 5.1.6.

⁴³ Size of small granules: between 0.75 and 2 mm.

⁴⁴ Size of large granules: between 2 and 6 mm.

Step 4

Calculate the daily grit dose ($DGritD_{repro}$)⁴⁵ for small and large granules for reproductive risk assessment.⁴⁶

$$DGritD_{repro} \text{ (for small granules)} = 386 \times \frac{G_{density}}{(15200 + G_{density})} \times G_{loading}$$

$$DGritD_{repro} \text{ (for large granules)} = 1306 \times \frac{G_{density}}{(71 + G_{density})} \times G_{loading}$$

When sufficient information is available, apply a time-weighted average (TWA) correction for the number of granules and for the active substance.⁴⁷

Step 5

Take the appropriate NOAEL (mg/kg bw/d) (see section 4.3 and 2.3.1).

Step 6

Calculate the toxicity-exposure ratio for the relevant granule size and compare the TER to the respective trigger value.

$$TER_{repro} = \frac{NOAEL}{DGritD_{repro}}$$

TER_{repro} > 5

No refined reproductive risk assessment required

TER_{repro} ≤ 5

Refined reproductive risk assessment required

Steps 4–6 must be repeated for each relevant reproductive endpoint and associated time of exposure (see section 4.3 and Appendix J).

5.1.3. Birds ingesting granules when seeking seeds as food

If it appears possible that the granules could be mistaken for weed seeds by seed-eating birds⁴⁸, then the granules should be assessed using the method described previously in the opinion of the Scientific Committee on Plants on fosthiazate (SCP, 2002). The potential risk can be illustrated by estimating a TER in a manner analogous to that used for ingestion of granules accidentally as part of soil ingestion, i.e. by assuming that granules and seeds are ingested in proportion to their availability.

⁴⁵ See note 1 of section 5.1.6.

⁴⁶ The number of soil particles is based on three samples from three Dutch soils, two sands and one clay. If appropriate, replace these numbers with data for other soils. This should be done in the case of applications to peaty soils as they probably have lower grit estimates (see SCP, 2002: estimated density of available for 0.5–0.85-mm grit particles is approximately 5000 per square meter).

⁴⁷ See note 3 of section 5.1.6.

⁴⁸ There are no indications available that mammals do forage on small seeds.

Acute risk assessment

Step 1

Calculate the acute daily granule dose (DGD_{acute}) for a small granivorous bird.⁴⁹

$$DGD_{acute} = 620 \times \frac{G_{density}}{(100 + G_{density})} \times G_{loading}$$

With:

$G_{density}$ = number of granules on soil surface

$G_{loading}$ = the amount of the active substance in one granule

Step 2

Take the appropriate LD_{50} (mg/kg bw/d) for birds (see section 2).

Step 3

Calculate the acute toxicity-exposure ratio and compare the TER to the respective trigger value.

$$TER_{acute} = \frac{LD_{50}}{DGD_{acute}}$$

$TER_{acute} > 10$

No refined acute risk assessment necessary

$TER_{acute} \leq 10$

Refined acute risk assessment necessary

Reproductive risk assessment

It is acknowledged that granules will only be present on a soil surface for a short time; however, reproductive RA is still required as there may be a long-term effect due to short-term exposure. The methodology outlined in section 3 should be followed. The initial exposure estimates should be based on the concentration in the granule. If a TWA approach is required, then the degradation/dissipation of the active substance of the granule will be necessary.

Step 4

Calculate the daily granule dose (DGD_{repro}) for a small granivorous bird for the reproductive risk assessment (see note 4 of section 5.1.6).

$$DGD_{repro} = 620 \times \frac{G_{density}}{(100 + G_{density})} \times G_{loading}$$

When sufficient information is available, apply a time-weighted average (TWA) correction for the number of granules and for the active substance (see note 3 of section 5.1.6).

⁴⁹ See note 4 of section 5.1.6.

Step 5

Take the appropriate NOAEL (mg/kg bw/d) (see sections 4.3 and 2.3.1).

Step 6

Calculate the toxicity-exposure-ratio and compare the TER to the respective trigger value:

$$TER_{\text{repro}} = \frac{NOAEL}{DGD_{\text{repro}}}$$

$TER_{\text{repro}} > 5$

No refined reproductive risk assessment required

$TER_{\text{repro}} \leq 5$

Refined risk assessment for chronic exposure required

Steps 4–6 must be repeated for each relevant reproductive endpoint and associated time of exposure (see section 4.3).

5.1.4. Animals ingesting granules when eating soil-contaminated food

The method for assessing the potential risk for birds and mammals exposed to granules as part of ingested soil when seeking food follows the one proposed in the EPPO scheme of 2003 (OEPP/EPPO, 2003).

Acute risk assessment

Step 1

Calculate the acute daily dry soil dose (DDSD_{acute}) for a small omnivorous bird and mammal⁵⁰.

$$DDSD_{\text{acute}} \text{ for mammal} = 0.097 \times \text{dosage [kg a.s./ha].}$$

$$DDSD_{\text{acute}} \text{ for bird} = 0.283 \times \text{dosage [kg a.s./ha].}$$

Step 2

Take the appropriate LD₅₀ value (see section 2).

Step 3

Calculate the acute toxicity-exposure ratios and compare the TERs to the respective trigger values:

$$TER_{\text{acute}} = \frac{LD_{50}}{DDSD_{\text{acute}}}$$

$TER_{\text{acute}} > 10$

No refined acute risk assessment required

$TER_{\text{acute}} \leq 10$

Refined acute risk assessment required

⁵⁰ See note 5 of section 5.1.6.

Reproductive risk assessment

It is acknowledged that granules will only be present on a soil surface for a short time. However, reproductive RA is still required as there may be a long-term effect due to short term exposure. The methodology outlined in section 3 should be followed. The initial exposure estimates should be based on the concentration in the granule. If a TWA approach is required the degradation/dissipation of the active substance of the granule will be necessary.

Step 4

Calculate the daily dry soil dose ($DDSD_{\text{repro}}$) for the reproductive risk assessment for a small omnivorous bird and mammal⁵¹.

$$DDSD_{\text{repro}} \text{ for mammals} = 0.005 \times \text{dosage in kg a.s./ha.}$$

$$DDSD_{\text{repro}} \text{ for birds} = 0.025 \times \text{dosage in kg a.s./ha.}$$

When sufficient information is available, apply a time-weighted average (TWA) correction for the active substance.⁵²

Step 5

Take the appropriate NOAEL (mg/kg bw/d), described in section 4.4 and 2.3.1.

Step 6

Calculate the toxicity-exposure ratios for mammals and birds and compare the TERs to the respective trigger values:

$$TER_{\text{repro}} = \frac{NOAEL}{DDSD_{\text{repro}}}$$

$TER_{\text{repro}} > 5$

No refined reproductive risk assessment required

$TER_{\text{repro}} \leq 5$

Refined reproductive risk assessment required

Steps 4–6 must be repeated for each relevant reproductive endpoint and associated time of exposure (see sections 4.3 and 4.4).

5.1.5. Animals consuming other food items with residues from granular applications

At present, no standardised schemes are available for assessing the risk of residues of granular formulations in other food items such as earthworms and plant seedlings. This is mainly due to the lack of transfer factors for calculating concentrations in the food items for birds and mammals, e.g. transferring the load of granules to a concentration in the earthworm and the seedling.

If it is expected that the substance will be taken up by the worm via the pore water, the same route should be followed as for bioaccumulation. If it is expected that the substance will be taken up via seedlings, e.g. systemic substances, the same risk assessment method as for oversprayed food items should be applied (see section 4.1). Appropriate generic focal species are a 28.5-g lark and a 21.7-g mouse.

⁵¹ See note 5 of section 5.1.6.

⁵² See note 3 of section 5.1.6.

No standardised scheme is available for assessing the possible exposure of birds and mammals to granules adhered to the surface of worms. This is a route of exposure, which has caused poisoning incidents in the past and should therefore be considered in every case. Again, the same approach could be used as for oversprayed food items. This will require information on the number of adhered granules or the load of active substance per g of earthworm. Appropriate species of concern for earthworm-eating birds and mammals are a 10-g shrew and a 100-g thrush.

As described in section 4.1, the ‘daily dietary dose’ (DDD) is defined by the food intake rate (FIR) and the body weight (bw) of the species of concern. FIR/bw values for the generic focal species are provided in Table 14. The risk for these generic bird and mammal species can be calculated by dividing the appropriate toxicity value [mg/kg bw] by the FIR/bw value multiplied by the concentration of the compound in the plant or on the earthworm [mg/kg food].

Table 14. FIR/bw values for generic focal species exposed to pesticide residues via ingestion of plant seedlings or by granules sticking to earthworms.

Generic focal species	Food	FIR/bw	Body weight bw [g]	Daily energy expenditure DEE [kJ]	Food energy FE [kJ]	Moisture content MC (%)	Assimilation efficiency AE (%)
Shrew	earthworms	1.34	10	33.8	19.3	84.6	85
Thrush	earthworms	0.96	100	242	19.3	84.6	85
Lark	leaves	2.26	28.5	104	17.8	88.1	76
Mouse	leaves	1.68	21.7	58.8	17.8	88.1	76

5.1.6. Explanatory notes to risk assessment for granules

Note 1. Selection of input parameters for exposure scenarios (ingestion of granules as part of grit ingestion).

Table 15 gives estimations for acute and reproductive risk assessment scenarios for a small generic bird (e.g. finches) and a large bird (e.g. partridge or woodpigeon).

Table 15. Estimation of input parameters for acute reproductive risk assessment for birds ingesting granules intentionally when seeking grit.

Exposure duration	Size of birds	Number of grit per day (DGritI)	Number of soil particles (SP _{surface})	f _{TWA} for number of granules	f _{TWA} for the active substance
Acute exposure	Large	2453	71	No	No
	Small	651	15200	No	No
Long-term exposure	Large	1306	71	Yes	Yes
	Small	386	15200	Yes	Yes

It is assumed in the assessment that small granules (size between 0.75 and 2 mm) are taken by small birds (e.g. finches) and that large granules (size between 2 and 6 mm) are taken by large birds (e.g. partridge and wood pigeon).

The acute exposure scenario (90th percentile) and reproductive scenario (geometric mean) estimates of the numbers of grit particles in the gizzards of a small and a large bird are based on research carried

out by de Leeuw et al. (1995). For small birds, data on six European, predominantly granivorous species were available. Greenfinch had 95 grit particles in the gizzard, chaffinch 65, linnet 100, twite 122, brambling 188 and goldfinch 43 (mean values). The geometric mean is 92 and the 90th percentile is 155 grit particles. For larger birds data on three species were available. The grey partridge had 676, woodpigeon 208 and pheasant 214 particles (geometric mean 311 and 90th percentile 584). To convert these gizzard counts into a daily intake, a conversion factor of 4.2 is used (see note 2). Sensitivity or influence is based on incorporation efficiency.

For the number of soil particles in the same size classes as the granules (i.e. 0.75 to 1.5 mm and 2 to 6 mm) the geometric mean of three Dutch soils have been used as default (Luttik and de Snoo, 2004). On average (geometric) 15200 soil particles of the size 0.75 to 1.5 mm can be found per m² and 71 soil particles of the size 2 to 6 mm.

The daily grit dose (DGritD) can be calculated with the following equation:

$$\text{DGritD} = \text{DGritI} \times \left(\frac{G_{\text{density}}}{SP_{\text{surface}} + G_{\text{density}}} \right) \times G_{\text{loading}} [\text{mg/kg/bw/d}]$$

In which:

- DGritI = daily grit intake of birds
- G_{density} = number of granules at soil surface
- SP_{surface} = number of soil particles at soil surface in the same size classes as granules
- G_{loading} = the amount of the active substance in one granule.

In the first-tier assessment it is assumed that the birds will obtain their entire daily granule dose (DGritD) from the treated area (PT = 1), lower values could be used when appropriate in higher tier assessments. In the reproductive risk assessment it is appropriate to include time weighted average factors (TWA); one for the decline in numbers of granules over time and one for the degradation of the active substance (see note 3).

The estimate of soil particle density is based on just one sample from each of three Dutch soils, one clay and two sands, which would be expected to have relatively high grit contents. Peaty soils contain much less grit and would therefore lead to a higher estimate of daily granule dose. Therefore, if granules may be used on peaty soils and peaty soils are considered as relevant in agriculture, data on grit densities on relevant soils should be obtained and used to modify the assessment calculations. Even for clay and sandy soils, it would be desirable to base the assessment on larger numbers of samples; however, these are currently not available.

Note 2. Grit turnover rate

On basis of Fischer and Best (1995), a 4.2 conversion factor will be used to take account for the turnover rate of grit. It should be noted that this value is only based on one experimental design using only one species. Further, the blank silica granules were intermixed with dog food and there was a great deal of scatter in the data depicting the relationship between granule consumption and gizzard granule counts.

Additional research is needed to validate the general applicability of using a conversion factor and to determine the degree to which such a factor may vary among species and under different environmental conditions.

Note 3. Time weighted average factors (f_{TWA})

In the reproductive risk assessments it is appropriate to use time weighted average residues rather than initial residues. The time weighted average factor (f_{TWA}) depends on the half-life of the compound or the half-life of the granules:

$$f_{TWA} = \frac{1 - e^{-kt}}{kt}$$

With:

$$k = \ln 2 / DT_{50}$$

$$t = \text{averaging time in days}$$

Note 4. Selection of input parameters for exposure scenarios (ingestion of granules as part of seed ingestion)

Granules are often smaller than most seeds taken by birds but are of comparable size to some of the smaller seeds of arable weeds e.g. *Stellaria media*, *Capsella bursa-pastoris*, *Veronica arvensis* and *Urtica dioica*. Some of these (e.g. *Stellaria*, *Capsella*) are among the plant species most commonly taken by birds. Plant groups known to be important in the diet of the seed-eating linnet include Polygonaceae, Chenopodiaceae, Gramineae, Caryophyllaceae, Cruciferae, and Compositae. It is therefore possible that granules may be ingested by birds searching for seeds as food.

Studies on UK arable fields show varying densities of crop and weed seeds up to about 20,000/m², based on soil cores to a depth of 20 cm (Jones, 1998; Jones and Maulden, 1999; Jones *et al.*, 1997). It is assumed that seeds taken by small birds average about 1 mm diameter and are therefore visible to birds only if they are contained in the top 1 mm of soil. Ploughing is intended to invert the soil and has been shown to bury over 90 % of new seeds from the surface to a depth of 5 cm or more, but additional ploughing in successive years tends to redistribute surviving seeds more evenly (Moss, 1998). Therefore, a uniform distribution of seeds is assumed in the top 20 cm, and 20000 seeds/m² in the top 20 cm would correspond to about 100 seeds/m² in the top 1 mm.

It is assumed that a linnet of 15.3 g will eat small seeds with an average caloric content of 21.7 kJ/g dry weight, an average water content of 9.9 % and an average assimilation efficiency of 80 % for birds. Based on allometric equations for dry food intake (see Appendix G) and an estimated moisture content of 9.9 %, a 15.3 g linnet would require 4.35 g/day or about 620 seeds per day (based on an average weight for canary seeds of 7 mg).

If the generic species is adequate for carrying out the first-tier risk assessment, the daily granule dose (DGD) can be calculated by using the following equation:

$$DGD = DGI \times G_{\text{loading}}$$

$$DGI = 620 \times \left(\frac{G_{\text{density}}}{100 + G_{\text{density}}} \right)$$

In which:

DGI = daily granule intake

G_{density} = density of granules at surface (including incorporation efficiency when the product label recommends incorporation of granules)

$G_{\text{loading}} =$ amount of active substance in one granule

In the first-tier assessment it is assumed that the birds will obtain their entire daily granule dose (DGD) from the treated area ($PT = 1$), lower values could be used when appropriate in higher tier assessments. In the reproductive risk assessment it is appropriate to include time weighted average factors (TWA): one for the decline in numbers of granules over time and one for the degradation of the active substance (see note 3).

Note 5. *Selection of input parameters for exposure scenarios (ingestion of granules as part of soil ingestion)*

Table 16 gives estimations for the acute and reproductive risk assessment scenarios for a generic bird and mammalian omnivorous species of 25 g. It is assumed that the animals will eat equal parts on dry weight consisting of non-grass herbs, insects and seeds with a caloric content of 17.8, 22.7 and 21.7 kJ/g dry weight respectively, and an assimilation efficiency of 76, 76 and 80 % for birds and 74, 88 and 83 % for mammals.

Table 16. Estimation of shortcut values for acute and long-term exposure via contaminated soil for a generic bird and mammalian omnivorous species of 25 g.

Exposure duration	Species	Daily Dry Food Intake (DDFI) [g kg ⁻¹ bw d ⁻¹]	% of soil in diet	Daily Dry Soil Intake (DDSI) [g kg ⁻¹ bw d ⁻¹]	RUD [mg/kg dry soil]	Shortcut value
Acute	Mammal	153	9.4	14.5	6.667	0.097
	Bird	236	18	42.5	6.667	0.283
Long-term	Mammal	153	3.8	5.8	1.333	$0.005 \times f_{\text{TWA}}$
	Bird	236	7.9	18.6	1.333	$0.025 \times f_{\text{TWA}}$

If the generic species are adequate for carrying out the first-tier risk assessment, the daily dry soil dose (DDSD) can be calculated by using the shortcut value(s) for soil ingestion:

$$\text{DDSD} = \text{Shortcut value} \times \text{dosage in kg a.s./ha [mg a.s./kg bw/d]}.$$

The underlying equation for calculating the shortcut value is:

$$\text{Short cut value} = \text{DDSI} \times \frac{\text{RUD}}{1000}$$

In which:

DDSI = Daily dry soil intake of the indicator species [g/kg bw/d]

RUD = Residue unit dose (concentration in soil as a result of an application rate of 1 kg a.s./ha in a soil layer of 1 cm in acute scenario and 5 cm in long-term scenario, see also note 6)

Further:

$$\text{DDSI} = \text{DDFI} \times \frac{\% \text{soil}}{100 - \% \text{soil}}$$

In which:

DDFI = Daily dry food intake of the indicator species [g/kg bw/d]
 %soil = Percentage of dry soil in dry diet of indicator species (see note 7)

And:

$$DDFI = \frac{DEE}{FE} \times \frac{AE}{100} [\text{g dry weight/d}]$$

In which:

DEE = Daily energy expenditure of the indicator species [kJ/d]
 FE = Food energy [kJ/dry g]
 AE = Assimilation efficiency [%]

Mean estimates for factors DEE, FE and AE can be found in Appendix G on food intake.

In the first-tier assessment it is assumed that the birds will obtain their entire daily dry soil dose (DDSD) from the treated area (PT = 1), lower values could be used when appropriate in higher tier assessments. In the reproductive risk assessment it is appropriate to include time weighted average factors (TWA) for the degradation of the active substance (see note 3).

Note 6. Residue per unit dose (RUD) for soil-applied pesticides

The values for RUDs in Table 16 of note 5 are based on an application rate of 1 kg a.s./ha and assuming broadcast seeding (no incorporation). For the acute exposure assessment, it is assumed that the compound is equally mixed in a layer of 1 cm soil, for the long-term exposure it is assumed that the compound is mixed over a layer of 5 cm. If other incorporation depths are specified by the product label, the RUD value and shortcut values for a number of depths are presented in Table 17. The calculations are based on a dry bulk density of 1500 kg/m³.

Note 7. Estimation of soil ingestion by birds and mammals

For acute risk assessment and for reproductive risk assessment it is assumed that respectively the 90th percentile and the geometric mean estimates of the percentages of soil in the daily diet are appropriate to use. These values are based on data collected by Beyer et al. (1994). For mammals the following data are available: <2, <2, <2, <2, <2, <2, 2.3, 2.4, 2.7, 2.8, 5.4, 6.3, 6.8, 7.7, 9.4, 9.4 and 17 % (geometric mean 3.8 % and 90th percentile 9.4 % (17 different species)). For birds data on 11 species are available (no data on passerines): <2, <2, 3.3, 7.3, 8.2, 9.3, 10.4, 11, 17, 18 and 30 % (geometric mean 7.9 % and 90th percentile 18 %). It is important to note that Beyer et al. estimates are expressed as dry weight/dry weight.

Table 17. Shortcut values for different incorporation depths (e.g. 10, 15, 20 and 25 cm).

Exposure duration	Species	RUD mg/kg soil (in layer of x cm)				Shortcut value			
		10 cm	15 cm	20 cm	25 cm	10 cm	15 cm	20 cm	25 cm
Acute	Mammal	0.667	0.444	0.333	0.267	0.010	0.006	0.005	0.004
	Bird	0.667	0.444	0.333	0.267	0.028	0.0191	0.014	0.011
Repro	Mammal	0.667	0.444	0.333	0.267	0.004 × f_{TWA}	0.003 × f_{TWA}	0.002 × f_{TWA}	0.002 × f_{TWA}
	Bird	0.667	0.444	0.333	0.267	0.012 × f_{TWA}	0.008 × f_{TWA}	0.006 × f_{TWA}	0.005 × f_{TWA}

5.1.7. Possible options for refinement

General guidance on refinement and higher-tier assessment is provided in section 6. The following options are most likely to be relevant:

- Avoidance studies in pens (laboratory) with animals that have been grit deprived for a few days and reasonable numbers of available grit and granules (section 6.2).
- Field studies to test for sublethal effects and mortality following application of granules (section 6.4).

In addition to the options described above, specialised field or laboratory studies could be conducted to obtain refined estimates of parameters used in the first-tier calculations like, e.g. the incorporation efficiency or the turnover rate. These studies should be designed to cover the range of values occurring in practice, including a realistic worst case. The results can then be used to carry out revisions of the first-tier exposure calculations.

5.2. Risk assessment for treated seed

Tier 1 assumes that granivorous birds and mammals feed entirely on readily available, freshly treated seeds. The failure rate of pesticides used as seed treatments to meet the standard EU triggers for acute and reproductive risks under such a scenario is likely to be high. Therefore, many cases will require refined assessment. At present, it is not possible to recommend standardised approaches for refined assessment. Therefore, a range of options for refinement are presented.

The outcome of a refined assessment would, in most cases, take the form of a weight-of-evidence approach, rather than a quantitative assessment (e.g. TER). Risk managers will have to decide on whether the evidence provided is sufficient to allow for a decision whether the intended level of protection is reached. Guidance is provided on the method for such a weight-of-evidence approach.

5.2.1. Selection of relevant risk assessment scenarios

Exposure of birds and mammals to pesticides used as seed treatment is primarily via dietary intake. Dermal exposure to seed treatments is unlikely to occur, especially when seeds are incorporated into the soil. Pesticides used as seed treatments are unlikely to be volatile since the protection of the seed would not be long-lasting. Hence, the contribution to exposure of birds and mammals from inhalation of pesticides from treated seeds is considered to be low. Significant contamination of drinking water after the use of a pesticide as seed treatment seems equally unlikely to be a critical route or to lead to TER greater than direct dietary consumption. Therefore, the following risk assessment focuses on the dietary route of exposure.

It should be noted that in early sections of this Guidance Document, the risk assessment process has started with a screening step. In this scheme there is no screening step and the assessment starts at Tier 1.

Pesticides used as seed treatment are normally applied to soils that have been specifically prepared (seed beds). Minimum tillage practices have increased throughout EU in the last decade, but even in case of seed treatment use in minimum tillage practices the soil surface is ‘worked’ to a depth up to 5 cm. No-tillage practices are rare (< 5 %) in Europe. Therefore, for potential ‘consumers’ in bird and mammal populations the scenario represented by a seed treatment resembles a bare-soil scenario. Herbivorous birds and mammals are not considered to be attracted to fields immediately after treated seed has been drilled. However it is possible that birds and mammals may consume seedlings that contain residues of the active substance or consume the seedling and the remaining seed. These issues are discussed below.

In general granivorous birds and mammals prefer a certain type of seed for their diet. Not all birds are attracted to all sizes and shapes of seeds. Therefore, in a Tier 1 assessment, small granivorous birds that feed on small seeds, and larger, medium-size birds that feed on large seeds such as maize, sugar beets and beans should be considered separately.

Work by Prosser (2001) indicated that some pelleted seeds were not readily taken as a food source by birds. However, the potential for pelleted seeds to be taken as source of grit must also be considered when making a risk assessment for birds. Mammals are not known to ingest grit.

Step 1

For pelleted seeds, an assessment for mammals is not required⁵³, but an assessment for birds must be conducted according to the scheme presented in section 5.1.2.

For non-pelleted seeds the standard scenario for risk assessment is a bird or mammal feeding on freshly drilled seeds. Throughout the present document, first-tier scenarios are set in which diets consist of a single food item. Therefore, at Tier 1, it can be assumed that seed-eating birds and mammals feed on treated seeds only (100 % diet).

Step 2

For non-pelleted seeds, select the appropriate generic focal species from Table 18.

Table 18. Type of seeds, corresponding generic focal species and their food intake rate per body weight.

Type of seeds	Indicator species	FIR/bw
‘Large seeds’ (maize/beans/peas)	Large granivorous bird	0.1
	Small omnivorous mammal	0.24
‘Small seeds’ (not maize, beans or peas)	Small granivorous bird	0.3
	Small omnivorous mammal	0.24

⁵³ Pelleted seeds may be consumed by wood mice (e.g. Pelz, 1989) but the Joint Working Group considered that the risk in these cases may be reduced due to animals cracking and discarding the pellet with most of the residue before ingesting the seed.

Step 3

For all seed treatments, including pelleted seeds, an additional scenario of birds and mammals feeding on crop seedlings should be considered in the risk assessment.

When consumption of newly emerged crop shoots (including roots and remaining seed) is likely to occur, it is necessary to conduct an additional risk assessment for herbivorous birds and mammals according to the methods provided in the modules for acute and reproductive risk assessment for spray products (section 4). In such an assessment, any information on the amount of substance likely to be present in newly emerged crop shoots should be taken into consideration. The scenario assessed here resembles mostly the ‘newly-sown grassland’ or ‘early-post emergence uses on cereals’ scenario for spray products. Relevant indicator species for this scenario are as such large herbivorous birds and mammals and small omnivorous birds and mammals. The generic focal species and the appropriate shortcut values for the risk assessment for pesticides present in newly emerged crop shoots can be selected from Table 19. Insectivorous birds and mammals are unlikely to present a critical case for this scenario. The FIR/bw needs to be multiplied by the concentration expected in the seedling to obtain a shortcut value suitable for use in the first-tier RA. As a conservative default for the Tier 1, it is assumed that the applied amount of pesticide is contained in a total mass of seedling that is five times the weight of the original seed (based on the relative water contents of seeds and the newly emerged grass and cereal shoots – see Appendix G). The values in Table 19 assume that root, seed and seedling are ingested by the animal and that all of the applied substance remains available. If data can be provided to justify less conservative values this could be considered in a refinement step. The acute and reproductive risk assessments for birds and mammals have to be carried out in the same way as for spray applications, outlined in sections 4.1 - 4.4, but using the shortcut values from Table 19. This is in addition to, and not a replacement for, the assessment for ingestion of treated seed (Step 4).

Table 19. Generic focal species and corresponding shortcut values for assessment of residues present in newly emerged crop shoots.

Generic focal species	Short-cut values for acute risk*
Small omnivorous bird	$0.5 \times \text{NAR}/5$
Small omnivorous mammal	$0.24 \times \text{NAR}/5$

NAR = Nominal loading/application rate of active substance in mg/kg seed.

* For the reproductive assessment, these shortcut values should be combined with appropriate time windows and default degradation/dissipation rates for residues (see sections 4.3 and 4.4).

5.2.2. First-tier RA and refinement options for birds and mammals feeding on treated seeds

For products used as seed treatment, risk assessments for acute as well as reproductive effects are needed.

Step 4

Calculate the acute and long-term TER values for generic focal species using the FIR/bw values from Table 18 and appropriate estimates of exposure.

$$TER_{acute} = \frac{LD_{50}}{NAR} \times \frac{FIR}{bw}$$

$$TER_{\text{longterm}} = \frac{NOAEL}{\text{Appropriate exposure estimate}}$$

With:

NAR = Nominal loading/application rate of active substance [mg/kg seed].

Information on how to determine appropriate NOAELs for different reproductive phases is provided in sections 4.3 and 4.4. For exposure estimates, the same time windows as in the sections on reproductive effects should be used, together with the nominal application rate and appropriate dissipation and degradation rates of the active substance on the treated seed.

Compare the resulting toxicity-exposure ratios to the respective trigger values:

TER_{acute} ≥ 10 and TER_{longterm} ≥ 5	No refined risk assessment required.
TER_{acute} < 10 and/or TER_{longterm} < 5	Select one or a combination of refinement options (section 5.2.3) and perform a weight-of-evidence assessment

5.2.3. Refinement options

The above procedures represent realistic but worst-case scenarios for individual animals. Based on currently used loading rate (NAR) for most seed treatment products, a large majority of cases will fail this first-tier assessment, so refined risk assessment will frequently be required. At present, it is not possible to provide advice on a fixed refinement approach. Therefore, a set of refinement options is outlined below. This set of options is not necessarily exhaustive and further refinement tools may be available or be developed in the future. General guidance on higher-tier assessment is provided in section 6.

Regardless of the options selected for refinement, the uncertainties associated with each option should be evaluated (see section 6.8) and the overall weight-of-evidence (WoE) should be assessed (see section 6.9). A summary of the main sources of uncertainty affecting the different refinement options is provided in Table 21.

Focal species (FS), PT and mixed diet composition

Actual focal species information may be available for the crop/region under assessment. Refinements can be performed using the food intake rate (FIR) and body weight data of the actual focal species rather than the generic FS in Table 19. PT values for the actual crop-specific FS as well as any information on the (mixed) diet of those species may be used for further refinements of the dietary exposure and TER. In any refinement of these factors, account should be taken of the guidance provided in section 6.1 on approaches and limitations of refined dietary exposure assessments. Additional care is required for treated seeds. First, simple dietary assessments assume that food obtained on treated fields follows the same dietary composition as measured for the general population in all habitats. This will probably underestimate the intake of crop seed for animals feeding on newly drilled fields. Therefore, the conservative assumption of taking only treated seed should be retained unless there is specific data on the foods taken on relevant fields. Second, when refining PT for seed treatments, it is important to take account of the range of variation between individuals and between days (not average values), because acute risks and also reproductive effects caused by short-term exposures depend on the amount of seed taken by an individual on a given day.

Availability of non-treated seeds

Bare soil and/or prepared seed beds are likely to contain a natural seed bank of weed seeds. The first-tier assumption of a bird/mammals diet consisting of 100 % treated seeds is likely to represent a worst-case approach. At higher tiers, where mixed diets are considered, it is therefore possible to adjust the percentage of treated seed in the diet. This is based on the availability of alternative seeds from the natural seed bank on the treated field, assuming that relevant data exist or can be generated for the scenario under consideration. However, it cannot be assumed that birds or mammals simply take treated seeds and weed seeds in proportion to their relative densities. Account must be taken of other factors that may influence relative uptake, including the relative visibility to birds and mammals of the seeds against the soil background, their relative energy contents and palatability. Modelling these factors is likely to be very uncertain and it may be more practical to study seed intake of animals directly (e.g. by analysis of faecal samples from animals known to be foraging entirely or mainly on the relevant fields).

Dehusking behaviour

Granivorous mammals and birds are known to dehusk seeds prior to consumption. In such cases the actual intake of a substance after feeding on treated seeds may be considerably less than was estimated from the nominal treatment rate. The extent of dehusking behaviour may vary among different species of birds and mammal as well as for different types of seed (crop). Therefore, in looking at any available experimental data on dehusking, the representativeness of the studies to the situation likely to arise in the field should be taken into consideration. Further discussion and guidance on this issue is provided in section 6.1.7.

Foraging area

It stands to reason that the risk for birds and mammals presented by a product used as a seed treatment is correlated with the area that a bird or mammal will have to forage to find sufficient seeds that add up to a lethal dose. Therefore, an indication of the degree of risk may be obtained by estimating the area that needs to be foraged by a bird or mammal to obtain a lethal dose.

This approach requires information on the density of seeds available on the soil surface after application (including an assessment of field incorporation rate). De Snoo and Luttkik (2004) reported that the soil incorporation rates achieved in different crops, with different machineries and different periods of the season, vary by 90 – 99.5 %. It is important to take into account that the scatter of treated seeds left on the soil surface after using a ‘soil-incorporation’ seed treatment is unlikely to be homogeneous. Larger densities of available seeds may remain on the soil surface, especially at those points where the applicator either enters or leaves the soil (due to turning of machinery or uneven soil surface), even when the overall incorporation efficiency of the treatment is high. Birds and mammals may be specifically attracted to these ‘hot-spots’ and any effect seen may be more related to those than to the incorporation-efficiency-adjusted nominal application rate (NAR). The potential of risk mitigation measures that are mentioned on the label may also be taken into account. These require e.g. the immediate (end-of-row) removal of spills after application in order to lower the availability of treated seeds on the soil surface

Data on incorporation rates should be relevant to the crop, soil type and conditions under assessment. Data from multiple sites may be needed to represent the range of variation. Sampling within each site should be designed to reflect within-field variation including any differences between end-row, field edge and field centre areas. Since animals are likely to concentrate their foraging in areas of higher seed density, the area containing sufficient exposed seeds to provide a lethal dose should be calculated for the higher densities encountered as well as the average. Appropriate allowance should be made for

variation of toxicity between and within species, i.e. by estimating the lethal dose as the LD₅₀ for test species divided by a part or all of the standard uncertainty factor of 10⁵⁴.

If the area that must be foraged to obtain a lethal dose is clearly unfeasibly large for any relevant focal species, even at the upper end of expected seed densities, it may be possible to conclude that the risk is low. If a lethal dose can be obtained from an area that is clearly small enough for a focal species to forage in a short period of time, this will indicate a cause for concern unless it can be demonstrated that other factors such as avoidance and metabolism will reduce the risk. However, interpretation of intermediate results may be very uncertain, unless they can be compared to good information on the range of foraging areas that can be covered by relevant species in relevant conditions. If existing information is inadequate to make this judgement, then consideration could be given to conducting quantitative observations in the field.

Meal size approach

The typical numbers of seeds that a bird can ingest in a single feeding bout has been investigated by Prosser (1999). Comparison of the number of seeds needed to attain a lethal dose with the data provided by Prosser may provide useful information on the likely risk of mortality. Appropriate allowance should be made for variation of toxicity between and within species, e.g. by estimating the lethal dose as the LD₅₀ for test species divided by part or all of the standard uncertainty factor of 10, or dividing the relevant endpoint by up to 5 for reproductive effects caused by one-day exposures.

Prosser's (1999) data on seed intakes are summarized in Table 20 below. It should be stressed that the methodology used by Prosser to derive these numbers was conservative in some aspects (e.g. it was a spill scenario) but not in others (the same bird may have returned to the feeding site several times a day, and one bout may not equate to a 'meal'). Therefore, before using these data, one needs to assess the degree of 'comparability' between the numbers derived under the set of experimental conditions and the field situation to be assessed. The range of variation in feeding bout size (as indicated in Table 20 will assist in evaluating the proportion of bouts that may approach a lethal dose. If it appears from the 90th percentile and maximum values that some bout sizes could be sufficient to provide a lethal dose, this will indicate a cause for concern unless it can be demonstrated that other factors such as avoidance and metabolism will reduce the risk.

Table 20. Mean and maximum number of large and small seeds taken by birds in a single feeding bout in field studies, summarised from Prosser (1999).

	Number of large seeds			Number of small seeds		
	Mean*	90 th percentile**	Maximum	Mean*	90 th percentile**	Maximum
Large granivorous bird	12	116	266	75	1744	4487
Small granivorous bird	3	11	11	12	85	240

* Geometric mean of mean values for different species and seed types.

** 90th percentile of maximum values for relevant species and seed types.

Food item preference and avoidance

Granivorous birds and mammals may be able to distinguish treated seeds from non-treated seeds and may show a preference for either treated or untreated seeds in their diet. This may be influenced by various factors including appearance, taste or surface texture of the treated seed, and aversive reactions

⁵⁴ Unfortunately, there is no generally accepted view on how much of the standard uncertainty factor of 10 should be considered as allowing for variation in toxicity between and within species.

to the active substance. Information on such preferences/avoidance behaviour can, in combination with data on the availability of treated and non-treated seeds on the soil surface, be used to refine the risk assessment.

No standard guideline for testing avoidance is as yet available. Studies conducted in the past were performed under choice as well as no-choice situations, with and without food-deprived animals (hunger stress). In applying a weight-of-evidence approach on avoidance studies the severity of the test method should be compared with the field scenario likely to arise. Important factors to consider when assessing avoidance are discussed in section 6.2.

Metabolism and body burden modelling

The rate of absorption, distribution, metabolism and elimination (ADME) of substances in the gastrointestinal tract of birds and mammals influences the toxicity of the product. In the first-tier risk assessment above, LD₅₀ values from gavage studies are used as an estimate of the toxicity of the substance. ADME-factors may be different for dietary uptake of products from seed treatment than in the gavage experiments. Therefore, metabolism and body burden models (see also section 6.3 of this GD and Appendix 23 of EFSA, 2008) can be used as a potential refinement step at higher tiers. The EFSA opinion on pirimicarb gives an example as to how such models may be applied in a weight-of-evidence approach (EFSA, 2005a).

Field studies

Since the screening assessment for seed treatments has not been calibrated by field studies, as is the case for the acute assessment on spray-product, classical field 'effect' studies can be used to refine assessments on the acute risk of seed treatments. Quality criteria should be applied to the studies regarding the relevance of the species that are present (e.g. diet, use of field), the representativeness of the field situation and the power of the study to detect effects (e.g. carcass search efficiency). Note that, although the lack of vegetative cover makes it easier to find carcasses in newly sown fields, it may also make intoxicated animals more likely to seek cover away from the field. Other important factors to consider when designing and interpreting field studies are discussed in section 6.4.

Historical data on poisoning incidents

When reviewing a previously authorised product, information on historical incidents may be available from official surveillance schemes and/or the scientific literature. Such data are very relevant to evaluating the protection goal of avoiding 'visible mortality', although only a fraction of visible casualties may be reported or documented. Furthermore, only a fraction of actual casualties will be visible, and therefore incident records are a very uncertain indication of the degree of undetected mortality. This is relevant when assessing the protection goal of avoiding long-term repercussions for abundance and diversity. These issues and the interpretation of incident data are discussed further in section 6.5.

Comparison to well-studied historical examples

Comparisons between the product under assessment and other products that have been well studied in the past may provide some assistance in characterising the possible risk, provided the uncertainties inherent in 'reading across' between products and scenarios are carefully assessed. For example, extensive information is available on the organophosphorus insecticide fonofos, which was used as a seed treatment on wheat in the UK. This was associated with a small number of bird poisoning incidents over a number of years (Prosser et al., 2006). Authorisation of the product was not withdrawn, so it may be inferred that the level of incidents was not considered clearly unacceptable, but it may have been close to the borderline of acceptability. Therefore, it may provide a useful, although approximate benchmark for the evaluation of other products with similar characteristics. For example, if another product required a smaller area of exposed seeds to obtain a lethal dose, when

compared to the same calculation for the historical use of fonofos, then this would be a cause for concern. On the other hand, if the new product required a much larger area to obtain a lethal dose, this might be an indication of lower risk provided that the avoidance and metabolism properties of the two substances were similar. In making such comparisons it would also be relevant to consider the anticipated extent of use of the new product, because fonofos was used on a relatively small area of wheat and would presumably have caused more incidents if used more widely. The validity of extrapolations implied by comparative inferences of this sort must be considered very carefully. Differences in avoidance and metabolism between products could have large effects. Uncertainty will be increased for comparisons involving different crops, different focal species, or different regions.

A more subtle, but important uncertainty arises from between-species variation in toxicity. As indicated in Appendix C, (Figure 1, histogram of variation between species), a sensitive species may be up to one or two orders of magnitude more sensitive than the standard test species. If the test species for the benchmark pesticide was itself a relatively sensitive one, and the test species for the new pesticide was a relatively insensitive one, then the benchmark comparison could severely underestimate the risk. A conservative work-around for this would be to apply part or all of the normal uncertainty factor of 10 to the new pesticide, but not the benchmark pesticide, when calculating the areas required for a lethal dose.

If, when all the uncertainties are considered, a comparison of this sort is still clear enough to form a judgement about risk relative to a well-studied 'benchmark' example, it may make a useful contribution to the overall weight-of-evidence.

Weight-of-evidence (WoE) approach

All the options above can potentially be used to refine a first-tier risk assessment. However, none of them is considered as the 'preferred' way forward in all cases, and a combination of several options may often be used. Therefore, higher-tier assessments should take the form of a weight-of-evidence approach, in which an overall conclusion on the characterisation of risk is formed, giving appropriate weight to each of the available lines of evidence. In principle, the weights given to different lines of evidence should be proportional to their degree of certainty. If one line of evidence shows with high certainty that effects are (or are not) expected, then this should be given more weight than a more uncertain line of evidence that indicates the possibility of either a positive or negative outcome. A general indication of the degree of uncertainty associated with different types of evidence is shown in Table 21, but this depends critically on the details of the evidence available in each case. Further guidance on evaluating uncertainty for each line of evidence is provided in section 6.8. Guidance on weight-of-evidence approaches for combining lines of evidence is given in section 6.9. The implications of uncertainty for decision-making and risk management are discussed in section 7.1.

Table 21. Summary of most important types of uncertainty affecting different types of evidence that may be available in higher-tier assessment of seed treatments. The actual magnitudes of the uncertainties will depend on the quantity and quality of data available in each case.

Line of evidence	Type of output	Major sources of uncertainty				Overall uncertainty
		Dietary exposure	Toxicity	Avoidance/metabolism	Uncertainty factor*	
First-tier dietary assessment	TER	Realistic for worst-case individual	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Ignored. May reduce risk little or very substantially, depending on pesticide.	10 (acute) 5 (reproductive)	Realistic worst-case individual for non-avoided pesticides. Conservative to very conservative for others.
Refinement of focal species and PT	Refined TER	More realistic for some individuals but refinement must still take account of variation between individuals	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Ignored. May reduce risk little or very substantially, depending on pesticide.	10 (acute) 5 (reproductive)	May underestimate risk for non-avoided pesticides. Probably conservative for others.
Availability of non-treated seeds	Refined TER	Increased realism, but relation between availability and intake is very uncertain	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Ignored. May reduce risk little or very substantially, depending on pesticide.	10 (acute) 5 (reproductive)	High uncertainty. May underestimate risk if animals actually focus on treated seed.
Dehusking	Refined TER	Need to take account that proportion of seeds dehusked varies between individuals and species.	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Ignored. May reduce risk little or very substantially, depending on pesticide.	10 (acute) 5 (reproductive)	May underestimate risk if overestimate degree of dehusking or its impact on residues.
Foraging area = Estimation of field area containing exposed seeds carrying toxic dose	Area containing LD ₅₀ (acute) or NOAEL (repro) (m ²)	Takes account of seed availability but this is highly variable and may be very uncertain.	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Ignored. May reduce risk little or very substantially, depending on pesticide.	Divide toxicity endpoint by 10 (acute) or 5 (reproductive)**	Uncertainty depends on how incorporation is assessed. In addition, interpretation of result may be very uncertain.
Meal size approach***	One meal = a % of LD ₅₀	Meal size is highly variable and will be very uncertain unless there are extensive data for focal species.	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Simple way to allow for avoidance. May be conservative if meal size estimate is worst case, and metabolism and recovery are rapid.	Divide toxicity endpoint by 10**	Uncertainty and conservatism depend critically on quality of meal size data and rate of metabolism and recovery.

Line of evidence	Type of output	Major sources of uncertainty				Overall uncertainty
		Dietary exposure	Toxicity	Avoidance/metabolism	Uncertainty factor*	
Metabolism and body burden modelling***	Peak net dose = a % of LD ₅₀	Less important than other sources of uncertainty for this approach.	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Parameters required by body burden model are usually very uncertain	Use LD ₅₀ /10 or other suitable estimate for toxicity to sensitive species**	Very uncertain unless conservative estimates for most/all inputs give peak dose < LD ₅₀
Avoidance studies***	Number of species tested, number showing lethal and sublethal effects	Test scenario should be realistic worst case. Proportion of real exposures approaching this is very uncertain.	Focal species can be up to 1 or 2 orders of magnitude more or less sensitive than test sp.	Conservative for test species only if test design is worst case. Extrapolation to other species is highly uncertain (see section 6.2).	No uncertainty factor.	Conservative for test species only if test design is worst case. Extrapolation of result to other species is highly uncertain.
Field study***	Number of sites, number showing evidence of mortality	Species exposed and degree of exposure vary widely between sites. It needs multiple sites to capture this.	Multiple sites reduce uncertainty by representing a wider range of species sensitivity.	Multiple sites reduce uncertainty by representing a wider range of species and conditions.	No uncertainty factor.	Low uncertainty if number of sites high. Extrapolation of results from single/few sites is highly uncertain.
Data on historical poisoning incidents***	Numbers of suspected and confirmed incidents	Representative of actual exposures, if data relate to product under assessment.	Representative of actual sensitivities, if data relate to product under assessment.	Representative of actual conditions, if data relate to product under assessment.	No uncertainty factor.	Reliability as measure of visible mortality depends on quality of surveillance scheme. Underestimates total (hidden) mortality.
Comparison to a well-studied 'benchmark' example.	Critical comparison of some or all of the lines of evidence listed above.	Uncertainty depends on similarity of dietary scenarios for the two pesticides considered.	Ratio of tested to sensitive species could differ substantially between the two pesticides. An uncertainty factor has to be applied to allow for this.	Uncertainty will be high unless comparable data on avoidance and metabolism exist for both pesticides.	Apply uncertainty factor to assessed pesticide but not benchmark to allow for possible difference in relative sensitivity of standard species.	Reliability of comparison depends critically on comparability to benchmark in terms of scenario, avoidance, metabolism, etc.

* Refined TERs may be compared to the standard first-tier trigger values but the level of protection they achieve will generally be lower than in Tier 1 and should therefore be re-evaluated in every refined assessment (see section 6.8).

** If part of the standard uncertainty factor is considered to address other issues, then only the part relating to between-species variation in toxicity should be used here.

*** These lines of evidence are usually applicable only for assessment of acute risks.

5.3. Risk assessment for substances with endocrine-disrupting properties in birds and mammals

Annex II, 3.6.5. of (EC) 1107/2009, the new Regulation on pesticides states that “An active substance, safener or synergist shall only be approved if, (...) it is not considered to have endocrine disrupting properties that may cause adverse effect in humans, unless the exposure of humans (...), under realistic proposed conditions of use, is negligible, (...)” 3.8.2. relates to non-target organisms: “An active substance, safener or synergist shall only be approved if, (...) it is not considered to have endocrine disrupting properties that may cause adverse effects on non-target organisms unless the exposure of non-target organisms to that active substance in a plant protection product under realistic proposed conditions of use is negligible.”

Taking this inclusion of cut-off criteria within the new Regulation into account, the risk assessment for endocrine-disrupting properties in birds and mammals might no longer be needed. Before carrying out the RA steps below, notifiers should therefore check the latest state of regulatory practice and discuss with their competent national authority.

In the context of risk assessment for birds and mammals endocrine-disrupting substances can be defined as materials that cause effects on bird and mammal reproduction through disruption of endocrine-mediated processes (see also Appendix 26 of EFSA, 2008). The environmental risk assessment performed under EC, 2002, is based on the ecological relevance of the observed effects, independent of the mode of action that are (or may be) responsible for such effects. Therefore the general procedure for risk assessment can also be used for substances with endocrine-disrupting properties.

Step 1

Study the information available from tests performed on other taxa (fish, amphibians, mammals and birds) for the substance under assessment. Information from structurally related substances may also be considered. If the data give rise to concerns of potential endocrine-mediated effects of the substance, then mammalian screening tests should be assessed to clarify the mechanism of action, and/or the potential of the test substance to cause endocrine-mediated effect in birds/mammals (*in vivo*). With regard to mammals, and in contrast to birds, a number of *in vitro* and *in vivo* screening tests for assessing endocrine-disrupting properties have become available in recent years and are in various stages of (pre-) validation (OECD, 2007a; NIEHS, 2002; US EPA, 2005; OECD, 2007b). In order to begin the assessment of endocrine-mediated effects in mammals and birds, further specific steps to be followed are given below.

Step 2

Study the information available from mammalian screening studies to clarify any potential of the substance to influence known endocrine mechanisms. In case (*in vitro*) screening studies in mammals show that the substance has an effect on a known endocrine mechanism, further assessment is needed to allow for the evaluation or generation of data relevant to risk assessment. The mammalian multi-generation study, performed for pesticide risk assessment, covers the entire reproductive cycle and therefore is able to provide information on overall productivity at the population level. In addition to mammalian screens, fish and amphibian screens exist that can address the question of the likelihood of a material to be an endocrine disruptor, as well as its probable mode of action (OECD, 2005; OECD, 2007c). This information should also be taken into account for the assessment as further weight of evidence. In cases where screens are ‘positive’, or where no screens are available but concerns for potential endocrine-mediated effects remain, Step 3 should be taken.

Step 3

Assess the standard (multi-generation) mammalian reproductive study or any available relevant mammalian *in vivo* study for potential endocrine-mediated effects on reproduction. Derive an endpoint value for these effects to be used in risk assessment for wild mammals.

Mammals and birds have similar hormones, hormone receptors and fundamental feedback mechanisms. However, one important difference between mammals and birds lies in the mechanism of sex differentiation. Both testosterone and estradiol, in appropriate relative concentrations, are required for reproductive development in birds (Ottinger and Abdelnabi, 1997; Ottinger et al., 2001). In the absence of estrogens the development is masculine. In mammals, however, embryos require sufficient levels of androgens to induce gonadal differentiation into testicular tissue. There are further important differences between birds and mammals regarding hormonal systems existing. Hence, if mammalian screening tests reveal the potential of a substance to influence endocrine processes, the absence of endocrine-mediated effects in mammalian *in vivo* studies is not sufficient to conclude a risk assessment on birds. It is not possible to use the endpoints from a mammalian risk assessment in an avian assessment. Such endpoints can only be used as a source of information.

Step 4

Assess all information available from the standard one-generation avian reproduction study or a specific modified one-generation study modified to include endocrine endpoints. The information provided may help in determining an appropriate strategy for further testing but will, in general, not provide conclusive information on endocrine-mediated effects. This is partly due to the fact that the one-generation avian reproduction study does not include exposure during all relevant stages of the bird's development or the measurement of other relevant endocrine-sensitive endpoints such as behaviour (e.g. parental care, nesting behaviour, territoriality and mounting behaviour). Currently, no internationally accepted testing methodology is available, that can be used to adequately assess the impact of endocrine mediated effects of a substance on the reproduction of birds.

A test design aimed specifically at the evaluation of endocrine effects that is currently under discussion in an OECD process is a two-generation study with Japanese quail (OECD, 2006a). While the ultimate objective of the test is still to be determined, the most likely objective of the study is to characterise dose-response relationships with subsequent conclusion on immediate and more long-term adverse consequences associated with exposure to potential endocrine-disrupting substances. In addition to the avian two-generation test, more targeted and smaller tests (e.g. partial life cycle or critical life-stage tests) may be developed in the future. Such tests should allow the evaluation of the impact of potential endocrine-disrupting substances on a specific portion of the avian life cycle and its associated endpoints. Smaller tests that focus on specific endpoints (including behaviour) may be more sensitive in evaluating the potential endocrine effect of a substance than a two-generation study, since the range of concentrations can be focussed around a specific endpoint. Individual studies of this nature have been performed (OECD, 2006a), but no test protocols have been developed to date.

Step 5

Assess any specific two-generation or sensitive life stage study in birds for endocrine-mediated endpoints. When assessing/selecting the appropriate test design and the appropriate endpoints, it is essential to evaluate all the available information on avian and/or other species. If available information allows, the likely mode of action and the part of the avian life-cycle likely to be the most sensitive (with associated behaviours) should be identified. Subsequently, an appropriate test design should be selected. There is no single test design that should automatically be followed. In addition, only those techniques should be applied that have been developed sufficiently to assess the various endpoints. While extensive work has been performed on a number of potentially relevant endpoints (OECD, 2006a; OECD, 2006b) there is still a substantial amount of development and validation work required. Hence, in using endpoints from such studies in avian risk assessment the uncertainty related to the fact that they are currently

in a research stage and therefore lack validation should be taken into consideration as a source of uncertainty when interpreting the assessment outcome.

5.4. Assessment of the risk from metabolites formed in potential food items

The primary focus of this document is to provide a framework on how to assess the risk of active substances to birds and mammals. It is, however, important to ensure that the risk from any metabolite(s) is also fully addressed. Birds and mammals can be exposed to metabolites that are formed in plants, fish and other birds or mammals that are consumed. Metabolites can also occur in soil which, in turn, can occur in soil organisms (e.g. earthworms) that are also eaten. Outlined below is a procedure that should be followed to ensure that the risk from metabolites in potential items of avian or mammalian food is assessed.

Step 1

Determine the metabolites present in plants, fish, other birds or mammals and other relevant food items that may be consumed by the relevant focal species.

Step 2

In order to assess the risk to **mammals**, it is necessary to refer to the evaluation of the mammalian toxicology data package. Information from studies on the metabolism of the active substance by the rat (or goat) will indicate whether the metabolite of concern occurs in mammals. If the metabolite of concern does occur at significant levels in a rat metabolism study then its toxicity may have been addressed as part of the assessment of the active substance. One important point to note is that the metabolite may occur at much higher levels, or proportions, in the plant or food item than in the rat or goat. If this is the case, care must be exercised, since the assumption that its presence in rats sufficiently addresses the risk may result in underestimation of the risk. This is illustrated by a substance that is formed in low levels in rats, however is formed in high levels in plants. Assuming that the risk is addressed by the metabolism study may underestimate the risk. In such a situation Step 3 should be taken. However, if the metabolite is adequately addressed in the mammalian toxicity data package, then still the risk to birds must be assessed (see Step 4).

Step 3

If the metabolite occurs at much higher levels, or proportions, in the plant or food item than in the rat, the availability of an acute rat or mouse study on the metabolite in the mammalian toxicology data package should be checked. Before requesting such a study, if it is not at hand, a reassessment of the amount of metabolite formed and the risk from the parent substance is required. This assessment should include an indication of how much more toxic the metabolite would need to be to raise concerns, i.e. to produce an acute TER of < 10.

Step 4

For **birds**, a similar approach to that outlined in Steps 1-3 for mammals should be used. The hen metabolism study should be consulted and the same approach as outlined above should be used. If a hen metabolism study is not available, it is recommended to consult the rat or goat metabolism studies. If the metabolite is detected in the study, then this may be sufficient for the assessment, depending upon the toxicity of the parent substance, the risk posed and the likely metabolic pathway, i.e. if the metabolite is likely to be formed in birds as well. These factors should be evaluated by a weight-of-evidence approach (see section 6.8).

Occasionally, there may be a soil or plant metabolite that does not occur at all or not at significant levels in either bird or mammal metabolism studies. This means that the potential effects have not been

assessed in studies using the active substance. Birds and mammals may, however, be exposed to this metabolite when consuming plants or organisms containing soil. In this situation it is necessary to assess the risk in the following ways:

- Carry out a quantitative structure-activity relationship (QSAR) assessment although there are no ‘off the shelf’ QSAR or structure-activity relationships (SAR) for pesticide metabolites. However, this should not preclude their use. When using a QSAR or SAR, it is necessary to ensure that the model is appropriate for the key chemical structures of the metabolite, i.e. that substances of the type being assessed have been included in the original training set. If not, this will cause much uncertainty regarding the output. One QSAR that was designed to model pesticide toxicity and might be useful for metabolites is the DEMETRA model.⁵⁵
- Carry out an SAR assessment. If the toxiphore is no longer present in the metabolite, this may indicate that the metabolite is of lower toxicity. However, it should be noted that a toxiphore to one organism (the target pest) may not be a toxiphore to another. Therefore, this approach should be justified, e.g. with reference to similar active substances with similar metabolic pathways, etc.
- Carry out an avian toxicity study on the metabolite. This should only be used for those metabolites that pose a potential high risk and where it is not possible to address this risk by other means.

5.5. Risks for birds and mammals through drinking water

Exposure of birds or mammals via drinking water is not explicitly included in the DDD calculations of the dietary risk assessment. Therefore, an approach is presented that allows estimating the possible risk arising from uptake of contaminated drinking water for two basic scenarios. Due to the incidental nature of occurrence of drinking water reservoirs on agricultural fields (as compared to the contamination of food items growing or dwelling on those fields), a separate assessment of this exposure route is considered appropriate at least on the first-tier level.

Most birds and mammals can in principle satisfy (at least parts of) their daily water demand via uptake of food. However, this potential depends on the water content of the diet items, which is lowest for seeds. Therefore, the assessment methodology for the risk to birds and mammals of pesticides in drinking water as provided below uses small granivorous animals as indicator species at Tier 1.

The two scenarios covered by the assessment both refer to small and smallest water reservoirs, namely pools in leaf whorls and puddles on soil (see Step 1 for the selection of scenarios and Step 2 for calculating exposure concentrations in water). Experience has shown that uptake of drinking water from larger water bodies is unlikely to pose a relevant risk. Uptake of drinking water by animals is estimated using allometric equations (Step 3). For situations where the calculated TER values suggest a risk, options for refinement and/or management are provided (Step 4). For further details see Appendix K.

Step 1

Selection of relevant scenarios. Two scenarios were identified as relevant for assessing the risk of pesticides via drinking water to birds and mammals:

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

⁵⁵ Details of this can be found at http://www.demetra-tox.net/index.php?option=com_frontpage&Itemid=1.

A leaf scenario is clearly the worst-case situation. It is relevant for spray applications only and should be considered for the following crop types and growth stages:

- Leaf vegetables (forming heads) at principal growth stage 4 until harvest (classification according to BBCH⁵⁶).
- Other leaf vegetables (e.g. cauliflower) at principal growth stage 4 or later, with a morphology that facilitates collection of rain/irrigation water in reservoirs that are large enough and easily accessible to attract birds and sufficiently stable over some hours.

A leaf scenario is not deemed relevant for small mammals. The equations for calculating exposure concentrations can be found under Step 2a. A leaf scenario is only deemed to be relevant for acute risk assessment. This is due to the fact that such pools in whorls are not likely to be formed very frequently in a field, since they require a specific combination of leaf morphology, weather conditions, formulation type and water volumes. Also a puddle scenario reflects events that may or may not occur on a single agricultural field, unlike the contamination of potential food items growing or dwelling on the fields. It is, however, likely to be more common than a leaf scenario and puddles may remain present in fields for longer periods of time. Therefore a puddle scenario is also recommended to be used in a first-tier approach towards the assessment of any risk to reproduction of birds and mammals. The lower probability of exposure on a population-relevant level as compared to dietary exposure may be considered when estimating overall uncertainties in the course of a refined risk assessment.

A puddle scenario, on the other hand, is relevant for all types of application that may cause contamination of soil. This also includes non-foliar applications of pesticides. If necessary, a puddle scenario may further be applied for a risk assessment for metabolites and degradation products, according to their toxic potential. The equations for calculating exposure concentrations can be found under Step 2b.

Step 2a

Calculation of exposure concentrations for a leaf scenario. A leaf scenario assumes a situation in which rainfall or irrigation occurs shortly after the application event. Based on measurements conducted at the sites of incidents, it was concluded that the worst-case concentration in water would correspond to the concentration in the spray solution (i.e. the product already diluted in the required amount of water) diluted by a factor of 5 (Hommes et al., 1990).

$$PEC_{\text{pool}} = \frac{C_{\text{spray}}}{5}$$

Step 2b

Calculation of exposure concentrations for a puddle scenario. To obtain an estimate for pesticide concentrations in puddles formed on a field after rainfall (predicted environmental concentration, PEC_{puddle}), it may be assumed that this concentration would be the same as the concentration in runoff water as calculated for the assessment of surface water exposure. Taking into account a relevant subset of parameters from FOCUS⁵⁷ surface water modelling (FOCUS, 2003), a simplified model can be proposed to calculate PEC_{puddle} in mg/L as a function of application rate and the organic carbon adsorption coefficient (K_{OC}) of a substance. Provided that the full application rate is considered, this approach assumes application to bare soil without degradation and thus reflects a worst case for crop-directed applications. Where appropriate, crop interception may be considered in the same way as for calculation of PEC_{soil} , PEC_{gw} and PEC_{sw} , in order to increase realism.

⁵⁶ Biologische Bundesanstalt, Bundessortenamt und Chemische Industrie

⁵⁷ Forum for the Co-ordination of pesticide fate models and their use

$$PEC_{\text{puddle}} = \frac{AR/10}{1000(w + K_{oc} \times s)}$$

With:

AR = application rate [g/ha]; divisor of 10 to achieve rate in mg/m²

w = 0.02 (pore water term: volume)

s = 0.0015 (soil term: volume, density, organic carbon content)

When multiple spray applications are considered, a MAF based on the DT₅₀ in soil (single first order kinetics, geometric mean as used for PEC_{gw} and PEC_{sw}) may be applied to achieve the effective application rate AR_{eff}.

$$AR_{\text{eff}} = AR \times MAF_m = AR \times \frac{1 - e^{-nki}}{1 - e^{-ki}}$$

With:

k = ln(2)/DT₅₀ (rate constant)

n = number of applications

i = application interval (d)

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals (see below), no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (K_{oc} < 500 L/kg) or 3000 in the case of more sorptive substances (K_{oc} ≥ 500 L/kg).

Step 3

Drinking water uptake by birds and mammals and calculation of TER values. The respective calculations for birds and mammals are performed on a level of generic focal species, i.e. basic ecological traits already form part of the considerations. According to the relatively low water content of their diet, granivorous species will face the greatest necessity to satisfy their daily water demand by additional uptake of drinking water. In line with the proposals made for dietary exposure, the following generic species should be considered for estimating the uptake of drinking water:

- Small granivorous bird (bw = 15.3 g)
- Small granivorous mammal (bw = 21.7 g)

For birds, drinking water rates (DWR) as published by DEFRA (2007) should be used. They are based on allometric equations for total water flux (WF) in different categories of birds and on data on the contribution of other sources on birds' water balance. For mammals, no DWRs are included in the report by DEFRA (2007), but it is possible to use the data on water flux from Nagy and Peterson (1988) and calculate DWR in the same way as for birds.

- Small granivorous bird
 $\log_{10}(\text{WF}) = -0.195 + 1.003 \times \log_{10}(\text{bw})$ for passerines
 linnet: WF = 9.8 mL/d; DWR = WF – (food water + metabolic water) = 7.0 mL/d, equivalent to 0.46 L/kg bw/d

- Small granivorous mammal
 $\log_{10}(\text{WF}) = -0.110 + 0.734 \times \log_{10}(\text{bw})$ for non-desert species
 wood mouse: $\text{WF} = 7.4 \text{ mL/d}$; $\text{DWR} = \text{WF} - (\text{food water} + \text{metabolic water}) = 5.1 \text{ mL/d}$,
 equivalent to 0.24 L/kg bw/d

TER values are calculated by division of the relevant ecotoxicological endpoint (leaf scenario: acute; puddle scenario: acute and reproduction) by the product of PEC_{pool} or $\text{PEC}_{\text{puddle}}$, in summary termed PEC_{dw} and the DWR related to bodyweight. It is suggested that the same acceptability criteria should apply as for the dietary risk assessment.

Step 4

Options for refinement or management

Leaf scenario

As regards calculated TER values, the leaf scenario obviously constitutes an extreme worst-case scenario. It can be shown that even active substances of moderate to low toxicity ($\text{LD}_{50} > 1000 \text{ mg/kg}$) will often fail this scenario. However, incidents reported in the pasts confirm that in fact a potential for adverse effects exists that may be realised when several conditions (application of pesticides followed by rainfall or irrigation in a period of relative drought) are simultaneously met. In such cases, typical approaches for refining the risk assessment, e.g. the estimation of a PT factor, are not possible, because birds will be attracted by the water source in a way that is not observed under more regular conditions. As a consequence, a risk identified in a leaf scenario will typically have to be managed.

In Germany, where incidents corresponding to this scenario did occur in the 1980s, risk mitigation options were studied. Specific label statements exist that both warn the user that a product is hazardous for birds, and provide measures to mitigate the risk:

- Apply only at early stages of crop development;
- Provide bird netting on the crop after application;
- Avoid sprinkling/irrigation of the crop until one day after application.

The puddle scenario should be considered for assessments where the leaf scenario is not relevant, e.g.:

- Mammals (all crops);
- Application on cereals and grasses for birds;
- Applications where the morphology of the crop at the time of application makes it unlikely for pools in whorls to be formed (e.g. early stages); and
- Non foliar applications.

A puddle scenario should also be applied if the risk with regard to a leaf scenario is managed by measures that would not prevent animals from drinking from contaminated puddles on soil.

Puddle scenario

Refinements to the exposure part of this scenario can be made by using runoff concentrations directly from relevant FOCUS step 3 scenarios. This would address degradation of the active substance in a dry period after application according to FOCUS weather data. Due to the incidental nature of puddle occurrence on agricultural fields, the potential for refinement of the assessment using the 'ecological parameters' for indicator/focal species (PT) is deemed very limited.

5.6. Bioaccumulation and food chain behaviour

Bioconcentration is defined as the net result of the uptake, distribution and elimination of a substance in an organism due to waterborne exposure, whereas bioaccumulation includes all routes, i.e. air, water, soil and food (EC, 2003). Bioaccumulation often correlates with lipophilicity, thus, for organic chemicals, a $\log K_{ow} \geq 3$ indicates a potential for bioaccumulation. If this condition is met, the three issues described below (a-c) should be considered. As bioaccumulation processes often are slow and substances may be persistent, a long-term assessment is appropriate. Relevant metabolites must also be considered. For background information with regard to food chain modelling see Romijn et al. (1993, 1994), Traas et al. (1996), Jongbloed et al. (1996) and Luttik (2003).

a) Food chain from earthworm to earthworm-eating birds and mammals

For the food chain ‘earthworm to earthworm-eating birds and mammals’ two different approaches are presented. The first is the same as in EC (2002) based on dry soil concentrations (see Steps 1a-5a below). The PPR Panel concluded in 2009 that for soft bodied soil organisms (earthworms, enchytraeids, nematodes) and plants in close contact with the soil solution, pore water mediated uptake of pesticides seems mainly responsible for the effects caused, and would therefore be the relevant metric for effects assessment, and consequently also for exposure assessment (EFSA, 2009). The second approach is based on pore water concentrations and includes the gut content of the earthworms (see Steps 1b-5b below). The inclusion of the gut content of worms is particularly of importance for soils with > 1 % organic matter. This approach is equivalent to the approach taken in the Technical GD for existing chemicals (EC, 2003).

Dry soil approach

Step 1a

Select a predicted environmental concentration for dry soil (PEC_{soil} with an appropriate TWA according to the reproductive assessment) from the environmental fate section.

Step 2a

Calculate the bioconcentration factor for the earthworm ($BCF_{earthworm}$):

$$BCF_{earthworm} = \frac{0.84 + 0.012 K_{ow}}{f_{oc} \times K_{oc}}$$

With:

K_{oc} = Organic carbon adsorption coefficient

f_{oc} = Organic carbon content of soil (take 0.02 as a default value)

The equation originates from works of Jager (1998). There, the bioconcentration⁵⁸ factor for the earthworm ($BCF_{earthworm}$) is defined as concentration in earthworm related to fresh weight to concentration in soil related to dry weight ($PEC_{worm\ fresh\ weight}/C_{soil\ dry\ weight}$). The model is empirically based on non-ionised, organic chemicals in the $\log K_{ow}$ -range from 1 to 8, and it should not be applied to other types of substances or highly reactive substances. If modelling seems inappropriate it may be necessary to determine bioconcentration factors experimentally.

⁵⁸ Process leading to a higher concentration of a substance in an organism than in environmental media to which it is exposed. (<http://sis.nlm.nih.gov/enviro/iupacglossary/glossaryb.html#bioconcentration>)

Step 3a

Estimate residues in earthworms:

$$PEC_{earthworm} = PEC_{soil} \times BCF_{earthworm}$$

Step 4a

Convert residue (PEC_{worm}) to daily dose by multiplying with 1.28 (mammals) and 1.05 (birds) respectively, and compare with relevant long-term NOAEL. Multipliers are based on a 10-g mammal eating 12.8 g worms (fresh) per day, and a 100-g bird eating 104.6 g per day, according to Smit (2005) (see Appendix L).

Step 5a

Compare the toxicity-exposure ratio to the respective trigger value:

TER > 5

No further refinement required.

TER < 5

Further refinement required (see section 6).

In addition to the refinement options in section 6, another option would be to carry out a BCF study with earthworms rather than to rely on the QSAR approach used at the Tier 1.

Further, rather than assuming equilibrium and calculating BCF values, another option is the modelling of the internal body burden of earthworms by using information on uptake and elimination kinetics in earthworms as well as information on dissipation kinetics in soil.

Pore water approach

(method equivalent to EC, 2003)

Step 1b

Select a pore water concentration ($C_{porewater}$ with an appropriate TWA according to the reproductive assessment) from the environmental fate section.

Step 2b

Calculate the bioconcentration factor for the earthworm ($BCF_{earthworm}$) related to porewater:

$$BCF_{earthworm} = \frac{(0.84 + 0.012 \cdot K_{ow})}{RHO_{earthworm}}$$

Where for $RHO_{earthworm}$ by default a value of 1 [$kg_{wwt} \times L^{-1}$] can be assumed (Jager, 1998).

Step 3b

Calculate the concentration in earthworms:

$$C_{earthworm} = \frac{BCF_{earthworm} \times C_{porewater} + C_{soil} \times F_{gut} \times CONV_{soil}}{1 + F_{gut} \times CONV_{soil}}$$

Where:

$$CONV_{soil} = \frac{RHO_{soil}}{F_{solid} \times RHO_{solid}}$$

With:

$CONV_{soil}$	conversion factor for soil concentration wet-dry weight soil	$[kg_{wwt} kg_{dwt}^{-1}]$
F_{solid}	volume fraction of solids in soil	$[m^3 m^{-3}]$
F_{gut}	fraction of gut loading in worm	$[kg_{dwt} kg_{wwt}^{-1}]$
RHO_{soil}	bulk density of wet soil	$[kg_{wwt} m^{-3}]$
RHO_{solid}	density of solid phase	$[kg_{dwt} m^{-3}]$

Step 4b

Convert residue ($C_{earthworm}$) to daily dose by multiplying with 1.28 (mammals) and 1.05 (birds) respectively, and compare with relevant long-term NOAEL. Multipliers are based on a 10-g mammal, eating 12.8 g worms (fresh) per day, and a 100-g bird, eating 104.6 g per day, according to Smit (2005) (see Appendix L).

Step 5b

Compare the toxicity-exposure ratio to the respective trigger value:

TER > 5

No further refinement required.

TER < 5

Further refinement required (see section 6).

In addition to the refinement options in section 6, another option would be to carry out a BCF study with earthworms rather than to rely on the QSAR approach used at the Tier 1.

Further, rather than assuming equilibrium and calculating BCF values, another option is the modelling of the internal body burden of earthworms by using information on uptake and elimination kinetics in earthworms as well as information on dissipation kinetics in soil.

b) Food chain from fish to fish-eating birds and mammals

A simple worst-case assessment can be conducted according to the following steps:

Step 1

Take the highest PEC_{water} based on the regulatory acceptable concentration (RAC^{59}) from the environmental fate section and multiply this value with an appropriate TWA value according to the reproductive assessment.

Step 2

Take the whole-body BCF_{fish} from the aquatic section.

⁵⁹ It might be impractical to have to wait for the RAC to be determined in the aquatic ecotoxicology section; instead the highest relevant PEC for bioaccumulation could be used. The RAC could be used as a refinement option.

Step 3

Estimate residues in fish:

$$PEC_{fish} = PEC_{water} \times TWA \times BCF$$

Step 4

Convert residue (PEC_{fish}) to daily dose by multiplying with 0.137 (mammals) and 0.205 (birds) respectively, and compare with the relevant long-term NOAEL. Multipliers are based on a 3000-g mammal, eating 425 g fresh fish per day, and a 1000-g bird, eating 159 g per day, according to Smit (2005) (see Appendix L).

Step 5

Compare the toxicity-exposure ratio to the respective trigger value:

TER > 5

No further refinement required.

TER < 5

Further refinement required (see section 6).

In addition to the refinement options in section 6, and rather than assuming equilibrium and calculating BCF values, another option is the modelling of the internal body burden of fish using information on uptake and elimination kinetics in fish as well as information on dissipation kinetics in water.

c) Biomagnification in terrestrial food chains

Substances that have a potential for biomagnification, i.e. the whole-body residue in an animal at steady state is higher than the residue in its food (biomagnification factor $BAF > 1$)⁶⁰, are of concern for terrestrial food chains. For substances with such a property, exposure may increase along the food chain, and top predators are particularly at risk. In Annex VI of Directive 91/414/EEC a trigger value of 1 is provided for the BAF (not quite correctly termed 'BCF') which is specified as related to fat tissue. This trigger implies some degree of precaution since, when exposed to lipophilic organic chemicals the whole body residue is lower than the residue in fat tissue. The following step-wise approach is proposed:

Step 1

Obtain the information from the toxicology section on the ADME studies and from the residue section on the metabolism studies with livestock. A brief conclusion from these assessments with regard to bioaccumulation is reported in the list of endpoints. If the bioaccumulation potential is stated as being low then, no further assessment is required. If this is not the case, Step 2 has to be followed.

Step 2

Estimate the food-to-organism bioaccumulation factor according to the following equation:

$$BAF_{organisms, food} = \frac{\alpha \times FIR}{k_2}$$

⁶⁰ See also IUPAC-definition: <http://sis.nlm.nih.gov/enviro/iupacglossary/glossarya.html>

With

- α = Fraction of ingested dose that is absorbed; available from toxicokinetic studies
- $k_2 = \ln(2)/T_{1/2}$ Rate constant for depuration; should also be available from toxicokinetic studies ($T_{1/2}$ = elimination half-life)
- FIR = Food intake rate relative to body weight.

Step 3

With the information provided in Appendix G, the FIR/bw can be calculated for any carnivorous or insectivorous species of concern.

Step 4

If the BAF according to this calculation is clearly below 1, no further assessment is required. If it is higher, possibilities for conducting a detailed food chain modelling as described in Appendix S should be considered.

6. Higher tier risk assessment – refinement steps

A higher-tier assessment is required when the results of assessments at lower tiers breach the relevant trigger values (e.g. $TER < 10$ for acute risks, 5 for reproductive risks⁶¹). The general aim of higher-tier assessment is defined by the ‘unless’ clause in point 2.5.2.1 of Annex VI of Directive 91/414/EEC. There it states that “no authorisation shall be granted ... unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact occurs after use of the plant protection product under the proposed conditions of use.”

The definition of ‘unacceptable impacts’ is discussed in detail in Appendix C. It indicates that unacceptable impacts include ‘long-term repercussions for abundance and diversity of non-target species’ and ‘visible mortality’. The term ‘clearly established’ is not defined, but suggests that a high level of certainty is required. However, as discussed in Appendix C, it is not practical to assess these protection goals directly in first-tier assessments. Therefore this Guidance Document has defined a surrogate protection goal for use in first-tier assessments. The actual and surrogate protection goals are defined as follows:

- The actual protection goal is to provide a high certainty that no visible mortality and no long-term repercussions on abundance and diversity will occur.
- The surrogate protection goal is to make any mortality or reproductive effects unlikely.

The surrogate protection goal is more conservative than the actual protection goal, but the actual protection goal is impractical⁶² to assess at Tier 1.

In higher-tier assessments, either protection goal can be used. It may be possible to show by refined assessment that the surrogate protection goal can be satisfied. However, if this is not possible then it would be necessary to address the actual protection goal directly. This could be done by assessing for example the percentage of mortality and the likelihood that it would be ‘visible’, or the probability of long-term repercussions for abundance and diversity. However, higher-tier assessments may also be based on the more conservative surrogate protection goal, if that is a more practical option for the case under assessment (e.g. a refined TER calculation, see section 6.1.).

⁶¹ Or alternative triggers if new ones are adopted.

⁶² Visible mortality doesn’t relate to any particular percentage of mortality, which could be predicted. Likewise, long-term population impacts require refined assessments and cannot be done at Tier 1 (see Appendix C).

A key first step before commencing any refined assessment is to define the objectives and scope for the case under consideration. This includes the types of effects (acute or reproductive) and scenarios to be considered and should be guided by the results of the first-tier assessments. It may be efficient to start by focussing on those scenarios which gave the worst (i.e. highest risk) results in the first-tier assessment. However, if refined assessment shows the risk for those scenarios to be acceptable, it may be necessary to conduct additional refined assessments for all other scenarios which breach the first-tier trigger values, unless it can be justified that the refined assessment can be extrapolated between scenarios.

In the following sections, specific options for higher-tier assessment are described in more detail. They are summarised in Table 22, with an indication of their possible contribution and some of the issues to consider when choosing between them.

There are no general rules for choosing which option(s) to adopt for refined assessment. However, it may be helpful to consider the following factors, together with any others which appear relevant:

- The degree by which the lower tier trigger values were breached. Stronger evidence is likely to be required if the triggers were breached by a large margin. This is especially true for assessment of acute risks from sprayed pesticides, as the field study analysis implies a rather strong expectation of mortality for pesticides which fail Tier 1 by more than a small margin (see Figure 4 in Appendix C). Removing this expectation would require correspondingly strong evidence in the higher-tier assessment.
- The general potential of each option to reduce the estimate of risk, and/or reduce uncertainty. Refinements of dietary exposure assessment may provide only limited benefit, but this may be sufficient if the first-tier triggers were not breached by a large margin. Field studies are much more effective for reducing uncertainty, but also more costly. Population modelling has the advantage of addressing long-term repercussions directly, but this may be outweighed by uncertainty about the extra parameters that have to be estimated.
- Indications from first-tier studies, e.g. indications of strong avoidance, rapid metabolism or rapid degradation may indicate that these would be fruitful targets for refinement.
- The availability and relevance of existing data, and the cost and practicality of generating new data.
- Ethical and policy preferences for minimising animal testing.

It might also be advisable to consult with the relevant authorities before finalising the choice of refinement options.

Since the variation in toxicity between species is one of the largest sources of uncertainty affecting risk assessment, it is a general issue that may influence the choice of refinement method. There is up to one or two orders of magnitude variation in acute LD₅₀ between the most and least sensitive bird species (Luttik and Aldenberg, 1997; also see Figure 1 in Appendix C). This implies up to one or two orders of magnitude uncertainty in estimating the LD₅₀ for the focal species⁶³, and therefore up to one or two orders of uncertainty in those refinement options that involve modelling effects on a focal species (including refined TERs and body burden modelling). It also implies up to one or two orders of magnitude uncertainty in the relation between any species chosen for testing and the species actually exposed in the field. This, in turn, implies at least⁶⁴ one or two orders of magnitude uncertainty in extrapolating from higher-tier studies with captive animals (e.g. avoidance studies and pen studies) to species actually exposed in the field. It also implies up to one or two orders of magnitude uncertainty when extrapolating from a single field study site to other study sites where different species may be present. The only refinement options that avoid this problem are wildlife incident data (which underestimate risk for other reasons, see section 6.5) and field studies with multiple sites in a sufficient

⁶³ This uncertainty is progressively reduced when LD₅₀s are available for more than one species.

⁶⁴ This will be increased by additional sources of uncertainty such as lab to field differences in exposure patterns and sensitivity.

diversity of conditions to encounter a representative range of species. This does not mean that field studies on multiple sites are the best option, because simpler or less costly options may be sufficient in many cases, but it does make it essential to take careful account of uncertainty about toxicity when using other options.

Regardless of the choice of options for the refinement of the assessment, it should be noted that, they are not sufficient on their own but should be considered as inputs to the final steps of risk characterisation and decision-making. Because there is often more than one line of evidence for characterising the risk, this will often require a weight-of-evidence approach. Practical approaches for risk characterisation and weight-of-evidence assessment are discussed in section 6.9. It is emphasised that weight-of-evidence assessment is not itself a method of refined assessment, nor is it a substitute for refinement options such as those listed in Table 22. Instead, it is an approach for weighing and combining the results of first-tier and refined assessments to form an overall characterisation of risk, as described in section 6.9. Guidance on risk management considerations in decision-making is included in section 7.1.

Table 22. Overview of options for higher-tier assessment. (Continued on next page.)

Refinement option	Possible objectives	Issues to consider	Section
Refined model of exposure for dietary route	Demonstrate that effects due to dietary exposure will not exceed an unacceptable level	<ul style="list-style-type: none"> • Addresses only dietary exposure (unless combined with estimation of other routes, see below) • Does not remove high uncertainty due to variation in toxicity between tested and focal species • Is difficult to interpret level of impact (e.g. mortality or population effects) implied by TER • Is difficult to assess level of protection without probabilistic calculations (comparison of refined TER with lower tier trigger value is not valid). 	6.1
Modelling non-dietary routes of exposure	Demonstrate that non-dietary routes are negligible, or estimate their contribution	<ul style="list-style-type: none"> • Equations exist for approximate estimates of drinking water intake and inhalation • Equations also exist for dermal exposure but require estimation of contact areas and transfer rates that will vary with species and habitat and would be very uncertain to estimate • High uncertainty estimating effects, due to variation in toxicity between tested and focal species. 	5.5 (dw only)
Specialised avoidance/ repellency studies with captive birds	Demonstrate that avoidance is sufficiently strong to ensure that lethal effects will not exceed an acceptable level	<ul style="list-style-type: none"> • Only addresses dietary route of exposure • Need to ensure test species is among the most sensitive for this pesticide (generally not known), or test at elevated concentrations to simulate situation for more sensitive species (which could introduce other factors, e.g. taste repellency not present at normal concentrations) • Need to ensure initial feeding rate is close to maximal not just for test species but also other sensitive species • Need to assume that the effect of other relevant factors, e.g. avoidance threshold and delay time, uptake, metabolism (EFSA, 2005a), is the same in untested species. 	6.2
Body burden modelling	Demonstrate that the ADME characteristics of the pesticide will prevent an unacceptable level of effects	<ul style="list-style-type: none"> • Can address all exposure routes IF non-dietary uptakes can be modelled with sufficient certainty • Extrapolation of avoidance threshold and lethal dose between species is highly uncertain • Estimates of ADME parameters have substantial uncertainty even for tested species (EFSA, 2005a) • Almost no knowledge of how ADME parameters vary between species and whether they do so in a correlated way. 	6.3
Field studies	Demonstrate that effects occur on acceptable proportion of occasions, or that the number of individuals and species affected is acceptable	<ul style="list-style-type: none"> • Addresses all routes of exposure • Need sufficient number and size of sites, and sufficient variety of ecological conditions, to ensure opportunity for sensitive species to be present and to be exposed in a representative range of conditions, and to give adequate statistical power to detect effects and/or quantify their frequency. 	6.4

Refinement option	Possible objectives	Issues to consider	Section
Semi-field studies (pen studies)	Demonstrate that under realistic exposure conditions, effects will not exceed an acceptable level	<ul style="list-style-type: none"> • Potentially addresses all exposure routes, if appropriately designed • Captive animals are confined to the treated area, so this aspect of exposure is conservative • Other aspects of exposure and effects may be unconservative (tend to underestimate risk): <ul style="list-style-type: none"> ○ Energy expenditure and hence food intake and exposure are reduced ○ The rate of feeding is unlikely to approach levels achieved by free-living animals, unless conditions are manipulated to achieve this (e.g. restriction of feeding time) ○ There is no way to ensure that the study species is more sensitive (has a lower LD₅₀) than other species exposed in the wild • Level of protection achieved is very uncertain, could be either conservative or very unconservative. 	6.4.5
Data on wildlife incidents	Demonstrate that acute mortality occurs at least under some circumstances	<ul style="list-style-type: none"> • Reported incidents may be a very small fraction of those that occur, so absence of reported incidents does not imply no occurrence. 	6.5
Population modelling	Demonstrate acceptably low risk of long-term repercussions for abundance and diversity	<ul style="list-style-type: none"> • Can provide quantitative estimates of long-term repercussions for abundance and diversity, the measure of population impact specified in Annex VI of Directive 91/414/EEC. • Relatively complex methodology requiring specialist population modelling expertise. • No guidance or officially-accepted methods for use in pesticide registration, so studies have to be produced and evaluated case-by-case. • Requires data on population parameters which may be difficult to obtain or very uncertain. • Requires estimates of impact on individuals as input, so uncertainty of these will also be included. • Overall uncertainty in estimated population impacts likely to be very uncertain. 	6.7
Refinements of phase-specific reproductive assessment	Demonstrate reduction in estimated risk when account is taken of relative timing of reproduction and pesticide applications	<ul style="list-style-type: none"> • Avoids highly conservative and unrealistic first-tier assumption that reproduction always coincides with period of maximum exposure. • Addresses only dietary exposure (unless combined with estimation of other routes, see above). • Does not remove high uncertainty due to variation in toxicity between tested and focal species. 	6.7 and App. 16
Additional toxicity studies	Reduce uncertainty about the distribution of toxicity between species, e.g. to justify reduction of uncertainty factors	<ul style="list-style-type: none"> • Although this reduces one of the most important sources of uncertainty, it has been discouraged for policy reasons, to minimise animal testing. • Even when more species are tested, there is still substantial uncertainty in estimating the LD₅₀ for any particular untested species (i.e. a focal species). • No established guidance on how to reduce uncertainty factors when more species are tested. 	2.3
Additional toxicity study on the identified critical life stage	Addresses the major concern highlighted in lower tier assessment, and generates more appropriate end-points for that phase	<ul style="list-style-type: none"> • Avoids the mismatch between the length of exposure in the study (e.g. 22 weeks for bird report study) and the length of the exposure estimate (1 or 21 day) in the risk assessment. • Difficult to decide as to how long the birds/mammals should be dosed before the sensitive stage is reached (in case of accumulating substances). • Subject to the normal uncertainty about extrapolation of toxicity between species. 	4.3, 4.4

6.1. Refined modelling of dietary exposure and risk

Under the former Guidance Document (EC, 2002), the most commonly used option for higher-tier assessment of both acute and reproductive risks was refinement of the worst-case dietary exposure model, replacing the default values with others that were considered more realistic, e.g. replacing PT (the proportion of food obtained from treated fields) = 1 with a value estimated from field observations or radio-tracking. This continues to be an option under this revised Guidance Document. However, it is essential that such refinements are supported by relevant evidence (see the following sections).

In addition, careful consideration must be given to how refined dietary risk estimates can be used in risk characterisation and decision-making. It is not valid simply to compare a refined TER to the same trigger value used at Tier 1 and assume that the same level of protection is achieved. Due to the importance of this issue, it is discussed first, followed by an overview of refined dietary assessment and then a series of sections providing guidance on individual components of the assessment.

6.1.1. Level of protection in refined dietary exposure assessment

The first-tier assessments have been carefully constructed to provide an appropriate level of protection (section 3 and Appendix C). This level of protection is a result of both the particular inputs used in calculating the first-tier TER and the size of the trigger value. If a refined TER is calculated with less conservative inputs, then the level of protection will decrease⁶⁵. Therefore it is essential that the level of protection should be reassessed for every higher-tier assessment, to ensure that it is still sufficient to meet the protection goals. This may be done by starting with the weight-of-evidence assessment carried out for the first-tier assessment (see Appendix C), and adjusting it to take account of the changes made to the dietary exposure parameters in the higher-tier assessment.

The need to re-evaluate the level of protection for every higher-tier assessment applies to all types of assessment (acute and reproductive risks for all types of pesticides). However, it requires different considerations in assessments for acute risks to birds from sprayed products, because for these assessments the level of protection has been established partly by comparison to the field data (section 3 and Appendix C).

For example, in the past, one of the most common refinements has been to reduce the value used for PT (e.g. based on radio tracking data) on the grounds that most individuals have PT less than 1. However, the birds that were present in the field studies used to evaluate the level of protection (LoP) for acute assessments of sprayed pesticides also had values of PT less than 1. Therefore the effect of lower values of PT in reducing acute risk is already reflected in the outcomes of the field studies. Consequently, the evaluated level of protection for Tier 1 (Appendix C) already takes account of lower PT values, so replacing PT = 1 with lower values in a refined TER will double-count their effect⁶⁶. The same logic applies to other common refinements including changes to PD and using pesticide-specific residue data, or arguments based on avoidance and/or metabolism: the same factors would also have been operating in the field studies (to varying extents) and will therefore be double-counted (to varying extents) if a refined acute TER is compared to the Tier 1 trigger value. This does

⁶⁵ It can be assumed that the relation between TER and level of protection asymptotes at some point. If the first-tier assessment was beyond this point, i.e. was extremely conservative, then moderate changes in the TER might not reduce the level of protection, but the field study analysis suggests that for acute risks to birds at least the first-tier assessment is not so conservative (Appendix C, Figure 4).

⁶⁶ To explain this another way: consider the points in the graph relating evidence of mortality in field studies to acute TER (Appendix C). The TERs in this graph are based on default TER of 1. If the default PT was set to a lower value, all the TERs will increase by the same factor, so all the points on the graph would shift to the right by the same amount. However, the probabilities of mortality for each point would remain unchanged as they reflect the actual outcomes of the field studies. Therefore, to retain the same level of protection, the TER threshold for acceptable risk would also need to be increased, again by the same factor.

not mean that refined TER calculations should not be done. Specifically, if there is evidence that one (or more) of the inputs to the TER calculation for a particular pesticide consistently differs from the range of values expected for the pesticides in the original field studies, in a way that reduces the risk, then the refinement can be supported. This might be the case if, for example, it could be shown that the distribution of PT (and particularly its upper tail, which is most relevant for acute risk), is lower than most of the distributions that would have been expected in the original field studies; or if, the pesticide is more strongly avoided in field conditions than most of the pesticides in the original field studies (organophosphates and carbamates). It is clear, then, that the level of protection provided by refined acute assessments must be re-evaluated case by case, including careful comparison with the field study calibration (Appendix C).

For all other types of assessment (apart from acute/spray), the level of protection for Tier 1 was based only on qualitative evaluation (due to lack of sufficient field data). For those types of assessments there is more scope for refinement, if they provide real evidence that can improve on the evidence and judgements that were available for the original evaluation of level of protection in Appendix C. This should therefore be done by starting with the weight-of-evidence assessment that was carried out for the first-tier assessment (see section 3 and Appendix C), and adjusting it to take account of the specific evidence provided by the refined assessment. Note that this requires reviewing not only the evaluation for the specific parameter for which refined data is provided (e.g. PT), but also the level of protection considering all parameters and uncertainties. This is necessary because, in reaching a judgement about the level of protection overall, account was taken of the fact that the default assumptions for some parameters (e.g. PT = 1) are conservative while others (e.g. exclusion of non-dietary routes) are unconservative (see Tables in Appendix C for detail).

In summary, **a refined TER calculation is one option for characterising the risk, but it is not valid to compare the resulting TER with the first-tier trigger value and assume that the same level of protection will automatically be achieved. Rather, the level of protection achieved by refined TERs must be re-evaluated in every higher-tier assessment** to evaluate whether the ‘unless’ clause is satisfied, i.e. whether it is established with sufficient certainty that no unacceptable impact will occur. Practical approaches for making this evaluation are discussed in section 6.8.

6.1.2. Overview of refined dietary exposure assessment

This section describes how to plan a higher-tier assessment of dietary exposure and introduces the sub-sections, which provide guidance on individual components of the assessment.

The first step of any higher-tier assessment should be to define the type(s) of effect, focal species, population, spatial scale and time period to be considered; define the measure of risk that will be produced; specify an appropriate assessment model to generate it; and decide how to deal with variability and uncertainty. Currently, there is no single established approach so this must be defined case by case according to the needs of the situation. Among the factors to be considered are the ones listed below. Note that some of the factors are more readily refined with existing methodologies (e.g. selection of focal species, inputs for exposure assessment) whereas others require methodology that is not yet well established for regulatory use (e.g. probabilistic modelling), or the use of additional animal studies which is discouraged for animal welfare and policy reasons.

Type of effects. The survey of Member States and stakeholders undertaken by EFSA (2008, Appendices 1a and 1b) indicated that visible mortality and population effects should be the focus of concern. Assessing population effects will require qualitative or quantitative assessment of the relationship between test endpoints (lethality, reproductive performance) and appropriate measures of population effect. The time period for exposure assessment is generally dictated by the type of effect considered (e.g. 1 day for mortality, 1 day or longer periods for reproductive effects).

Focal species. For higher-tier assessment of the risk for birds and mammals it is usual to focus on ‘focal’ species to avoid modelling exposure for multiple species. These FS are selected to represent a

realistic worst case and could comprise more than one species. See section 6.1.3 for guidance on how to identify appropriate focal species.

Population and spatial scale. The first-tier assessment implies a hypothetical population of animals confined to a single treated field. Higher tier assessment often uses data on the proportion of an animal's daily diet obtained in habitat treated with pesticide' (PT). This implies a population of animals moving in landscape with both treated and untreated areas. This opens up additional questions. Should the assessment refer only to the subset of individuals which visit treated fields, or include also individuals which never do so? Should it be assumed that a pesticide is applied to every field of the relevant crop? Should it be assumed that these fields are treated simultaneously or over a period of time? Is it assumed that food availability and dietary choices of the focal species are different or the same in different crops and habitats, and in treated versus untreated crops? These questions have significant implications for the design of the exposure model (see below). Introducing increasing realism rapidly makes the exposure model very complex, so it is common to start with a relatively simple scenario that is designed to be conservative, and only incorporate more complex representations of reality when this proves necessary.

Measure of risk to be produced. In the past, refined assessments for birds and mammals have generally used the same measure for risk characterisation as the first-tier assessment: the toxicity-exposure-ratio (TER). Consideration could also be given to alternative measures of risk such as percentage of mortality, percentage of reproduction attempts affected, or higher level endpoints such as population change over a specified period. These may be more interpretable for risk managers, but require additional data or assumptions (e.g. slope of the dose-response to estimate percentage of mortality).

Exposure model. The form of model required to estimate dietary exposure depends on the population considered, how the assessor decides to represent spatial scale (see above), and on the timescale of the assessment. Other influential factors include the number of food types considered and whether these are the same in each part of the landscape. Crocker (2005) shows how the assumptions made can influence the form of dietary exposure model required. However, it must be noted that the equations presented by Crocker (2005) include a factor to represent avoidance, although Crocker identifies several problems with this in his text. EFSA (2004, 2005a) have concluded that including avoidance in exposure modelling in this way (at least for substances where avoidance is determined by a threshold dose, rather than by a concentration-related sensory response) is not appropriate. Appendix G includes a simple form of dietary exposure model that allows for multiple foods and the presence of untreated habitat. Consideration should also be given to the inclusion of other routes of exposure in the assessment. Otherwise these must be considered as significant sources of uncertainty (potential under-estimation of risk) in the overall characterisation of risk (section 6.8). See Appendix 2 of EFSA (2008) for a discussion of the importance of dermal exposure.

Toxicity model. The form of the model required for toxicity depends upon the measure of risk required, and on how extrapolation between species will be accounted for. If the desired output for a risk assessment is a TER, its calculation requires an estimate of the LD₅₀ or NOAEL. In principle, this should be an estimate of the relevant toxicity endpoint (LD₅₀ or NOAEL) for the focal species being assessed. In practice, the focal species is never tested, so its LD₅₀ or NOAEL is uncertain and could lie either above or below the tested species. This uncertainty can be represented by a distribution in a probabilistic risk assessment, although the shape and parameters (mean and variance) of the distribution are uncertain. In deterministic assessments it is usual to make the conservative assumption that the focal species is more sensitive than the tested species, and use an extrapolation factor to allow for this. The TER trigger value used in first-tier assessments is (or includes) such an extrapolation factor. In higher-tier assessments, one option is to continue using the geometric mean of the LD₅₀s or NOAELs for the tested species, and divide it by the same extrapolation factor as in Tier 1. This should provide at least the same average level of protection in the effects assessment as was present in Tier 1, but does not quantify that level of protection (EFSA, 2005a; and section 2.3.1 and Appendix 7 of EFSA, 2008). Another option is to use one of the other methods 3-5 as described by EFSA (2005a).

These methods are designed to achieve a specified level of protection and to take account of the decreased uncertainty when more species are tested. However, for birds and mammals, methods 3 - 5 are currently applicable only to the LD₅₀, because they require estimates of variation between species that are not available for other bird and mammal endpoints⁶⁷.

If the required output is not a TER but another measure of risk, different model structures and data or assumptions may be required. For example, the estimation of the percentage of mortality would require an estimate of the slope of the dose-response as well as the LD₅₀, and again these should refer to the focal species. Slopes are available from some but not all LD₅₀ studies, and extrapolating the slope to untested focal species will be very uncertain. There is even less information about variation between individuals in other responses (e.g. reproductive effects).

Methods for dealing with variability and uncertainty. Consideration of variability and uncertainty is an essential requirement for addressing the ‘unless’ clause. The variability of impacts must be considered to decide whether they are acceptable, and uncertainties in the assessment must be considered to decide whether acceptability is ‘clearly established’.

At Tier 1, variability and uncertainty are addressed by including some conservative assumptions in the assessment and comparing the result with a trigger value that is considered to provide an appropriate level of protection. An indication of the level of protection achieved by the first-tier acute assessment is provided by the analysis of field study data in Appendix 2 of EFSA (2008).

As explained at the start of this section, the first-tier trigger values are not applicable in higher-tier assessments. Therefore, other methods must be used to take account of variability and uncertainty. The range of different impacts that are made possible by the variability and uncertainty of exposure and effects needs to be taken into account. There are two options for doing so:

- *Scenario analysis.* This is a practical approach that simply involves repeating the assessment for a limited number of selected scenarios. In each scenario, a single value is assumed for each variable or uncertain parameter, leading to a single estimate of impact. Different values can be selected for different scenarios, e.g. a 90th percentile residue might be assumed in one scenario and a 50th percentile residue in another. Each scenario can be described in terms of its assumptions, e.g. when residues and PT are at their 90th percentiles, and an uncertainty factor of 10 is applied to the geometric mean of the LD₅₀s, the TER is X. If the scenarios include a range from worst case to ‘best case’ assumptions then the range of results gives an indication of the range of possible impacts.
- *Probabilistic modelling.* This uses probability distributions to represent sources of variability and uncertainty that influence the assessment, and produces a distribution that estimates the variability and uncertainty of the impact.

Scenario analysis has the advantage of being simple to compute, and is useful for indicating the range of possible impacts. If even the worst-case impact is acceptable, no further assessment is required. However, if the best-case impact is acceptable but the worst-case is not, the relative probability of the different scenarios needs to be considered. Scenario analysis may not be sufficient for this, since it only shows that a range of impacts are possible. It does not provide any quantitative estimate of how often a given impact will occur, nor of how uncertain the impact is for each scenario. Therefore the assessor will have to make a subjective assessment, based on the nature of the assumptions made for each parameter⁶⁸. This is very difficult, because the influence of different parameters depends not only on the value that is chosen, but also on the shape and width of their distributions and how they are combined in the model. For example, it might be thought that taking the 99th percentile of one parameter and means for all other inputs would result in a conservative estimate of impact, but if the

⁶⁷ See Luttik et al. (2005) for a discussion of inter-species extrapolation of long-term toxicity.

⁶⁸ It is suggested that this should be done using the approaches outlined in sections 6.8 and 6.9 for weight of evidence and qualitative evaluation of uncertainty.

model were insensitive to the parameter that is set to the 99th percentile then the result could actually be close to the mean impact. The difficulty of evaluating the conservatism of a refined dietary assessment subjectively is illustrated by Figure 2.

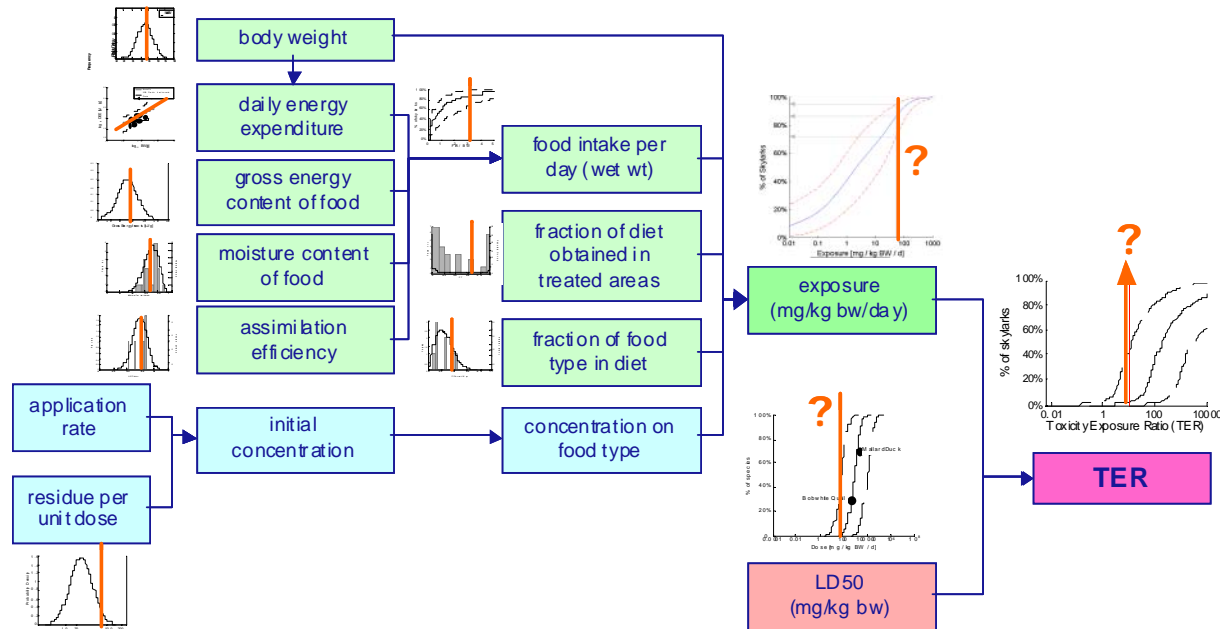


Figure 2. A deterministic refined assessment of dietary exposure and risk involves choosing a single value for each of the parameters and using them to estimate a single value for the output (e.g. TER or % mortality). These single values are illustrated by the thick lines in the graphs for each input and output. The conservatism of the output (i.e. where the deterministic TER sits within the ‘true’ distribution of TERs) depends on the combined effect of the conservatism of all the inputs and is difficult to judge without quantitative (probabilistic) modelling.

Probabilistic modelling is a more complex approach but may be worth considering if scenario analysis proves insufficient for decision-making. Probabilistic modelling takes account of the full distribution of values for each input and uses them to estimate a distribution for the output. Thus it estimates both the range of possible impacts and their relative probabilities, providing a quantitative basis for addressing the ‘unless’ clause. However, it is much more complex than scenario analysis and requires significant statistical expertise to be applied correctly. Also, it is not yet generally accepted for use in regulatory assessment, and there is no established guidance for its use in relation to pesticide risks (although useful guidance has been published in other areas, e.g. US EPA, 1997).

Regardless of the use of either scenario analysis or probabilistic modelling, it will never be practical to quantify all sources of variability and uncertainty. Therefore, in order to properly address the ‘unless’ clause, it is essential for every refined assessment to be accompanied by a list of unquantified sources of variation and uncertainty, and a qualitative evaluation of their potential influence on the assessment outcome. Some approaches for this are discussed in section 6.7.

Whatever the outcome of a refined assessment, it should not be the sole basis for decision-making. Instead, decision-making should consider all relevant lines of evidence, including the outcome of the first-tier assessment. The outcome of the first-tier assessment is especially important in the case of acute risks from sprayed pesticides, because its relevance to effects in the field has been characterised

by the analysis of field studies (Appendix 2, EFSA, 2008). Some approaches for weighing different lines of evidence to form an overall characterisation of risk are discussed in section 6.9. It is emphasised that weight-of-evidence assessment is not a replacement for quantitative refinement of the dietary exposure assessment. Instead, it is an approach for weighing and combining the results of first-tier and refined dietary assessments, together with the results of any other refinement options that may be used, to form an overall characterisation of risk.

The following sections provide guidance on methods to assess some of the parameters required for a refined exposure assessment. Some of these methods can be costly to implement, therefore it is advisable to consider carefully the contribution they might make to refine the assessment. In general, it will be efficient to concentrate resources on those parameters that contribute most to the uncertainty of the assessment outcome. However, the choice of which parameters to refine will also be influenced by other factors. For example, toxicity is probably the biggest source of uncertainty in bird and mammal assessments, but for ethical and policy reasons testing of additional species is strongly discouraged. This limits the contribution that refined modelling of exposure and effects can make to higher-tier assessment.

6.1.3. Identification of focal species

This chapter describes the identification and selection of species used in the risk assessment for birds and mammals.

Indicator species

The risk assessment starts by using ‘indicator species’. This is a realistic worst case and acts as a screening step by eliminating all those substances that clearly pose a low risk to birds and mammals. This ‘indicator species’ is not a real species but it is representative of all species that may occur in a particular crop at a particular time. It has a high food intake rate, and consumes one type of food which in turn has high residues on or in it (see Tables 6 and 8). The indicator species is fixed and can not be altered, if refinement is required, then it is necessary to progress to the next stage and use a ‘generic focal species’.

Generic focal species

If the active substance, and associated product and its use, fails the screening step, it is possible to refine the risk via the use of a ‘generic focal species’. This is not a real species, however it is considered to be representative of all those species potentially at risk. A ‘generic focal species’ is based on ecological knowledge of a range of species that could be at risk. It should be noted that this species still has a high food intake rate, however it may consume a range of food types rather than just one as for the indicator species. The ‘generic focal species’ is also considered to be a representative of the types of birds or mammals that occur across Member States (see tables in Annex I). The generic focal species is fixed and can not be altered. If refinement is required, then it is necessary to progress to the next tier and to use a ‘focal species’.

Focal species

If an active substance, and its associated product and use, fails when the ‘generic focal species’ is used, it is possible to further refine the exposure element of risk via the use of a ‘focal species’ (FS). This is a real species that actually occurs in the crop when the pesticide is being used. The aim of using a ‘focal species’ is to add realism to the risk assessment insofar as the assessment is based on a real species that uses the crop. It is essential that the species actually occurs in the crop at a time when the pesticide is being applied. Further, it is essential that this species is considered to be representative of all other species from the feeding guild that may occur in the crop at that time highlighted at earlier stages of the risk assessment. As a ‘focal species’ needs to cover all species present in the crop, it may become necessary to assess the risk for more than one species (considering different feeding guilds or different breeding times) to ensure that the chosen ‘focal species’ has the highest exposure. Details on

how to determine a focal species for a specific crop are presented in Appendix M of this Guidance Document.

6.1.3.1. Identification of focal species using targeted observation data

The identification of focal species using targeted observation data can involve one of two methods, i.e. the transect method and the field survey method. Both methods involve surveying fields with the appropriate crop, its correct growth stage and at a time of the year that is relevant to the proposed use. It should be noted that it is necessary to survey a range of fields to enable an indication of the range of birds that may occur as well as the frequency with which they occur in each field and per survey. Once the survey data have been collected it is necessary to determine the focal species. The selection of the species 'covering' all other species present in the field, needs to take into account issues such as feeding strata, food intake rate, body weight of potential focal species and diet to ensure species with the highest potential exposure are considered. It should be noted that a focal species is not automatically the species that was most frequently seen, but that it should represent the feeding guild(s) that has/have raised concern at earlier stages in the risk assessment as well as other species.

6.1.3.2. Extrapolation of study results from one MS or zone to another

Studies to determine a focal species in one Member State or one zone, may possibly be taken into account to support uses of pesticides in other zones, however, straight 'read across' is not possible. A focal species occurring in one MS or one zone could only be used for the risk assessment for another zone if it satisfies the criteria outlined above, i.e. the species being present, prevalent, occurring frequently and, more importantly, representing the feeding guild(s) that has/have raised concern at earlier stages in the risk assessment.

In summary:

- In order to refine the risk assessment a focal species should be identified and be determined using appropriate techniques (see Appendix M of this Guidance Document).
- In determining a focal species, it is important to consider the risk highlighted and hence select a species that is representative of the feeding guild highlighted at lower tiers.
- In selecting a focal species, it is essential to ensure that the chosen species covers all other species. It may be necessary to have more than one focal species, to ensure that all appropriate species are covered.

It is possible to extrapolate from a focal species from one MS or one zone to another, providing it satisfies all relevant criteria in terms of being present, prevalent, occurring frequently and representing feeding guilds at risk.

6.1.3.3. Identification of focal species using other sources of information

The ideal and most reliable way to determine a focal species is via field work (see section 6.1.3). However, it may be possible to determine a focal species by evaluating published data. In the grey literature, data are available for which the aim has been to determine focal species in certain crops at certain times of the year⁶⁹. If these data are to be used, it is essential to ensure that the crop and time of the year, as well as the agricultural environment are relevant for the assessment.

Other data that may be used to determine focal species may include survey or census information. When considering such data, it is important to ensure that it includes information not only on the identity of species that are present in a particular crop but also their quantity. It should be noted that a

⁶⁹ See e.g. http://www.pesticides.gov.uk/uploadedfiles/Surveys_short1.pdf

simple absence- or presence- correct/type survey alone will not provide sufficient information. It is also important to ensure that the survey or census was carried out at an appropriate time of the year and that the crop in question was at an appropriate growth stage. Finally, it is also essential to ensure that there are sufficient sites visited. A survey on one field only is unlikely to provide sufficient information on the prevalence and abundance of potential focal species.

6.1.4. Measured residues and residue dynamics

The most relevant substance-related parameters that determine the exposure term in the DDD equation are the initial residue unit doses (RUD) on food items and the dissipation rate of the substance. Application rate and number of applications also determine exposure, but are fixed according to the intended use. In principle, additional information provided by applicants on substance- and use-specific residue levels can be used to refine the RUDs for each food category mentioned in Appendix F or for a food item introduced in higher-tier assessment. Recommendations on arthropod residue field studies to refine food residues in higher-tiered bird and mammal risk assessments can be found in Appendix N. In the same way, substance- and use-specific information on the decline of residues on plant food items can be used to refine the current default DT_{50} of 10 d (see section 6.1.4.1).

It should be noted that, in particular the RUD values for cereals and grass, non-grass herbs and for insects as presented in Appendix F are already derived from relatively large (in the case of plant food items) datasets comprising GLP studies carried out according to the label. Therefore, any additional residue study conducted according to normal standards would tend to rather broaden this existing database than to replace a RUD derived from it. However, refinement of RUDs is still possible if it can be clearly justified⁷⁰ that the deviating new residue data mainly reflect substance- or use-specific properties rather than normal variation.

6.1.4.1. Measured residues and residue dynamics in plant food items

Level of residues. The exposure assessment in the DDD equation is in first instance based on measured residue levels in food items, in this case plants. It has already been stated above that the RUDs from Appendix F may in principle be replaced by more substance- and use-specific parameters if these are available from experiments and fulfil certain criteria.

- The confined residue studies performed for the residue risk assessment are considered a valuable source of information also for an assessment of bird or mammal exposure. For this reason, the default RUDs for ‘grass and cereals’ as well as for ‘non-grass herbs’ are now based on 132 and 230 individual confined residue studies, respectively, for different active substances. Nonetheless, it should be kept in mind that these studies are targeted at deriving maximum residue levels (MRL) and pre-harvest intervals (PHI) for human consumption risk assessment. It must be carefully checked whether the worst case for MRLs and PHIs is also a worst case for bird and mammal exposure, e.g. with respect to application timing. Trials with the first sampling point at day 0 should typically allow reliable conclusions on residue levels under realistic conditions, provided that plant parts sampled were those that can actually be eaten by birds or mammals.
- If an intended use comprises more than one application and respective confined residue trials are available with sampling that begins immediately after the last application, the results can be used directly in the exposure assessment. No additional multiple application factor (MAF) is required.

⁷⁰ This justification could logically take one of two main forms: *either* sufficient field data (on multiple sites and under varying conditions) *or* clear mechanistic evidence (e.g. on spray deposition or retention), confirmed by at least some field data, to demonstrate that the substance or use under consideration *differs from the general pattern* represented by the data underlying the default values.

- It should be kept in mind that the RUDs for crop plants also act as a surrogate for residues on other potentially contaminated plants on the field. If the crop in question is not eaten, but residue studies for other crop plants indicate occurrence of significant residues in non-crop plants, this information should not be neglected in the risk assessment.

There may be reasons for applicants to perform additional studies explicitly targeted at the ecotoxicological risk assessment. Factors to consider when designing such a study to determine more realistic residue levels on potential food items are outlined below:

- The proposed treatment regime should be in line with the worst case ‘good agricultural practice’. For example, if the product is to be used at 1000 g/ha on cereals from growth stage BBCH 60 onwards, then the study should be carried out at growth stage BBCH 60.
- The sites and conditions should be representative of the proposed usage. Data from a field study conducted in a northern Member State should in general be used for a northern MS risk assessment. However, it may be possible to use data from a region A to support uses in a region B if it is obvious that the conditions in region A tend to be worse than in region B so that the risk will not be underestimated. The acceptability of this should be considered on a case-by-case basis.
- More than one site should be used as between-site variations are likely to be greater than within one site. The number of sites should cover an appropriate range of situations to ensure that the data are representative of the proposed uses. Also, statistical advice should be sought when establishing the number of sites and the sampling scheme.

The result of any measurement program will be a distribution of residue data accompanied by descriptive statistics. The selection of values (90th percentiles or arithmetic means) should be the same as for the generic RUD data, provided that the parameters are reliable from a statistical point of view. If a time-weighted average residue concentration is required for the risk assessment, it can be either determined parametrically with an estimated DT₅₀ or by considering the observed area-under-curve.

Dissipation and degradation of residues. Dissipation and degradation of residues from plant material may be more rapid than in other environmental media. The different routes of residue decline comprise physical parameters like volatilization or wash-off, physico-chemical factors like photolysis, abiotic chemical degradation as well as biotic metabolism and dilution due to plant growth. The integrated result of these processes is usually visible in form of an initial rapid decline in surface residues followed by a phase of slower dissipation (Willis and McDowell, 1987). In principle, the assumption of first order kinetics is less appropriate for such type of processes. Nevertheless, only very few data are typically available on residue decline on the scale of hours during the first day. However, these would be required for achieving a reliable fit of a more complex kinetical model. Since the DT₅₀ from first order kinetics tends to underestimate dissipation at earlier time points for the described overlap of partly very rapid processes, but will not overestimate it, this approach is recommended to ensure a worst case.

Willis and McDowell (1987) presented a review of approximately 450 DT₅₀ values (81 chemicals) for a broad spectrum of vegetative plant materials (grass, cereals, forage crops, cotton, vegetables, tobacco, and foliage of fruit trees). Mean DT₅₀ values and standard deviations for total residues were as follows:

- Organochlorines: 5.8 ± 6.0 d
- Organophosphates: 3.3 ± 2.6 d
- Carbamates: 2.7 ± 1.2 d
- Pyrethroids: 5.9 ± 5.0 d

Due to the time schedule of sampling in the original studies the authors expect that many of the half-lives may be overestimates. This bias in mind and taking into account that the data base includes very

stable substances such as organochlorines, it is reasonable to use a DT_{50} of 10 days as a default value if the DT_{50} comes into play in the exposure assessment.

With regard to the level of residues, it is possible to replace the default DT_{50} by a more appropriate substance- and use-specific value based on experimental evidence.

- Risk depends upon the rate of dissipation and degradation under practical use conditions. Thus data from confined residue studies covering all routes of loss are more relevant than plant metabolism studies which are focussed on metabolisation.
- The confined residue studies performed for the residue risk assessment include also studies with several sampling points to allow conclusions on residue decline in plants. However, they are usually not targeted at deriving a DT_{50} or at describing residue dynamics on a time scale of few days after the initial exposure peaks. Still, studies with sampling starting directly after the initial application often exist and allow kinetical analyses. Care must be taken that the concentrations at individual data points refer to the same plant item (e.g. whole plant or green plant parts). With a change from fresh to dried samples or from whole plants to, e.g. grains only the consistent parts of the dataset can be used for deriving kinetical parameters.
- When only few sampling points are available for analysis of results from one trial site, the fit of the model, and consequently, the kinetical parameters become very uncertain. In such cases, pooling of data from comparable trial sites may be considered, but it must be accompanied by a justification why those trial sites can be considered comparable.

Due to the mentioned limitations of confined residue studies, it may be advantageous to conduct targeted plant dissipation studies if refinement of the DT_{50} is intended.

- As regards the representativeness of sites and conditions, the same requirements as for the determination of residue levels are valid. However, like the default DT_{50} , the analysis does not aim at plant-specific kinetics, but at a value that can be used also for plant food items not tested in the analysis.
- To ensure that a meaningful DT_{50} is determined, sampling points should primarily cover the first few days after application, e.g. day 0, 1, 2, 5, 10 and 20. If there is evidence from the residues package that the substance is likely to have a short half-life, for example from the residues or fate and behaviour, then the number of sampling points may be reduced. It should be noted that the number of sampling points should be justified. If the substance is applied several times per season, it is not always necessary to repeat sampling through the season. However, if the product is likely to accumulate, then repeat sampling should be conducted.

After determination of a DT_{50} , the MAF and TWA factors can be adjusted accordingly.

6.1.4.2. Measured residues and residue dynamics in arthropod food items

Much less is known about residue levels and residue dynamics of pesticides in arthropods than in plants. First, this is related to the problems connected with the sampling of small mobile targets and with the analysis of low sample masses. Second, this is due to the fact that these data are not requested as plant residue studies within the risk assessment for human health assessment. Nevertheless, increased concern about the risk to birds and mammals has triggered various activities to elucidate the questions on the fate of pesticide residues in and on arthropods populations.

As the most distinct difference to the earlier concept, the RUDs for arthropods are no longer based on residues on surrogate items, but on results from targeted laboratory, semi-field and field studies. Instead of former size classes, biological aspects such as foraging strata of birds or mammals now form the relevant background of the exposure assessment. If a refinement of these standard parameters

is intended, comparable approaches and concepts like those used for obtaining the current default values should be used.

The state of knowledge and the state of agreement between stakeholders at the time of writing this document is reflected in Appendix N. Only few core points will be mentioned and discussed below. For more detailed information, readers are referred to Appendix N and to possible future revisions of that document.

Laboratory vs. field. Although studies in the laboratory take place under better controlled conditions and allow tight sampling schemes, factors determining height and time course of residues like uptake from vegetation, food-web interactions etc. can only be observed in field studies. However, field studies are subject to much more natural variation than laboratory studies, so it is essential to conduct sufficient studies (at different sites and under varying conditions) to demonstrate that differences from the default values are statistically significant.

Selection of study sites. One test site is considered to represent an individual study⁷¹; however, to obtain information on intra-site variability of the residue values, 3-5 replicates should be planned per site. To minimise bias due to immigration and emigration, the replicates must be sufficiently large and arthropod sampling should be avoided in the border structures.

Application of the test item. The application(s) should be performed according to the recommendations of the product label and according to good agricultural practice.

Test organisms. Attention should focus on organisms likely to be consumed by the potential focal species and also the composition of the species' diet. This information is thus needed before initiation of the study. In order to obtain a meaningful classification, it is recommended that arthropods are sampled according to typical foraging strata of birds or mammals.

Sampling. Sampling techniques should be selected and performed in a way to minimise bias in test results. Desiccation of samples and cross-contamination should be avoided. Composition of individual samples must be recorded to allow meaningful interpretation of results. In case of insecticides, taking knock-down samples is recommended for obtaining information on residue levels in dead or dying arthropods directly after application. Sample numbers must be high enough to allow statistical evaluation.

Reporting and data interpretation. The main results from tests are initial and/or peak residue concentrations, as well as data on residue dynamics. Due to a number of reasons, first order kinetics is not considered appropriate for describing residue dynamics in arthropod populations. The most important of these reasons is the potential uptake of residues by arthropods in the first days after application. Thus, quantitative description of residue dynamics should not simply be based on MAF or TWA factors alone. If refinement is intended, it is necessary that the relevant application scenario is appropriately reflected in a test. Only if that is ensured, a MAF_{90} can be derived from the highest peak measured or a $MAF_m \times TWA$ from the area under the residue vs. time curve. Care must be taken that the quality of the data (e.g. application pattern, number of sampling points) is sufficient to support conclusions on average residue levels.

6.1.5. Steps to refine the PT factor

PT is defined as the 'proportion of an animal's daily diet obtained in habitat treated with pesticide'.

⁷¹ Note that, as for residues on plant food items, more than one site should be used to take account of between-site variation (see section 6.1.4.1).

6.1.5.1. Criteria for performing radio tracking studies and evaluating observational data

At the screening step as well as the generic focal species step, it is assumed that individuals find all their food in the treated area, therefore $PT = 1$. In reality, birds and mammals in the agricultural landscape may visit a variety of habitats within a single day and may obtain their food from a variety of fields. Therefore, in higher-tier risk assessment, it may be possible to use more realistic estimates of PT . In order to do this, it is necessary to obtain a measure of the amount of treated food ingested by individual birds and mammals in a particular field. This measure can be obtained by radio-tracking individuals, however, this is an indirect measure and certain assumptions need to be made, namely:

- That the amount of active time spent by an animal in a given crop is directly proportional to the food it eats there; and
- That the crop has been recently treated with pesticide.

If these assumptions are accepted, it can be further assumed that 50 % of the daily food intake of an individual bird that spends 50 % of its day in a given crop is likely to be contaminated with pesticide. Likewise, an individual that spends 70 % of its day will obtain 70 % of its food from the treated crop.

Details on the use of radio-tracking data to estimate PT are provided in Appendix P however, outlined below is a brief summary of the key issues that should be considered.

6.1.5.2. Radio-tracking and inclusion of individuals in the estimate of PT

Radio-tracking should be carried out on those species considered to be ‘focal species’ (FS). There are two main methods for the selection of individuals to radio-track:

- a) To focus on the crop and to radio-track only those individuals that were caught in (or in close proximity to) the target crop;
- b) To focus on the species and to radio-track individuals captured in local farmland habitats where they are most abundant.

Both approaches provide useful data. However, it is necessary to consider that the estimated PT will generally be different. This will be a reflection of the fact that they are derived from different populations. The birds or mammals studied in (b) represent the whole farmland population whereas the birds or mammals in (a) are a subset that spends potentially more time in the crop of concern.

Having selected either (a) or (b) and obtained radio-tracking on the birds or mammals, it is necessary to further consider which individuals from this dataset are used to determine PT . One option is to consider all birds or mammals that visited the crop or had the potential to visit the crop. This would give an indication of the risk to the population at a farmland scale. Alternatively, only those birds that visited the crop, i.e. consumers only, could be selected to assess their risk. Using consumers only will not give an indication of the risk to the wider population that was in the vicinity of the target crop but did not happen to visit it during the observation period. Alternatively, considering all birds that had the potential to forage in the crop of concern will give an indication of the risk to the wider farmland population. It may perhaps include birds that were quite unlikely to visit the crop, e.g. because their breeding territories did not overlap the target crop or they had a strong preference for some other feeding habitat.

Considering all of the above, it is recommended that for focal species caught within the crop, PT should be estimated from all individuals - whether they used the crop of concern or not. For the focal species caught in the general farmland, PT should be estimated from only those individuals proved by radio-tracking to be consumers, i.e. $PT > 0$. It should be noted that the inclusion or exclusion of individuals with $PT = 0$ is a trivial calculation. It is further recommended that the risk from both groups is included, i.e. if radio-tracking data are available from birds or mammals caught in the

general landscape, then two PT values should be calculated, one for all the birds and one for only those with $PT > 0$. Likewise, for those birds or mammals caught in the crop of concern, PT should be calculated for those individuals with a $PT > 0$ as well as for all individuals.

Whichever choices are made in collecting data and deriving refined estimates for PT, it is essential in all cases to evaluate the impact of the refinement on the overall level of protection provided by the assessment, taking account of the issues discussed in section 6.1.1.

6.1.5.3. Radio-tracking contact time as an estimate of foraging time

Data from radio-tracking studies are used to provide an indication of the exposure through the consumption of treated food. Therefore, it is necessary to distinguish between the time spent in the crop 'actively or potentially foraging' and the time spent in the crop 'inactive or not foraging' for food. Therefore, the output from a radio-tracking study is the amount of (potential) foraging time in the crop expressed as a proportion of the total time spent (potentially) foraging during the day.

6.1.5.4. How long should individuals be followed?

Ideally, radio-tracking of an individual should encompass the activity period of a single day; however, this might not always be possible. In this case it is necessary to consider the following questions:

- Is the sampling regime likely to introduce biases into the estimation of PT, such as by favouring particular times of day when the animal is engaged in particular behaviours or by leading to greater sampling of the animal when it is either in or outside the crop?
- Does the shorter observation time produce a significant bias on estimates of PT? Can the likely bias that shorter observation may have on the estimation of PT be estimated and corrected for? Can it be indicated whether the bias will have conservative or non-conservative effects on the risk assessment?

6.1.5.5. How to use PT in deterministic case calculations

In selecting a suitable refinement of PT, it is necessary to determine what level of protection is required. For example, if the first-tier PT of 1 was replaced by a median or mean, this would suggest that the risk assessment will only relate to those 50 % individuals that fall under this PT, provided that no other parameters drive the risk assessment. However, in reality other variables contribute significantly to the overall risk and therefore the true proportion protected will be a result of the combined effect of all the input parameters (see Figure 2 in section 6.1.2).

Therefore, selecting a percentile for PT does not automatically provide the same percentile of TERs, due to the potential affect of the other parameters. Therefore, selecting the 90th percentile does not mean that 90 % of the population will be protected. If it is desired to know the level of protection provided by a certain PT percentile, it would be possible to estimate this by using probabilistic methods to take account of the combined effect of all the parameters.

6.1.5.6. Use of other sources of information in refining PT

Radio-tracking studies will not be available for every combination of crop and focal species. In cases where radio-tracking data are not available, an attempt may be made to refine PT using other types of information. However, it should be recognised that this will generally involve a much higher level of uncertainty, which must be taken into account in risk characterisation and decision-making.

If radio-tracking data are available for other species or crops, this may provide a useful starting point from which to extrapolate to the species and crop of interest. In some cases, it might be reasonable to treat the available data as a direct surrogate for the species and crop of interest, but with additional

uncertainty due to the extrapolation. In other cases it might be considered that some adjustment should be applied to the data to make it more relevant to the species and crop of interest. In both situations, the extrapolation should be clearly documented and justified with reference to relevant supporting evidence, e.g. regarding the ecological similarity of the species and crops involved, or from other types of data (e.g. observational studies).

Many types of information other than radio-tracking may contribute to the assessment of PT. The most useful are systematic visual observations (e.g. transect surveys) and mark-release-recapture studies, but even these are subject to substantial uncertainties. For example, visual observations of unmarked individuals cannot determine how PT varies between individuals, and can estimate average PT (which may not be sufficient for risk assessment) only if the size of the local population is known. Less systematic data, such as informal or incidental observations, nest locations and general ecological or natural history knowledge can contribute to expert judgements about PT, but these are inevitably highly uncertain. Other difficulties affecting interpretation of information on PT are listed in section 2.1 of EFSA (2004).

It is therefore recommended that:

- Every estimate of PT (apart from the conservative default $PT = 1$) be based on a detailed and critical evaluation of all the relevant evidence and be fully justified and documented,⁷²
- The evaluation should always include consideration of the range of PT for individual animals, which for many species may actually extend from 0 to 1, as well as the average;
- Every estimate of PT be accompanied by a realistic indication of its uncertainty;
- Estimates that have been developed for one species-crop combination should not be extrapolated to other species-crop combinations without a fully documented and justified reassessment of the relevant evidence.

6.1.6. Steps to refine the information on composition of vertebrate diet (PD factor)

PD is defined as “composition of diet obtained from treated area”. Birds and mammals will be exposed to pesticide residues on or in food items obtained from crops or areas where pesticides are used. Outlined below is brief information regarding the dietary composition of both the indicator and generic focal species (see Appendix Q for detailed information) and energy, moisture content and assimilation efficiency of diets (Appendix L).

6.1.6.1. Diet used in the screening step

For the screening step, the diet is deemed to be a single type of food (e.g. only seeds or only arthropods etc.) that is considered to be both realistic and worst case in terms of amount required to fulfil the dietary requirements as well as the initial residues. The screening step diet is fixed and cannot be changed. For further details of the screening step diet, see Annex I, and Tables 6 and 8.

6.1.6.2. Diet used for the ‘generic focal species’

The diet used for the risk assessment for ‘generic focal species’ is a more realistic one. The methodology used to develop these diets is outlined in Appendix Q. In determining these diets, all available literature has been considered, and a quartile approach has been adopted to try and account for the range of a particular food item that may occur in the diet. Hence, in determining the diet of the

⁷² The documentation should be concise but sufficiently detailed to enable readers to critically evaluate the basis for the estimates taken for use in the risk assessment. An example of the degree of detail and depth that may be required is provided by the combination of section 2.2 and Appendix 1 in EFSA (2004).

generic focal species 'lark', use was made of all the published information on the diet of all lark species so as to obtain a generic diet. With regard to the screening step, these diets are fixed and should not be altered. If there is concern, i.e. the TER is breached, it is necessary to progress to the next step.

6.1.6.3. Diet used for the 'focal species'

If a more refined assessment of diet is required, this should be based on the focal species. In order to do this, two approaches are possible. The first and most robust way is to carry out specific studies to determine the diet of focal species. The second approach is to consult published studies, some of which may have been used to determine the diet for the indicator and generic focal species. Details of these two approaches are outlined below.

1. Specific studies on the diet of focal species are conducted in appropriate landscapes (crop or agricultural mosaic) according to a robust methodology as described in Appendix Q for birds. In principle, the method of faeces analysis can also be used for mammals but more common is the analysis of stomach content for mammals caught in snap-taps (mice, voles etc.) or shot by hunters (hares, rabbits etc.) There are two types of methodology for birds - namely faecal analysis and stomach flushing. Both methods rely on catching birds in or close to the crop of concern and then determining what they have eaten. Since dietary composition may vary between crops, it is essential that the birds have access to the crop of concern and are known to have actually foraged in the crop of concern. For several small mammal species the analysis of faeces and of contents of dissected stomachs is recommended and the same rules and methods can be applied as for birds (see Appendix Q).
2. Alternatively, additional published literature may be used, but only if it takes account of the crop or agricultural mosaic as well as variability and uncertainties in time and space that may be due to preference and availability.

In both cases, it must be taken into account that there is not a single true value of PD, rather it varies between individuals, between sites/habitats and over time. If multiple studies are available, differences between them may represent either true variation and/or uncertainty due to differences in measurement methods. If a single value is used for refined assessment the impact of the variability of PD in the field must be taken into account when evaluating the overall level of protection provided by the assessment.

In summary, it is therefore concluded that:

- It is possible to refine the diet that a focal species obtains from the treated area by conducting specifically designed studies. These studies should be conducted using the appropriate focal species, the correct crop and during the correct time of year.
- It is possible to refine the diet using published data. However, the underlying studies need to be relevant in terms of the species, the crop, and the relevance of the agricultural mosaic.

6.1.7. Dehusking

Residues on treated seeds (direct treatment, pelleted or incrustated seeds) will be mainly located on the outside of the seeds (husk, testa, pericarp), whereas concentrations in the inner parts of the seeds (endosperm, embryo) will be significantly lower. Thus, exposure of granivorous birds or mammals may be markedly reduced when they dehusk seeds before consumption. However, incorporation of dehusking as a mitigating factor in the DDD equation requires careful consideration of various parameters.

In the case of birds, dehusking is mainly observed in smaller species. Some respective observations have been reported, e.g. by Prosser (1999), comprising species such as finches, sparrows and

yellowhammer. Studies have shown that dehusking of seeds can substantially reduce avian exposure to pesticides in some cases. Nevertheless, it is important to note that dehusking is not all-or-nothing: not all small species dehusk, and some species dehusked some but not all of particular seed types. In the wild, the actual amount of seeds dehusked may be dependent on stressors such as feeding pressure, predation or competition (Prosser, 1999). For birds with a bodyweight above 50 g, it must be assumed that dehusking does not occur (Edwards et al., 1998). Larger granivorous birds typically have the capability to destroy even hard-shelled seeds within their gizzard.

For granivorous mammals such as rodents, dehusking or cracking of seed or fruit shells is often a part of their typical behaviour. Distinct anatomical features such as incisors or folds of skin that prevent material from entering the mouth while being gnawed (DEFRA, 2005) indicate that rodents will probably minimise the uptake of husks when eating seeds. Ludwigs et al. (2007) presented some experimental indications for the occurrence and efficiency of dehusking with regard to mice and cereal seeds. Qualitative data on wood mice dehusking cereal or weed seeds or cracking sugar beet seeds can be found in Barber et al., 2003; Westerman et al., 2003; Tew et al., 2000; and Pelz, 1989.

Quantitative information on the actual effectiveness of dehusking is very scarce. In the study of Edwards et al. (1998), seeds were manually dehusked before analysis. The data of Ludwigs et al. (2007) are based on seeds actually dehusked by animals. These data further indicate that not only the amount of dehusked seeds but also the exposure mitigation achieved by dehusking is very dependent on seed structure.

Due to the lack of reliable data and the known uncertainties, dehusking should only be considered in higher-tier assessments with case-specific justifications. Evidence must be provided that dehusking may actually play a role under field conditions for the relevant focal species. If this is the case, the available information should be checked for the conditions under which dehusking occurs and the extent to which it has been observed for this species. Specific care should be taken for seed treatments with a high toxicity per single seed. If the LD₅₀ is already reached with one or few seeds/particles, consideration of dehusking in the risk assessment might not be justified.

To obtain an estimate on the actual efficiency of dehusking, studies with the relevant focal species, the relevant seed type and the relevant product are preferable, since extrapolation is always connected with increasing uncertainty. If specific data are not available, the risk assessment can start with more generic information, in order to identify the general potential of this mitigating effect. Particularly in the case of birds, the assessment should always be performed for a second species that does not dehusk. If this assessment indicates a higher risk for the non-dehusking species, this species should become the species of concern. Further considerations on dehusking are not meaningful in such a case, unless it can be proven that the risk to the non-dehusking species is acceptable in a further refined assessment. If the overall risk is still determined by the potential effects on the dehusking species, careful reconsideration of any generic assumptions made in the first instance is required. It may become necessary to conduct targeted studies on the actual exposure of focal species under realistic conditions to conclude on an acceptable risk.

It is therefore recommended that:

- If dehusking is to be considered in a higher-tier assessment, case-specific evidence must be provided that it may actually play a role under field conditions for the relevant focal species;
- Available information on actual extent of dehusking and on relevant environmental conditions for such behaviour should be thoroughly discussed;
- Studies with the relevant focal species, the relevant seed type and the relevant product should be considered in preference to other studies requiring extrapolation;
- Particularly for birds, a risk assessment for a dehusking species should always be accompanied by an assessment for a second species that does not dehusk, in order to conclude on the actual species of concern.

6.2. Avoidance

A degree of avoidance of food contaminated with pesticides, commonly seen in dietary studies with captive animals, has the potential to reduce exposure and hence risk in the field. It can be a combination of several different responses including (a) a reduction in the rate of feeding due to novel or unpleasant characteristics of the contaminated food (e.g. taste or odour) and (b) temporary cessation of feeding due to sublethal intoxication. It is hard to determine the precise mechanism(s) of avoidance for a given pesticide, so attention should focus on its effectiveness in reducing exposure and effects, and on how this may vary under field conditions. Avoidance can occur with treated seeds and granular formulations as well as sprayed pesticides; and the principles of this section apply equally to each. The majority of this section focuses on evaluating the impact of avoidance on acute risks; consideration of avoidance for reproductive risks is discussed more briefly at the end of the section.

In the former Guidance Document (EC, 2002), a multiplicative factor (AV) to represent the effect of avoidance was included in the equation for estimating exposure. This might be appropriate if the degree of avoidance was constant over time, as might (or might not) apply if the avoidance response was purely of type (a) above. However, for many substances (including but not restricted to organophosphate and carbamate pesticides), where the type (b) response is important, avoidance is absent or limited at the start of feeding and becomes significant only after the animal reaches a certain threshold dose. This cannot be represented appropriately by a simple multiplicative factor in the exposure model (EFSA, 2004), which is the reason for the current exclusion of AV from the standard exposure model (section 4). This does not mean that avoidance cannot be considered in risk assessment. But it does mean that avoidance cannot generally be characterised by a simple multiplicative factor such as AV.

In cases where avoidance occurs as a threshold effect, the threshold is likely to be less than the lethal dose. Nevertheless, mortality can still occur in an acute exposure scenario: since the avoidance response is not immediate, animals that feed rapidly may ingest a lethal dose before the onset of the response. For less toxic substances, where several feeding bouts would be required to ingest a lethal dose, the availability of uncontaminated foods and the ability of the animal to select them become more important. Many other factors that may influence the avoidance response and its potential to reduce risk in the field are discussed in section 4.1 of EFSA (2004).

Currently, no internationally accepted guidelines for testing avoidance exist. Two national guidelines exist (INRA, 1990; BBA, 1993) but neither of these ensures a high feeding rate, which, as mentioned above, is a critical factor in acute exposures. Reductions in food consumption may also be measured in dietary toxicity tests (Luttik, 1998), but again these do not ensure a high feeding rate. Various other methods exist, including some intended for testing the efficacy of avian repellents for protecting crops (discussions see OECD, 1996). However, due to the complexity of factors affecting avoidance, interpreting data on avoidance from captive studies and assessing its implications for risk in the field is difficult and uncertain, as shown by the example of EFSA (2004).

Since it is not generally appropriate to represent avoidance as a multiplicative factor reducing consumption, consumption should not be the primary endpoint of avoidance studies for acute risk assessment. Instead, any new studies should focus on the critical question for avoidance, i.e. on whether it is able to prevent mortality and serious sublethal effects under realistic worst-case conditions. Thus, mortality and serious sublethal effects should be the primary endpoints, unless the aim is to generate data on other parameters for use in a modelling approach (see section 6.3).

An alternative to testing avoidance for acute exposures is to model the avoidance response and its interactions with other key factors such as metabolism. This involves modelling the effects of feeding rates and ADME processes on body burdens of the active substance as well as the threshold doses for avoidance responses and lethality. Approaches for body burden modelling are discussed in section 6.3 and an example of its use in a regulatory context is provided by EFSA (2005a). However, there is no standard approach, therefore the appropriateness of any model must be fully documented and justified in each case.

When data or models on avoidance are used as part of an acute risk assessment, careful consideration must be given to the substantial uncertainties involved. Particular attention should be paid to uncertainties that concern the relevance of the study or model to the exposure situation in the field, and to uncertainties that affect extrapolation between species. Questions to consider include:

- What rates of feeding occur in the field?
- Do the feeding rates achieved in laboratory studies or assumed in models correspond to the maximum rates occurring in the field? If not, how much higher will risk be at the maximum rates? If avoidance will not prevent adverse effects at the maximal rate, it will be necessary to consider the distribution of feeding rates in the field to assess how often adverse effects may occur.
- Does the availability of untreated foods provided in studies or assumed in models correspond to realistic worst cases in the field? For acutely toxic substances, absence of untreated food is a realistic worst case⁷³. For longer-term exposures, what evidence is there that animals could learn to avoid contaminated food?
- Is the species tested in studies or considered in a model among the most sensitive to the substance? This is critical for acute scenarios, because the opportunity for an avoidance response to prevent mortality (i.e. the time interval between reaching the avoidance and reaching lethal doses) will be smallest for the most sensitive species. This is a serious problem for avoidance testing, because the relative sensitivity of the tested species (i.e. its position in the species sensitivity distribution for that substance) is extremely uncertain (1 or 2 orders of magnitude). Therefore, even if no adverse effects are seen in a tested species, more sensitive species may be adversely affected in the field. Potentially, this issue could be addressed by testing multiple species, but this option raises concerns of ethics and policy. In a modelling approach, it may be possible to account for variation in sensitivity between species by using a species sensitivity distribution⁷⁴.
- What assumptions are made or implied about extrapolation between species of the many other factors affecting the avoidance response? Even if a tested species is known to be sensitive, could other factors affecting avoidance (e.g. metabolism) be less favourable in other species? This could be addressed by testing multiple species, but as mentioned above, this raises concerns of ethics and policy. This problem is also serious for modelling approaches, since almost nothing is known about between-species variation in the avoidance threshold dose and the various ADME processes. In the absence of such information, a possible approach is the exploration of the effect of a range of plausible but conservative assumptions. If the risk appears low when using conservative assumptions, this may be sufficient for a conclusion (e.g. section 2.3.2.7 in EFSA, 2005b).

In the light of these issues, the recommendations with regard to consideration of avoidance in refined assessments of acute risk are as follows:

- Reductions in food consumption in the standard 5-day dietary LC₅₀ study are not sufficient to demonstrate that avoidance will prevent mortality in the field. They only indicate that avoidance may be worth to be considered further, using the following approaches.
- If specialised avoidance studies with the substance exist already, their implications for risk should be interpreted very carefully, taking full account of the issues discussed above.
- Before undertaking any new animal studies, it should first be considered whether modelling can provide sufficient certainty for decision-making, following the approaches outlined in section 6.3 and illustrated by EFSA (2005b).

⁷³ This is because it is a realistic worst case to assume that an animal encountering a contaminated food source in the field will continue to feed on that single food until its appetite is satisfied, unless avoidance occurs.

⁷⁴ See EFSA (2005, section 2.3.2.2) for an example of this.

- If new animal studies are to be carried out, they should be designed, justified, conducted and interpreted very carefully, taking account of the issues discussed above⁷⁵. The test species should be chosen or trained to feed at the maximum rate expected in the field, ideally based on suitable field observations. The primary test endpoint should be the occurrence of mortality and serious sublethal effects, unless the aim is to generate other data for use in a modelling approach. If no adverse symptoms are seen, it is important to determine whether this is due to avoidance or simply due to the low sensitivity of the test species⁷⁶. It is recommended to consult the competent authorities before proceeding with any new studies.
- If there is evidence from one or more of the above approaches that avoidance will reduce the risk of mortality, it should be considered carefully whether it is reasonable to extrapolate this conclusion to other species in the field. If there is significant doubt about this, the testing of additional species could be considered (if justified).
- All of the above approaches require very detailed documentation and justification, including explicit discussion and analysis of the uncertainties, as illustrated by the examples of EFSA (2004, 2005b). The uncertainties should be considered when evaluating the level of protection provided by the refined assessment (see sections 6.7 and 6.8).

Reproductive risk may be reduced if avoidance causes reductions in exposure over longer time periods, e.g. if it results in the animal learning to select less contaminated food items, or moving to untreated areas. This could be caused by either of the mechanisms mentioned at the start of this section (type (a) or (b)). Demonstrating this type of response experimentally requires a different type of study design than avoidance in acute scenarios, e.g. longer time periods and access to both treated and untreated food, rather than short time periods with treated food only. However, as for avoidance in acute scenarios, it is essential to consider the realism of the test conditions and how responses may differ in the field. For example, a test with treated and untreated portions of an attractive food presented concurrently side-by-side may significantly exaggerate the degree of avoidance that would be seen in the field, where animals may have to switch to less-preferred foods, or leave the treated area, to obtain untreated food. It is also essential to consider how responses seen in tested species extrapolate to other species. Devising test methods and assessment approaches to take account of such factors requires further research, so in the meantime any consideration of avoidance in reproductive assessments should be undertaken case by case and with special care.

6.3. Metabolism & avoidance – application of body-burden models and dietary toxicity data

In EC (2002) and in this Guidance Document, risk assessments models, at least at lower tiers, use the daily dietary dose (DDD) as main input parameter. Implicitly, the use of the DDD brings along some restrictions:

- A) The animal (bird or mammal) itself is considered a black-box. ‘Dose’ refers only to the amount of substance administered to the animal, and ignores internal process such as absorption in the gastrointestinal tract, elimination (faeces and urine) and metabolism and their kinetics.
- B) The assessment is made based on the ‘day’ as a unit of time, and as such precludes the use of other (shorter) time scales as the basis for the risk assessment.

⁷⁵ Note also that avoidance studies should not be performed for treated seeds or granules where it is expected that a lethal dose is contained in a single seed or granule. In such cases avoidance cannot prevent mortality, although it is possible regurgitation may do so, and attention should focus instead on assessing what proportion of the population will be exposed (and hence the possible level of mortality).

⁷⁶ This may be determined from the LD₅₀ for the species, if available. If a new toxicity study is required, an approximate lethal dose study (e.g. up-and-down method) should be chosen, to minimise animal use.

Within the registration process of plant protection products under Directive 91/414/EEC, often data from metabolism studies (ADME) within rat, live-stock or hen are available. These would allow for an alternative in risk assessment to avoid the above mentioned restrictions. Where risk-refinement is necessary based on results from lower tier assessments, 'metabolism' data should be evaluated by the risk assessor for options to reduce the uncertainty associated with the risk assessment. ADME studies may provide information on:

- Data on adsorption rates in the gastrointestinal tract
- Data on metabolism (kinetics/rate of formation)
- Data on elimination rates
- Data on potential de-activation/de-toxification steps

Besides the specific 'metabolism/ADME' studies on rat, livestock or hen, available toxicity studies (gavage/dietary) can be re-evaluated to potentially obtain useful information allowing the risk-assessor to overcome the restrictions of the DDD approach. A comparison of data from gavage and dietary studies can be particularly useful, since large differences between these two types of dosing may indicate metabolism playing a significant role in the expression of the intrinsic toxicity of a substance. Therefore, even cases where specific ADME studies are not available for the substance under assessment, metabolism is a refinement option.

Metabolism data may provide a way to include food avoidance as a refinement factor at higher tiers. The use of the avoidance factor (AV) as it was included in the standard algorithm in the previous Guidance Document (EC, 2002) is no longer considered suitable. However, there is wide agreement among scientists that food avoidance is an important factor, that frequently occurs in the field, and which, as such, should be considered when refining risk assessments (but see also section 6.2). ADME data and comparison of gavage with dietary studies can provide a means to take account of avoidance in risk assessment.

Several publications were made over the last years, presenting models, which allowed for the use of absorption, metabolism and elimination in the refinement of the risk assessment for birds and mammals (EFSA, 2005a). A more in-depth overview and discussion of the body burden (BB) model is given in Appendix 23 to EFSA (2008). This Appendix also specifies which type of data is required as input to BB-models and provides the assessor with information on the type of output that is gained with these models, as well as information on the manner in which this output can be used in risk assessment.

The body burden model(s) provide(s) the risk assessor with a tool:

- To include potential activation or de-activation (de-toxification) and elimination processes of a substance within the animal in the risk-assessment;
- To study the influence of absorption rates of a substance in the gastrointestinal tract on avoidance and risk posed to terrestrial vertebrates;
- To use the experience gained in human risk assessment and pharmaceutical research;
- To refine the assessment of the bioaccumulation potential of any substance and/or its metabolites;
- To include other routes of exposure (dermal/inhalation) into the risk assessment. However there are currently no examples for this being used in regulatory assessment of risks to wildlife.

Since ADME studies are not always available, and due to the fact that subtracting metabolism relevant information from available toxicity studies can be complex, BB-type models may not be a suitable tool for lower-tier assessment for terrestrial vertebrates. However, they are potentially a powerful tool for risk refinement. Currently available data could be used as input parameters for the BB-model. Alternatively, relatively simple dietary studies could be designed that would provide the input data

needed. Such studies use relatively low numbers of individuals and often do not inflict stress (toxic effects, starvation) on the test animals. Therefore, for animal welfare reasons, BB-type models may form an alternative refinement option to conducting further laboratory toxicity and field studies.

BB-type models could be considered as a potential tool for higher-tier risk assessment. It should be stressed however, that BB-type models are a research area rather than an established methodology in environmental risk assessment. Moreover, extrapolation of ADME data from one species to another is hampered by uncertainty due to the lack of research on this topic. Therefore, when such models are to be used, the assessment should always be accompanied with a justification of why this model is considered to be applicable for the specific case one is dealing with. Furthermore, if an assessor wishes to use BB-type models, it is strongly recommended to consult with a toxicologist/metabolism specialist.

6.4. Field studies to detect or quantify mortality or reproductive effects

This section focuses on the use of field studies to detect or quantify mortality or reproductive impairment of wild birds and mammals⁷⁷. The use of field tests for other purposes is considered in other sections (to identify focal species, section 6.1.3; to measure residues on wildlife foods, section 6.1.4; to quantify use of treated crops, section 6.1.5; to quantify dietary composition, section 6.1.6). Sometimes, a single field study may serve several of these purposes.

Field studies of mortality and reproductive effects are neither simple nor inexpensive but they have some important advantages. Aimed at the direct measurement of the effects of concern under realistic field conditions, such studies can take account of all routes of exposure and – depending on the number of study sites – all relevant sources of variation.

An internationally agreed standard protocol for avian and mammalian field studies does not exist. The US EPA protocol (OPPTS 850.2500 - Field testing of terrestrial wildlife) is still current, although field studies are no longer requested by US EPA as part of higher-tier assessment. For Europe, papers and recommendations from two workshops held in the 1980s are available (Greaves et al., 1988; Somerville and Walker, 1990; Anonymous, 1990), but no official guidance or protocol exists.

6.4.1. Field study objectives

In view of the potential costs and difficulties of field studies, it is essential to ensure that the objectives of such studies are clearly defined and appropriate for the needs of the risk assessment they will serve. Specification of the objectives should include the type(s) of effects that are to be assessed, the population in question and spatial and temporal scales. To enable the design of a study of appropriate power, it is desirable to know in advance the levels of effects that are considered acceptable, as well as the degree of certainty that is required to prevent the acceptable limit being exceeded. Since such questions address risk management, it is desirable to discuss them in advance with the relevant authorities.

6.4.2. Number of study sites: intensive versus extensive approach

A key issue in a workshop held in 1988 was the contrast between ‘extensive’ and ‘intensive’ approaches (Somerville and Walker, 1990). The ‘extensive’ approach uses simple techniques such as carcass searching and census methods but employs a large number of sites to cover a broad spectrum of use conditions. It provides true replicates for statistical evaluation and thus allows for estimation of

⁷⁷ In this section, ‘field studies’ refers both to studies of effects following experimental pesticide applications (i.e. applications made as part of a regulatory study) and also to ‘active monitoring’ of effects following applications of approved products in agricultural practice. It excludes ‘passive’ wildlife incident monitoring or surveillance, involving investigation of suspected incidents reported by farmers and members of the public, which are dealt with in section 6.5.

the probability of effects. The ‘intensive’ approach on the other hand involves more detailed investigations but on a smaller number of sites, or on one site only. It puts more emphasis on evaluating the potential for effects by using a combination of methods to study factors influencing exposure and risk.

The recommendations of the 1988 workshop tended to favour the intensive approach (Anonymous, 1990). However, this should be reconsidered in the light of developments since that time. Research has demonstrated wide variation in PT between individuals, of residues between sites and of toxicity between species. Each of these conditions will contribute to wide variation of exposure and effects between sites. Consistent with this observation, the analysis of field studies suggests that the same pesticide use may cause lethal effects on some occasions but not others (Appendix 2 of EFSA, 2008). This implies that studies on small numbers of sites could be very misleading. Failure to detect lethal effects at one or a few sites cannot be interpreted as a reliable indication of the frequency of lethal effects over many sites. Furthermore, this cannot be addressed by selecting ‘worst-case’ sites, as it is not possible to know in advance which sites will have high residues or which species will be most sensitive, nor is it possible to ensure that individuals of sensitive species with high PT will be present. However, these issues can be addressed by assessing the occurrence of effects at a larger number of sites, as in the ‘extensive’ approach.

It may be objected that a high quality study done with modern methods on a small number of sites should be sufficient to refute a potential risk indicated by the first-tier assessment, given that the latter has been ‘calibrated’ with historical field studies of variable quality. This would be true if most or all of variation in existing field studies is due to variable quality. However, due to the wide variation in residues, PT and toxicity and other factors influencing risk, it is clear that a large part of the variation must be real. Effects may occur at some sites but not others. Therefore, even when high quality modern methods are used, it will still be necessary to study multiple sites to determine with adequate certainty whether effects will occur. It is concluded that an ‘extensive approach’ with suitable methods and an appropriate number of sites (see below) is preferable to field studies with fewer sites.

The number of sites required will depend on a number of factors. These include the sensitivity of the field study methods for detecting effects, the level of effects that is considered acceptable (this might be defined in various ways, e.g. as the percentage of sites with any effects, the percentage of individuals affected over multiple sites, or the percentage of sites exceeding some specified level of effects), and the level of certainty required. Statistical methods for determining the number of sites required are included in the US EPA guidance (OPPTS 850.2500). However, it was suggested at the 1988 workshop that these methods could lead to a high frequency of false positives and required further consideration (Gould, 1990). Therefore, if field studies of effects became more frequently used, it would be desirable to undertake a new initiative (e.g. research and/or a workshop) to develop appropriate methods for determining number of sites. It would also be desirable to develop guidance on how to take account of the number of sites used when evaluating the results of studies (including existing studies with small numbers of sites). In the meantime, expert statistical help should be sought on a case by case basis, both to determine and justify the number of sites for new studies, and to evaluate the results of existing studies.

6.4.3. Methods for detecting effects in the field

The choice of methods and their detailed implementation in each case should be driven by the study objectives, including the type of effects that are of interest and the degree of certainty required in detecting and quantifying them. It should be noted that using multiple sites does not remove the need for adequate methods to detect effects at each site. Available methods include (but are not limited to):

- Systematic searching for dead or sublethally-affected individuals. This should include the treated area as well as adjacent habitats where exposed individuals might go to rest, roost or take cover (see Fryday et al., 1996). Searches should be carried out at appropriate times to maximise detection of casualties, taking account of the mode of action of the substance, while

minimising disturbance that could artificially reduce exposure. Pre-treatment searches on at least two occasions are advisable to remove pre-existing animal remains and assess the level of natural mortality to aid interpretation or analysis of post-treatment mortalities. Search efficiency and rate of carcass removal by scavengers should be estimated using dummy carcasses.

- Radio-tracking to monitor activity and survival of tagged individuals (e.g. Prosser et al., 2006). The number of individuals should be sufficient to measure the level of mortality with the desired level of certainty. Casualties must be recovered very promptly and in a condition that is adequate to diagnose the cause of death.
- Post-mortem examination to diagnose cause of death: this may include residue analysis, biomarker assays (e.g. enzyme inhibition) and histology.
- Capture-mark-release-recapture studies to monitor population changes, which include changes in age structure, especially in small mammals.
- Monitoring of sublethal effects using biomarkers (e.g. enzyme inhibition). Repeated sampling from the same individuals may be desirable to control for high natural variability in biomarker levels, although this must be balanced against the risk that repeated capture will alter the behaviour of the animals and hence will bias the results.
- Visual observations to monitor populations and activity of birds and large mammals. Interpretation of results is difficult if the animals are not individually marked.
- Monitoring of reproductive performance of birds. Large samples of nests are required to ensure that an adequate number are active at the time of pesticide application.

Before choosing and using study methods, relevant literature should be consulted. Such literature includes the US EPA guidance (OPPTS 850.2500) and workshop publications cited earlier (Greaves et al., 1988; Somerville and Walker, 1990). However, in order to address the objectives of each study, the methods described or recommended in these sources should be considered, modified and justified case by case.

Careful consideration should also be given to other aspects of study design, including the following:

- Selection of appropriate study sites, e.g. should they be representative or aim towards a worst case? In order to take account of variation in sensitivity between species⁷⁸, sites with contrasting species assemblages (e.g. in different regions) may be preferable to similar sites in a single region.
- A broad range of species should be studied to take account of the wide variation in toxicity between species.
- Representativeness of the method, timing and rate of pesticide applications: should these be highly controlled or reflect normal variations in agricultural practice?
- The number and type of control sites and pre-application observations.
- The manner in which the cause of mortality or other observed effects will be determined, and how uncertainty in attributing effects to the pesticide will be addressed when interpreting the results (e.g. will carcasses with low residues, or those that were not analysed, be considered as pesticide casualties or not?).
- The way to ensure that the activities of investigators on the treated area do not cause under-estimation of exposure and risk, e.g. by reducing the time wildlife spend in the treated area or by reducing the rate at which they feed.

⁷⁸ The number of species associated with a crop in one region may be high, but only a few species in each region will have high PT in that crop. Therefore in order to have a reasonable chance of encountering a species with both high PT and high sensitivity, sites in multiple regions may be needed.

6.4.4. Interpretation of existing field studies

In principle, all of the issues discussed above in relation to study design, e.g. number of sites, representativeness of sites and methods, attribution of cause of effects, the need for statistical advice, should also be considered when interpreting existing studies. Primary focus should be placed on the evaluation of (a) the certainty that effects did or did not occur at the sites studied, (b) what can be inferred about the occurrence of effects in general (over many sites). These evaluations will usually require expert statistical advice as well as expertise in biology, ecology and residue chemistry. In particular, it should be remembered that, because of the intrinsic variability of exposure and effects between sites, a small number of sites, even when subjected to high quality study, provide a very uncertain estimate of the occurrence or frequency of effects over many sites. This impact of this and other uncertainties affecting the outcome of field studies may be evaluated using the approaches described in section 6.8. This can then provide a basis for evaluating the weight that should be given to the field evidence, relative to the first-tier assessment and other types of higher tier evidence (weight of evidence assessment, section 6.9).

6.4.5. Pen studies

Pen tests are a form of semi-field study in which the product is applied according to practical use conditions, either by applying it within an aviary or pen or by setting up an open-bottom cage in the field after treatment. Such tests are only rarely conducted with mammals and birds, and there is no currently-recognised standard method. Detection of effects is facilitated by the confinement of the study animals within the pen, and by the use of replicated treated pens and controls. Formerly, these studies were considered as worst-case because the captive animals are confined to the treated area. However, this is invalidated by other factors. First, energy expenditure and hence food intake are reduced. More importantly, the rate of feeding is unlikely to approach levels achieved by free-living animals⁷⁹. Finally, there is no practical way to ensure that the study species is more sensitive (has a lower LD₅₀) than other species exposed in the wild. This last issue is critical, because the wide variation in toxicity between species means that untested species could be up to one or two orders of magnitude more sensitive than those used in the study. Therefore, it is recommended that new pen studies should not be conducted, unless for very specific purposes such as to investigate avoidance responses⁸⁰. For the same reasons, great care should be exercised when interpreting existing pen studies. The ecological realism of the study for the tested species should be carefully assessed, and the results should not be extrapolated to other species.

6.4.6. Conclusions and recommendations for use of field studies

The above considerations lead to the following conclusions and recommendations regarding field studies:

- Field studies that measure effects in the wild have a substantial advantage over other refinement options, because they avoid uncertainties associated with extrapolation from models or laboratory studies to the field. Further, they reduce uncertainties associated with extrapolating sensitivity (toxicity) from studied species to those exposed in the field. Semi-field studies (pen studies) do not have these advantages and are not recommended.
- Despite their advantages in reducing uncertainty, field studies of effects are not always the best option for refined risk assessment. In many cases, especially when the first-tier assessment ‘fails’ by only a small margin, other simpler and less costly options for refinement may be sufficient.

⁷⁹ Low feeding rates may greatly reduce risk by increasing the opportunity for avoidance responses and metabolism of the pesticide (EFSA, 2005a). This probably explains the failure of some existing pen studies (e.g. Pascual and Hart, 1997) to show mortality despite mortalities being documented for the same species in the wild.

⁸⁰ If the purpose of a pen study is to investigate avoidance, the PPR Panel’s recommendations in section 6.2 apply.

- Field studies to detect or quantify avian reproductive effects are significantly more difficult than field studies to detect or quantify mortality.
- When field studies are conducted, it is essential to define the objectives very clearly in advance. It is further desirable to discuss these with the relevant authorities if possible.
- An ‘extensive’ approach with multiple field study sites is recommended in preference to ‘intensive’ approaches where fewer sites are studied in more detail. More work (research and/or a workshop) would be desirable to develop guidance on how to determine an appropriate number of sites. In the meantime, expert statistical advice should be sought case-by-case on this issue.
- Care is required to ensure that the methods chosen for detecting effects in field studies are appropriate to the study objectives and provide adequate statistical power to be useful for risk assessment and decision-making.
- Results of new or existing field studies require critical evaluation, which will frequently require expert statistical advice. The primary focus should generally be to evaluate (a) the certainty that effects did or did not occur at the sites studied, and (b) what can be inferred about the occurrence of effects in general (over many sites).
- Uncertainties affecting the interpretation of field studies may be evaluated using the approaches described in section 6.8. This can then provide a basis for evaluating the weight that should be given to the field evidence, relative to the first-tier assessment and other types of higher tier evidence (weight of evidence assessment, section 6.9).

6.5. Use of wildlife incident data

When reviewing an authorised substance, it may be possible to use data from incidents involving wildlife (see e.g. Hardy and Stanley, 1984, Hardy et al., 1986, Fletcher and Grave, 1992; Mineau et al., 1999)⁸¹. These generally relate to lethal effects. For countries that have organised schemes to investigate and document reported incidents, the frequency of incidents can be regarded as a measure of visible mortality, which is one of the protection goals for higher-tier assessment. However, incident reporting is unlikely to be useful when assessing reproductive effects. Severe and widespread reproductive impacts have been detected in the past, e.g. the historical declines of raptor populations due to eggshell-thinning caused by DDT⁸² and DDE⁸³. However, much lower levels of effect would be sufficient to breach the protection goal of ‘no long-term repercussions on abundance and diversity’, and it is extremely unlikely that these lower levels of effect would be detected by casual observation.

It is important to recognise that the recorded frequency of poisoning incidents can be regarded as a measure of ‘visible mortality’. It is very likely to underestimate the level of mortality actually occurring. This is due to the fact that the probability of victims being noticed, collected, reported to an authority and identified as being affected by plant protection products is likely to be low (Baillie, 1993). This depends on numerous factors, including:

- Large animals are more conspicuous than small animals (Baillie, 1993);
- Mass mortality (e.g. of species which feed in flocks) is more conspicuous, and more likely to be reported, than single carcasses;
- Specimens with a high conservation interest are more likely to be reported than common species;

⁸¹ This section refers to ‘passive’ wildlife incident monitoring or surveillance, involving investigation of suspected incidents reported by farmers and members of the public. It excludes ‘active monitoring’ which is a form of field study and is dealt with in section 6.4.

⁸² DDT = dichlorodiphenyltrichloroethane

⁸³ DDE = dichlorodiphenyl dichloroethylene

- Animals receiving a life-threatening exposure to pesticide are likely to seek cover before they die (Fryday et al., 1996), making them unlikely to be found by casual observers;
- Birds are highly mobile and after exposure may travel a significant distance before becoming incapacitated. This reduces the likelihood that their deaths (if observed) will be suspected of association with pesticides and hence reduces the likelihood that they will be reported and investigated. On the other hand, birds exposed to very fast acting substances (a few minutes) are more likely to be found on the treated field;
- Passive monitoring is extremely unlikely to detect effects other than severe overt symptoms (e.g. incapacitation or convulsions) and mortality, and therefore provides virtually no information on reproductive effects;
- Incident investigation schemes do not exist in all countries and their organisation varies between countries (de Snoo et al., 1999).

For these reasons, an absence of incidents does not necessarily indicate the absence of risk or of impact. Conversely, the reporting of incidents confirms that effects occur at least under some circumstances. Furthermore, information on the types of species involved and nature of the effects and the circumstances under which they occur may be helpful when planning refined risk assessment, e.g. by identifying potential focal species, potentially relevant routes of exposure, and possible options for mitigating the risk.

It is concluded that assessments of existing (previously authorised) active substances should always include documentation and interpretation of any incidents of mortality or reproductive effects that have been reported via passive monitoring, but that absence of such reports for a particular pesticide should not be interpreted as evidence of low risk. Nevertheless, absence of such data for large-scale uses on bare soils is a stronger indication for low mortality than absence of such data for uses on smaller areas of growing crops. These and other uncertainties affecting the interpretation of incident data should be assessed using the approaches of section 6.8 and taken into account when weighing incident data against first-tier assessments and other types of higher tier evidence (section 6.9).

6.6. Phase-specific reproductive risk assessment

The screening and Tier 1 assessments do not distinguish between different phases of reproduction. In reality, different phases of reproduction may differ both in their exposure and their toxicological sensitivity to the pesticide. Furthermore, only a proportion of birds will be exposed and, for those that are exposed, the peak exposure may not occur during the most sensitive reproductive phase. These factors may be addressed by phase-specific risk assessment. To gain the full benefits of this approach requires detailed data that may not be available in some cases (e.g. time of application of the pesticide, time of breeding phases for focal species etc.). However, the phase specific approach may be an effective approach if the data are available. For further information see Appendix J.

6.7. Assessment of population-level effects

The survey of Member States and stakeholders undertaken by EFSA (2008) indicated that visible mortality and population effects should be the focus of concern for bird and mammal risk assessment. In principle, it would be desirable to assess these effects directly. This is not practical in first-tier assessments, but may be an option at higher tiers.

Assessing population effects quantitatively by population modelling is possible but very challenging. The methodology is complex and requires specialist population modelling expertise. Examples of population models exist in the research literature, e.g. Topping et al. (2005), Sibly et al. (2005),

Roelofs et al. (2005) and Wang and Grimm (2007)⁸⁴. However, there is no established guidance on population modelling, and there are no officially-accepted models for use in pesticide registration, so models have to be produced and evaluated/approved case-by-case.

Population modelling requires data on population parameters, which vary between species and countries and may be difficult to obtain and/or very uncertain. It may also require data on the spatial distribution of bird or mammal populations relative to the spatial distribution of pesticide use; information that is lacking or highly uncertain in most Member States. All these uncertainties have to be seen as additions to the usual uncertainties affecting estimates of exposure and effects for individuals, since these are needed as inputs for modelling population effects. Furthermore, the individual effects need to be provided in terms of the incidence of mortality (not just exposure relative to LD₅₀) and the incidence of different types of reproductive effect (not just exposure relative to NOAEL for most sensitive endpoint). This again requires additional parameters, which introduce additional uncertainties. Overall, therefore, estimates of population impacts are likely to be extremely uncertain. Nevertheless, quantitative modelling of population effects is an option for higher tier assessment, provided that the necessary expertise and data are available and provided that proper account is taken of all the uncertainties involved (methods for dealing with uncertainty are discussed in section 6.8). However, due to the complexity of these approaches it is recommended that they be discussed with the relevant authorities before proceeding.

It is also possible to consider the potential for population effects in a qualitative way, i.e. a reasoned argument expressed in words. Of course, all of the complexities mentioned above are still present, and it is not possible to account accurately for these in a qualitative evaluation. Therefore, a qualitative argument should concentrate on major factors that influence the population consequences of individual effects. Factors that could potentially reduce the risk of population consequences include:

- The proportion of the population that is exposed to an active substance at any one time (including the area likely to be treated in relation to population distribution);
- Extrapolation from no-effect to effect levels for reproductive effects; and
- The potential for an affected population to recover through reproduction (in unexposed periods) or immigration (from unexposed areas).

However, consideration must also be given to factors that may increase risk, e.g. multiple exposures from return visits to the treated field or other adjacent fields, and the likelihood that species that are already declining (as many farmland species are) will have little or no ability to absorb additional effects.

Any qualitative evaluation of population effects will be extremely uncertain, due to the large uncertainties affecting the magnitude of the factors involved, the way they interact, and their impact on population effects, and the contribution of other factors that it is not possible to include in a qualitative evaluation. Therefore it is essential that the evidence, reasoning and uncertainties are fully documented in every case. This should include a table such as that illustrated in section 6.8, to list the uncertainties and indicate their potential impact on the assessment outcome. The degree of uncertainty should be clearly explained to risk managers so they can take proper account of it in decision-making (see section 7).

6.8. Approaches for characterising uncertainty in higher-tier assessments

Point 2.5.2.1 in Annex VI to Directive 91/414/EEC states that no authorisation shall be granted unless it is "clearly established" that no unacceptable impact occurs. The term 'clearly establish' implies a requirement for some degree of certainty. First-tier assessments use standardised scenarios and

⁸⁴ These examples are provided as an indication of the types of approaches that are available, no endorsement is implied.

decision rules which are designed to provide an appropriate degree of certainty (see section 3 and Appendix C). Higher tier assessments are not standardised, and so the degree of certainty they provide has to be evaluated case by case. The need for risk assessments to include characterisation of uncertainty has also been emphasised at senior policy levels in the EU⁸⁵.

Methods for characterising uncertainty can be grouped into three main types:

- Qualitative methods: using words to describe the certainty of an outcome, or to describe how different the true outcome might be compared to an estimate.
- Deterministic methods: generating deterministic quantitative estimates of impact for a range of possible scenarios. This shows the range of possible outcomes (e.g. a range of TERs) and can be accompanied by qualitative descriptions of their relative probabilities (traditional ‘worst-case’ assessments are an example of this).
- Probabilistic methods: these give numeric estimates of the probabilities of different outcomes. These probabilities may be estimated statistically (e.g. when quantifying measurement or sampling uncertainty, or as outputs from probabilistic modelling). However, they may also be estimated subjectively, by expert judgement.

All uncertainties affecting an assessment should be considered at least qualitatively. To reduce the risk of overlooking important uncertainties, it is recommended to systematically consider each part of the assessment (e.g. different lines of evidence, different inputs to calculations, etc.) and list all of the sources of uncertainty together with a description of the magnitude and direction of their potential influence on the expected level of impact. As well as evaluating each individual source of uncertainty, it is also essential to give an indication of their combined effect. It is recommended to use a tabular approach to facilitate and document this process, as illustrated in Table 23. This is based on an approach used in some recent EFSA opinions (EFSA, 2005a; 2007b; 2007c; 2008), but adapted to increase clarity by introducing separate columns to describe uncertainties that act in different directions.

Research in social science has shown that there is a general tendency for experts to underestimate uncertainties. It is therefore important that risk assessors should be aware of the potential magnitude of common uncertainties in the assessment of risks to birds and mammals. For example, the ratio between the acute LD₅₀ for tested and untested species can be over one order of magnitude different (Luttik and Aldenberg, 1997). This implies up to 1 or 2 orders of magnitude uncertainty in estimating the LD₅₀ for the focal species in a refined risk assessment. Similarly, assessors should be aware of the potential magnitude of measurement uncertainties (e.g. in residue or radio-tracking data), and of the potential magnitude of sampling uncertainty associated with small and moderate sized datasets.

In some cases, a qualitative evaluation of uncertainties may be sufficient to establish clearly (i.e. with sufficient certainty) that unacceptable levels of impact will not occur, as is required by the ‘unless’ clause in Annex VI. In other cases, a purely qualitative evaluation of uncertainty may not give a sufficiently clear picture of the range of possible outcomes. In such cases, one option is to obtain additional data to reduce uncertainty. This may usefully be targeted on the uncertainties that appeared largest in the qualitative evaluation. However, an alternative option is to refine the characterisation of the uncertainties progressively, by evaluating some of them using first deterministic methods and then, if necessary, probabilistic methods. This implies a tiered approach to the treatment of uncertainties, which starts by evaluating all uncertainties qualitatively and progresses either by reducing uncertainty (by obtaining additional data) or by refining the evaluation of selected uncertainties (either deterministically or probabilistically), until the point where it can be ‘clearly established’ whether an unacceptable impact will occur (as required by the ‘unless clause in Annex VI).

⁸⁵ E.g. “Even though it is not a subject that lends itself easily to quantification, I would urge you to take account of the risk manager’s need to understand the level of uncertainty in your advice and to work towards a systematic approach to this problem.” (Madelin, 2004).

Table 23. Tabular approach recommended for qualitative evaluation of uncertainties in refined assessments.

The +/- symbols indicate whether each source of uncertainty has the potential to make the true risk higher (+) or lower (-) than the outcome of the refined assessment. The number of symbols provides a subjective relative evaluation of the magnitude of the effect (e.g. +++ indicates an uncertainty that could make the true risk much higher). If the effect could vary over a range, lower and upper evaluations are given (e.g. + / ++). If possible, the user should indicate the meaning of different numbers of symbols (e.g. two symbols might be used to represent a factor of 5, and three symbols a factor of 10). See Appendix C for some practical examples.

Source of uncertainty	Potential to make true risk lower	Explanation	Potential to make true risk higher	Explanation
Concise description of first source of uncertainty	Degree of negative effect (e.g. ---)	Short narrative text explaining how this factor could make true risk lower		
Second source of uncertainty			Degree of positive effect (e.g. +++)	Short narrative text explaining how this factor could make true risk higher.
Add extra rows as required for additional sources of uncertainty	-	Note: many uncertainties may act in both positive and negative directions	+	
Overall assessment	Narrative text describing the assessor's subjective evaluation of the overall degree of uncertainty affecting the assessment outcome, taking account of all the uncertainties identified above. The overall assessment should be a balanced judgement and not simply a summation of the plus and minus symbols.			

It is unlikely that it will ever be practical – or necessary – to quantify all uncertainties, so every deterministic or probabilistic assessment should be accompanied by a qualitative evaluation of the unquantified uncertainties. Also, it should be remembered that deterministic and probabilistic methods often require assumptions (e.g. about distribution shapes) that are themselves uncertain, and these additional uncertainties should be included in the qualitative evaluation. Therefore, every refined assessment should contain at least a qualitative evaluation of uncertainties. Individual first-tier assessments do not require an evaluation of uncertainty, because the uncertainties affecting the first-tier procedure have already been evaluated; furthermore, entries in the tables established for the first-tier procedures (in Appendix C) may be a useful starting point when evaluating uncertainty for refined assessments.

The overall magnitude of uncertainty associated with an assessment will often be very large. This should not be regarded as implying a failure of risk assessment; on the contrary, it provides essential information for decision-making (Madelin, 2004).

It should be noted that for pesticides where several different types of refined assessment are used (e.g. refined dietary modelling followed by an avoidance study or field study), the uncertainties affecting each one will be different. In such cases it is recommended to evaluate the uncertainties affecting each approach separately, including a separate version of Table 24 for each. The contribution of the multiple assessment approaches (multiple lines of evidence) in reducing overall uncertainty can then be evaluated by weight-of-evidence in the final risk characterisation (see next section).

In summary, it is recommended that:

- Every refined risk assessment should be accompanied by at least a qualitative evaluation of the uncertainties affecting it, using a systematic tabular approach such as that illustrated in Table 23.

Evaluations already done for the first-tier assessment procedures (Appendix C) may be useful as a starting point when evaluating uncertainty in refined assessments. In assessments with multiple lines of evidence, the uncertainties affecting each line of evidence should be evaluated separately.

- In cases where qualitative evaluation of uncertainty is not sufficient to determine whether it is clearly established that no unacceptable impact will occur, the assessor may either (a) seek further data to reduce the uncertainty, or (b) refine the evaluation of the existing uncertainties using quantitative methods (which can be either deterministic or probabilistic).

6.9. Risk characterisation and weight-of evidence assessment

Risk characterisation is the final step of risk assessment. At this point, all relevant information or evidence that has been gathered is used to produce an overall characterisation or description of the risk, in a form that is suitable for decision-making.

To be useful for decision-making, the risk characterisation should focus on evaluating whether the relevant protection goals are satisfied for the pesticide under assessment. As explained in the introduction to section 6, higher-tier assessment may address one or both of the following protection goals:

- The actual protection goal - to ensure a high certainty that there will be no visible mortality and no long-term repercussions on abundance and diversity;
- The surrogate protection goal - to make any mortality or reproductive effects unlikely.

The surrogate protection goal is more conservative than the actual protection goal, but more practical to assess.

Most refined assessments do not measure or estimate visible mortality and long-term repercussions directly. Evaluating these by extrapolation from simpler measures of risk (e.g. a TER) is very uncertain. Furthermore, neither the level of certainty required, nor all other aspects of the decision-making criteria⁸⁶ are defined. It is therefore recommended to adopt a tiered approach to risk characterisation, as follows:

1. First, to consider whether the evidence provided by the risk assessment is sufficient to satisfy the surrogate protection goal of making any mortality or reproductive effects unlikely. If so, it can be assumed there is also a high certainty that no visible mortality or long-term repercussions, nor short-term population effects will occur. This is a more conservative criterion than is implied by the 'unless' clause, but it is more practical to assess and enables firm conclusions to be reached without requiring more precise definition of the 'unless' clause criteria.
2. If the evidence does not satisfy the surrogate protection goal of making any effects unlikely, then attention should shift from establishing the lack of effects to assessing the *levels* of mortality and reproductive effects that may occur, as well as their implications for the likelihood of visible mortality and long-term repercussions on abundance and diversity. It should be recognised that the additional uncertainty inherent in this more complex assessment may make it difficult to meet the Annex VI criterion of 'clearly establish'.

Often, risk characterisation will involve combining several different types of refined assessment, each providing a separate indication of the risk. For example, an applicant might submit a refined dietary exposure assessment, together with some avoidance studies. These need to be integrated in an overall risk characterisation that takes appropriate account of each, so as to provide the best basis for decision-making. This process of combining available 'lines of evidence' to form an integrated conclusion or

⁸⁶ E.g. there is no firm definition of the spatial and temporal scale for assessing 'long-term repercussions', nor of what constitutes 'visible' mortality, nor of the acceptable magnitude for short-term population effects.

risk characterisation is frequently referred to as ‘weight-of-evidence’ assessment (e.g. EC, 2002; Hull and Swanson, 2006). This term reflects the principle that the contribution of each line of evidence should be considered in proportion to its weight.

It is emphasised that weight-of-evidence assessment is not itself a method of refined assessment, nor is it a substitute for refinement options such as those listed in Table 22. Instead, it is an approach for weighing and combining lines of evidence resulting from first-tier and refined assessments to form an overall characterisation of risk.

In the context of this document, a line of evidence might be the completed output of any of the refinement options, such as a refined dietary exposure assessment, an avoidance study (or several avoidance studies considered together), a body-burden model, or a field study designed to measure mortality. Note that some refinement options, such as field studies to measure PT, are not lines of evidence in themselves but rather contributions to a line of evidence (PT is an input for refined exposure modelling).

A qualitative⁸⁷ approach to weight-of-evidence assessment is recommended, as follows:

- Consider all relevant lines of evidence, including the first-tier assessment. Retention of the first-tier assessment is appropriate in all cases, as it is relevant to consider whether it was borderline or failed by a large margin. In addition, the first-tier assessment of risk for sprayed pesticides deserves special consideration in weight of evidence, because it is given increased weight as a predictor of mortality in the field (see below) in the analysis of field studies (see Appendix C).
- Evaluate the uncertainties associated with each line of evidence. This should be done by applying the approaches described in the preceding section to each line of evidence separately. The characterisation of overall uncertainty for each line of evidence is then used in the weight-of-evidence assessment, as in principle the weight given to each line of evidence should be proportionate to its certainty (see below).
- Form overall conclusions by using expert judgement to combine all lines of evidence, weighted according to their certainty, and give more weight to the most certain, but also take due account of the less certain. High certainty implies high weight. If one line of evidence implies a much narrower range for the risk than another line of evidence (i.e. higher certainty), then the true risk is most likely to fall inside the range of the former.
- Be sure to take full account of the uncertainties and to include a fair description of the range of possible outcomes in the final risk characterisation. Identify the outcome that is considered most likely, but do not give it more emphasis than is justified by the evidence.
- If different lines of evidence conflict (e.g. a low TER but no effects in a field study), this should be considered a form of uncertainty. No line of evidence should be completely discounted unless it is wholly invalid or irrelevant. Instead, as stated above, each line of evidence should contribute to the overall conclusion in proportion to its certainty.
- If the overall characterisation of risk is expressed qualitatively, choose words very carefully to describe the outcome and its uncertainty as clearly as possible. For example the phrase ‘on balance’ is often used to focus on one of several possible outcomes, e.g. “on balance, it is concluded there will be no mortality”. This type of statement is not appropriate, because it fails to communicate the degree of certainty (e.g. ‘on balance’ could mean 51 % certainty, or 99 %) ⁸⁸.
- A weight-of-evidence assessment is inevitably subjective. Different assessors may vary in their weighing of the evidence, especially when uncertainty is high. Therefore, it is essential to

⁸⁷ Quantitative approaches could also be used to combine lines of evidence, but this requires each line of evidence to be expressed in the same units together with a quantitative measure of its certainty.

⁸⁸ Note that the standard of evidence required by the ‘unless’ clause is ‘clearly establish’, which is much stronger than ‘on balance’.

document the assessment in detail, including the outcome and uncertainty for each lines of evidence considered, and explaining how they were combined to reach conclusions about the overall outcome and its uncertainty.

A systematic tabular approach is recommended for documenting the weight-of-evidence assessment, such as that illustrated in Table 24. The tabular format provides a concise yet clear summary of the lines of evidence considered and how they were combined. It also helps the reader to evaluate whether the assessment was balanced, and aids consistency of approach between pesticides.

It should be noted that Table 24 summarises the major types of uncertainty for each line of evidence, and not just the overall uncertainty. This is recommended because it helps the assessor to take account of some important strengths and weaknesses of different types of refined assessment, as can be seen from the example in Appendix C (Table 4). Note that uncertainty entries for the first-tier assessment may be copied from the corresponding uncertainty table shown in Appendix C.

The subjectivity of weight-of-evidence assessment can impede the formation of an independent view when this is based on the assessment of another person. Therefore, when a weight-of-evidence assessment is submitted by an applicant, it would be prudent for the regulatory authority to conduct their own weight-of-evidence assessment separately, compare their conclusion with that of the applicant, and consider the reasons for any differences.

It is sometimes objected that characterising uncertainty is unhelpful in decision-making. In fact, it is essential for risk assessors to characterise uncertainty, as is clear from Directive 91/414/EEC ('clearly establish') and from policy statements by the European Commission (Madelin, 2004; EC, 2000). Furthermore, practical options exist for dealing with uncertainty in decision-making. As stated in section 6.8, two of the principal options are to request more data to reduce uncertainty, or to request more refined evaluation or analysis of the existing uncertainty. A third option is to counter the uncertainty by applying risk mitigation options (see section 7), so that the chance of adverse impacts is limited to an acceptable level⁸⁹. However, choosing between options for dealing with uncertainty involves risk management considerations outside the scope of this document such as the acceptability of effects, the degree of certainty required and potentially other factors such as the cost and time required for further refinement, the need to respect legal deadlines for authorisations, and the consequences of risk mitigation or non-authorisation (e.g. reduced efficacy, reduced choice of pest control options in agriculture, risk of resistance, etc.).

In summary, it is recommended that:

- Every refined risk assessment should conclude with an overall characterisation of risk, in terms relevant for decision-making. It is recommended to begin with the consideration of whether the evidence makes any mortality or reproductive effects unlikely (the surrogate protection goal). Where this is not satisfied, attention should turn to characterising the levels of mortality and reproductive effects that may occur, and using this to evaluate whether there is a high certainty of no visible mortality and no long-term repercussions on abundance and diversity (the actual protection goal).
- The overall characterisation of risk should be derived by a qualitative weight-of-evidence assessment considering all relevant lines of evidence and their uncertainties using a systematic tabular approach (see e.g. Table 24). If the overall characterisation is expressed qualitatively (in words) rather than quantitatively, great care should be taken to describe the outcome and its uncertainty as clearly as possible.

⁸⁹ "In cases where both the potential risk and scientific uncertainties are high, the risk manager may conclude that a precautionary approach is appropriate." (Madelin, 2004).

- The first-tier assessment should always be included as one of the lines of evidence, and given appropriate weight (this will be higher for acute risks of sprayed pesticides than for other types of assessment).

Table 24. Tabular approach recommended for qualitative weight-of-evidence assessment, summarising the conclusion and uncertainties for several lines of evidence and using them to develop an overall conclusion (see Appendix C, Table 4) for a practical example.

The +/- symbols indicate whether each source of uncertainty has the potential to make the true risk higher (+) or lower (-) than the indicated outcome. The number of symbols provides a subjective relative evaluation of the magnitude of the effect (e.g. - - - might indicate an uncertainty that could reduce risk by an amount equivalent to reducing a TER by about a factor of 10). If the effect could vary over a range, lower and upper evaluations are given (e.g. - / ++ or + / ++).

	Lines of evidence (add more columns if appropriate)		
	First-tier assessment (should always be included)	Second line of evidence	<i>Add one column for each line of evidence</i>
Main contributions to uncertainty:			
Concise description of first major source of uncertainty	+ and – symbols (see legend)		
Second uncertainty			
Add one row for each major source of uncertainty			
Conclusions for individual lines of evidence	Insert overall assessment for each line of evidence		
Overall conclusion	Insert overall conclusion giving appropriate weight to each line of evidence, taking account of their relative certainty (more uncertainty = less weight). The overall conclusion should be a balanced judgement and not simply a summation of the plus and minus symbols.		

7. Risk management and decision-making

7.1. Risk management considerations⁹⁰

The survey of Member States and stakeholders undertaken by EFSA (2008) indicated that visible mortality and population effects should be the focus of concern for bird and mammal risk assessment. Due to the difficulties of assessing these directly the approach taken in the procedures for first-tier assessments, and in most of the options for refined assessments, is to focus on individual effects, such that the population is protected (see section 3 and Appendix C for a full discussion of these issues). This introduces a degree of conservatism as a means of dealing with the many and large uncertainties

⁹⁰ Risk management is outside the remit of EFSA. The guidance in this section was developed by the Joint Working Group (see also EC, 2009).

that would affect assessments of effects at the population level. In cases where the assessment outcome breaches the standard decision-making criteria, risk managers may wish to consider whether the degree of conservatism is appropriate.

This question could be approached from two quite different directions. The first is for risk assessors to refine their assessment. This could be done via any of the options for refinement considered in section 6, including moving from assessing individual effects to assessing population effects. Population effects may be assessed either quantitatively or qualitatively, although both involve substantial uncertainties that must be taken into account (section 6.8). Of course, any scientific evaluation of population effects should be fully documented and justified, as a separate section of the risk assessment (as for any refined assessment). Any additional assessments should not be considered in isolation but should be weighed against evidence from the first-tier assessment and any other refined assessment options, to form an overall characterisation of the predicted effects and their associated uncertainties (section 6.9)⁹¹.

The second possibility (which may be used in conjunction with the first) is for risk managers to weigh the scientific assessment of risk against other risk management considerations. Plant protection products are applied for the benefits they provide. Where risk managers consider that these benefits outweigh any predicted adverse effects from the risk assessment (taking account of their uncertainty), they may take the decision that authorisation is justifiable. For example, use of a plant protection product on a minor crop may be deemed essential and pose a lower threat to a population than use on a major crop, although the potential for aggregation of effects over multiple minor crops may also be relevant. Any risk management considerations affecting the final decision, either for no authorisation or for authorisation, must be explained in full. One of the benefits of this approach will be to assist other competent authorities when making their decisions on applications for mutual recognition or, in future, zonal authorisations.

7.2. Risk mitigation options

If at least one substantial area of use has been identified as acceptable in the risk assessment at the EU level, i.e. the TER is higher than the appropriate Annex VI trigger values, but a high risk is still indicated for other areas of use, it may be appropriate to consider risk mitigation options. These options are use-specific. It must be assessed in each case if their effectiveness can be determined on a Member State basis (e.g. in the context of a national authorisation) or if it must be determined during the process of Annex I inclusion of the active substance. In any case, the effectiveness of risk mitigation measures must be demonstrated before Annex I inclusion, as prescribed by the European Court⁹². Outlined below are possible options which could be considered if a high risk is indicated.

7.2.1. Risk from seed treatments

If a high risk from a seed treatment is predicted, labelling should instruct the immediate removal of spills. Furthermore, it may be appropriate to consider that the seed be drilled or incorporated immediately after application. If seed is incorporated, its availability to birds and mammals will be reduced and hence if an acute risk has been highlighted, this will be reduced as birds and mammals will take longer to find and consume treated seed. It has to be assessed, of course, whether consumption is reduced sufficiently thereby to conclude that the risk is acceptable. In order to do so, agronomic practices should be considered, for example, the likelihood of seed germination and the effectiveness of seed treatment on incorporated seeds. This risk management option has been

⁹¹ Assessments of population consequences tend to be very uncertain and must therefore be weighed carefully against other lines of assessment that address individual effects but with less uncertainty (see sections 6.7-6.9).

⁹² Judgement of the Court of First Instance in Case T-229/04 of 11 July 2007 - Kingdom of Sweden v Commission of the European Communities; annulment of the inclusion of paraquat into Annex I of Directive 91/414/EEC; paras 224 and 227, among others.

considered in detail by Pascual et al. (1999b) and further information regarding risk management options for cereal seed is presented in Pascual et al. (1999a and b).

7.2.2. Risk from granules

If a high risk from granules has been highlighted, the removal of spills should be required and the feasibility of incorporating them at the time of application be considered in order to reduce their availability to birds. As for seed treatment, agronomic implications should be considered when assessing this as a risk management option.

7.2.3. Risk from spray applications

If a risk to birds and mammals has been indicated from the use of a spray, this risk may be reduced by decreasing the application rate and/or application frequency. However, this may significantly affect the efficacy of the product. Alternatively, spot or row treatment may be appropriate depending upon the pest or disease being treated. Changing the method of application from spray to a more targeted approach, e.g. bait or paste/paint may reduce the risk to birds and mammals but the success of this approach will depend upon the disease or pest being treated. If a reproductive risk to birds or mammals has been highlighted, then it may be appropriate to restrict the time of application to the non-breeding time of birds or mammals or to limit the number of applications and hence reduce exposure.

Regardless of the ultimate choice that is made between options of risk management, any impact on the effectiveness and usefulness of the product should be evaluated so it can be taken into account in decision making.

RECOMMENDATIONS

The Commission recommends that it is acceptable that an applicant applies already this current Guidance Document. For all dossiers submitted as of 1 July 2010 this current Guidance Document should be applied. This Guidance Document should be revised in 2012 taking into account experience from using it. Member States are encouraged to use a questionnaire that will be made available to provide feedback to EFSA.

DOCUMENTATION PROVIDED TO EFSA

1. EFSA, 2008. Scientific Opinion of the Panel on Plant protection products and their residues on the Science behind the Guidance Document on risk assessment for birds and mammals. *The EFSA Journal* (2008) 734, 1-181
2. Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. *Journal of the European Union, L 230, 19.8.1991, p. 1–32.*
3. Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. *Official Journal of the European Union, L 309/1-50, EN, 24.11.2009*

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⁹³ Available at: http://randd.defra.gov.uk/Document.aspx?Document=PS2308_2672_FRP.doc

⁹⁴ Available at: http://randd.defra.gov.uk/Document.aspx?Document=PS2330_6382_FRP.doc

⁹⁵ Available at: http://ec.europa.eu/food/plant/protection/evaluation/guidance/wrkdoc19_en.pdf

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APPENDICES

See separate documents.

Name	Appendix title
A	Bird and mammals Tier 1 tables
B	Combined effects of simultaneous exposure to several active substances
C	Evaluation of the level of protection provided by the proposed first-tier assessment procedures
D	Proportions of List 3a substances failing under current and proposed lower tier procedures for acute risk assessment
E	Impact of crop interception on residues on plant food items
F	Residues of plant protection products on food items for birds and mammals
G	Calculating exposure for the dietary intake approach
H	Multiple applications and residue dynamics in the environment
J	Detailed guidance on how to carry out the repro risk assessment
K	Background information on the assessment of uptake via drinking water
L	Energy, moisture content and assimilation efficiency of bird and mammal food
M	How to determine a focal species
N	Recommendations on arthropod residue field studies
P	How to estimate PT
Q	How to determine bird and mammal diets
R	Nestling scenarios for long-term assessments
S	Bioaccumulation of chemicals in terrestrial vertebrates

ABBREVIATIONS

ADME	absorption, distribution, metabolism and excretion
AE	Assimilation efficiency
AFSSA	Agence française de sécurité sanitaire des aliments
AR	Application rate
a.s.	Active substance
AV	Avoidance factor
BAF	Bioaccumulation factor
BB	Body burden
BBCH	Biologische Bundesanstalt, Bundessortenamt and Chemical industry
BCF	Bioconcentration factor
bw	body weight
C	Concentration
CSL	Central Science Laboratory (now: The Food and Environment Research Agency)
d	Day
DDD	Daily dietary dose
DEE	Daily energy expenditure
DT ₅₀	Time for 50 % degradation
dw	Drinking water
DWR	Drinking water rates
EC	European Commission
EEC	European Economic Community
EFSA	European Food Safety Authority
EPCO	EFSA Peer Review Co-Ordination
EPPO	European and Mediterranean Plant Protection Organization
ETE	Estimated theoretical exposure
EU	European Union
F1	Initial offspring generation
F2	Second generation
FE	Food energy
FIR	Food intake rate
FOCUS	Forum for the Co-ordination of pesticide fate models and their Use
FS	Focal species
g	Gram
GD	Guidance Document
GLP	Good Laboratory Practice
gw	Ground water
HD5	hazardous dose to 5 % of the species
IUPAC	International Union of Pure and Applied Chemistry
<i>k</i>	rate constant
kg/ha	Kilogram per hectare
kJ	Kilojoule
K _{OC}	Organic carbon absorption coefficient
K _{OW}	Octanol-water partition coefficient
L	Litre
LC ₅₀	Lethal concentration; the concentration at which 50 % of the test organisms die.
LD ₅₀	Lethal dose; the dose at which 50 % of the test organisms die.
LoP	Level of protection
lt	Long-term
LTE	long-term exposure assessment
MAF	Multiple application factor
MC	Moisture Content
mg/kg	Milligram per kilogram
mg/L	Milligram per litre
MRL	Maximum residue levels
MS	Member State
n	Sample size

NAR	Nominal application rate
NIEHS	National Institute of Environmental Health Sciences
NOAEL	No observed adverse effect level
NOEC	No observed effect concentration
NOED	No observed effect dose
NOEL	No observed effect level
OECD	Organisation for Economic Co-operation and Development
OPPTS	US EPA's Office of Pesticide Programs and Toxic Substances
PD	Composition of diet obtained from treated area
PEC	Predicted environmental concentration
PHI	pre-harvest interval
ppm	Parts per million
PPR Panel	Scientific Panel on Plant Health, Plant Protection Products and their Residues
PRAPeR	EFSA's unit for the pesticide risk assessment peer-review
PSD	Pesticide Safety Directorate
PT	Proportion of an animal's daily diet obtained in habitat treated with pesticide
QSAR	Quantitative structure-activity relationship
RA	Risk assessment
RAC	Regulatory acceptable concentration
RIVM	Netherlands National Institute of Public Health and the Environment
RUD	Residue unit dose
SANCO	European Commission Health and Consumer Protection Directorate General
SAR	Structure-activity relationship
SCFCAH	Standing Committee on the Food Chain and Animal Health
SCP	Scientific Committee on Plants
SETAC	Society of Environmental Toxicology and Chemistry
SP	Soil particle
STE	short-term exposure assessment
SV	shortcut value
sw	Surface water
TER	Toxicity-exposure-ratio
TWA	Time weighted average
US EPA	United States Environmental Protection Agency
WF	Water flux
WG	Working Group
WoE	Weight of evidence

LIST OF TABLES

No.	Title of table
1.	Extrapolation factors based on the number of individuals tested at the limit dose.
2.	Factors for converting endpoints from mammalian toxicity studies from ppm to mg a.s./kg bw/d.
3.	LD ₅₀ mg/kg bw for various bird species and their use in the calculation of the geometric mean.
4a	Illustration of how to combine two studies on the same species (Example a)
4b	Illustration of how to combine two studies on the same species (Example b)
4c	Results following the combination of all these results as if it were one study.
5.	Crop groups and crop species
6.	Acute shortcut values (based on 90 th percentile residues) for avian indicator species.
7.	Multiple application factors for 90 th percentile residue data (MAF ₉₀) for selected application intervals and n = 1-8 applications (considering a default DT ₅₀ of 10 d on foliage).
8.	Acute shortcut values (based on 90 th percentile residues) for mammalian indicator species.
9.	Multiple application factors for 90 th percentile residue data (MAF ₉₀) for selected application intervals and n = 1 – 8 applications (considering a default DT ₅₀ of 10 d on foliage).
10.	Indicator species and shortcut values (based on mean residues) for the avian reproductive assessment.
11.	Multiple application factors assuming mean residues (MAF _m), for use in reproductive assessments.
12.	Indicator species and shortcut values (based on mean residues) for the mammalian reproductive assessment.
13.	Multiple application factors assuming mean residues (MAF _m), for use in reproductive assessments.
14.	FIR/bw values for generic focal species exposed to plant seedlings or by granules sticking to earthworms.
15.	Estimation of input parameters for acute reproductive risk assessment for birds ingesting granules intentionally when seeking grit.
16.	Estimation of shortcut values for acute and long-term exposure via contaminated soil for a generic bird and mammalian omnivorous species of 25 g.
17.	Shortcut values for different incorporation depths (e.g. 10, 15, 20 and 25 cm).
18.	Type of seeds, corresponding indicator species and their food intake rate per body weight.
19.	Generic focal species and corresponding shortcut values for assessment of residues present in newly emerged crop shoots.
20.	Mean and maximum number of large and small seeds taken by birds in a single feeding bout in field studies, summarised from Prosser (1999).
21.	Summary of most important types of uncertainty affecting different types of evidence that may be available in higher-tier assessment of seed treatments.
22.	Overview of options for higher-tier assessment.
23.	Tabular approach recommended for qualitative evaluation of uncertainties in refined assessments.
24.	Tabular approach recommended for qualitative weight-of-evidence assessment, summarising the conclusion and uncertainties for several lines of evidence and using them to develop an overall conclusion.
	Tables of Annex I
I 1	Shortcut values for avian generic focal species.
I 2	Shortcut values for mammalian generic focal species

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 90th percentile RUDs should be used for acute assessments.

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th 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 10-29	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

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Cereals	BBCH \geq 40	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	3.3	7.2
Cereals	Late season- Seed heads	Small granivorous/insectivorous bird "bunting"	Yellowhammer (<i>Emberiza citronella</i>)	12.5	27.0
Cotton	BBCH 10 - 19	Medium insectivorous bird "pranticole"	Collared Pratincoles <i>Glareola pratincola</i>	2.3	4.2
Cotton	BBCH \geq 20	Medium insectivorous bird "pranticole"	Collared Pratincoles <i>Glareola 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 \geq 50	Small omnivorous bird "sparrow"	House sparrow (<i>Passer domesticus</i>)	2.8	4.4
Fruiting vegetables	Fruit stage BBCH 71-89	Frugivorous bird "crow"	Crow (<i>Corvus brachyrhynchos</i>)	32.0	57.4
Fruiting vegetables	BBCH 10 - 49	Small granivorous bird "finch"	Linnet (<i>Carduelis cannabina</i>)	11.4	24.7
Fruiting vegetables	BBCH \geq 50	Small granivorous bird "finch"	Linnet (<i>Carduelis cannabina</i>)	3.4	7.4
Fruiting vegetables	BBCH 10 - 49	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	10.9	24.0
Fruiting vegetables	BBCH \geq 50	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	3.3	7.2
Fruiting vegetables	Fruit stage BBCH 71-89	Frugivorous bird "Starling"	Starling (<i>Sturnus vulgaris</i>)	20.7	49.4
Fruiting vegetables	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	11.3	26.8
Fruiting vegetables	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	9.7	25.2
Grassland	New sown grass seeds	Small granivorous bird "Sparrow"	House sparrow (<i>Passer domesticus</i>)	9.4	20.4
Grassland	Late season (seed heads)	Small granivorous bird "finch"	Linnet (<i>Carduelis cannabina</i>)	11.4	24.7
Grassland	Growing shoots	Large herbivorous bird "goose"	Pink-foot goose (<i>Anser brachyrhynchus</i>)	16.2	30.5
Grassland	Growing shoots	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	11.3	26.8
Hop	BBCH 10 - 19	Small insectivorous bird "finch"	Chaffinch (<i>Fringilla coelebs</i>)	9.1	23.8
Hop	BBCH \geq 20	Small insectivorous bird "finch"	Chaffinch (<i>Fringilla coelebs</i>)	10.6	25.3
Hop	BBCH 10 - 19	Small granivorous bird "finch"	Goldfinch (<i>Carduelis carduelis</i>)	11.4	24.6

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Hop	BBCH 20 - 39	Small granivorous bird "finch"	Goldfinch (Carduelis carduelis)	5.7	12.3
Hop	BBCH \geq 40	Small granivorous bird "finch"	Goldfinch (Carduelis carduelis)	3.4	7.4
Leafy vegetables	BBCH 10 - 49	Small granivorous bird "finch"	Serin (Serinus serinus)	12.6	27.4
Leafy vegetables	BBCH \geq 50	Small granivorous bird "finch"	Serin (Serinus serinus)	3.8	8.2
Leafy vegetables	BBCH 10 - 49	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0
Leafy vegetables	BBCH \geq 50	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	3.3	7.2
Leafy vegetables	Leaf development BBCH 10-19	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (Columba palumbus)	37.0	90.6
Leafy vegetables	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	11.3	26.8
Leafy vegetables	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	9.7	25.2
Legume forage	BBCH 10 - 49	Small granivorous bird "finch"	Linnet (Carduelis cannabina)	11.4	24.7
Legume forage	BBCH \geq 50	Small granivorous bird "finch"	Linnet (Carduelis cannabina)	3.4	7.4
Legume forage	BBCH 10 - 49	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0
Legume forage	BBCH \geq 50	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	3.3	7.2
Legume forage	Leaf development BBCH 21-49	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (Columba palumbus)	22.7	55.6
Legume forage	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	11.3	26.8
Legume forage	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	9.7	25.2
Maize	BBCH 10 - 29	Medium granivorous bird "gamebird"	Partridge (Perdix perdix)	3.0	6.6
Maize	BBCH 30 - 39	Medium granivorous bird "gamebird"	Partridge (Perdix perdix)	1.5	3.3
Maize	BBCH \geq 40	Medium granivorous bird "gamebird"	Partridge (Perdix perdix)	0.8	1.6
Maize	Leaf development BBCH 10 to 19	Small insectivorous/worm feeding species "thrush"	Robin (Erithacus rubecula)	5.7	10.5
Maize	BBCH 10 - 29	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Maize	BBCH 30 - 39	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	5.4	12.0
Maize	BBCH \geq 40	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	2.7	6.0
Maize	BBCH 10 - 29	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	22.7	55.6
Maize	BBCH 30 - 39	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	11.4	27.8
Maize	BBCH \geq 40	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	5.7	13.9
Maize	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	11.3	26.8
Maize	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	4.8	12.6
Oilseed rape	late – late (with seeds) (BBCH 30-99)	Small insectivorous bird "dunnock"	Dunnock (<i>Prunella modularis</i>)	2.7	7.4
Oilseed rape	early (shoots) (BBCH 10-19)	Large herbivorous bird "goose"	greylag goose (<i>Anser anser</i>)	15.9	39.0
Oilseed rape	late (with seeds) (BBCH 80-99)	Small granivorous bird "finch"	Linnet (<i>Carduelis cannabina</i>)	11.4	24.7
Oilseed rape	BBCH 10 - 29	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	10.9	24.0
Oilseed rape	BBCH 30 - 39	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	3.3	7.2
Oilseed rape	BBCH \geq 40	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	2.7	6.0
Oilseed rape	BBCH 10 - 19	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	22.7	55.6
Oilseed rape	BBCH 20 - 29	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	3.5	4.0
Oilseed rape	BBCH 30 - 39	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	1.1	2.4
Oilseed rape	BBCH \geq 40	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (<i>Columba palumbus</i>)	0.9	2.0
Oilseed rape	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	5.9	10.9
Oilseed rape	BBCH 20 - 29	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	2.8	7.7

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Orchard	Spring Summer,	Small insectivorous bird "tit"	Bluetit (<i>Parus caeruleus</i>)	18.2	46.8
Orchard	Not crop directed application all season	Small insectivorous/ worm feeding species "thrush"	Robin (<i>Erithacus rubecula</i>)	2.7	7.4
Orchard	Crop directed application BBCH 10 - 19	Small insectivorous/ worm feeding species "thrush"	Robin (<i>Erithacus rubecula</i>)	2.1	5.9
Orchard	Crop directed application BBCH 20 - 39	Small insectivorous/ worm feeding species "thrush"	Robin (<i>Erithacus rubecula</i>)	1.6	4.4
Orchard	Crop directed application BBCH ≥ 40	Small insectivorous/ worm feeding species "thrush"	Robin (<i>Erithacus rubecula</i>)	0.8	2.2
Orchard	Not crop directed application all season	Small granivorous bird "finch"	Serin (<i>Serinus serinus</i>)	12.6	27.4
Orchard	Crop directed application BBCH 10 - 19	Small granivorous bird "finch"	Serin (<i>Serinus serinus</i>)	10.1	21.9
Orchard	Crop directed application BBCH 20 - 39	Small granivorous bird "finch"	Serin (<i>Serinus serinus</i>)	7.6	16.4
Orchard	Crop directed application BBCH ≥ 40	Small granivorous bird "finch"	Serin (<i>Serinus serinus</i>)	3.8	8.2
Ornamentals /nursery	Application to plant	Small insectivorous bird "tit"	Bluetit (<i>Parus caeruleus</i>)	18.2	46.8
Ornamentals /nursery	Application to plant – exposure to underlying ground	Small insectivorous/worm feeding species "thrush"	Robin (<i>Erithacus rubecula</i>)	2.7	7.4
Potatoes	BBCH 10 - 39	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	10.9	24.0
Potatoes	BBCH ≥ 40	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	3.3	7.2
Potatoes	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	11.3	26.8
Potatoes	BBCH ≥ 20	Small insectivorous bird "wagtail"	Yellow wagtail (<i>Motacilla flava</i>)	9.7	25.2
Pulses	BBCH 10 - 49	Small granivorous bird "finch"	Linnet (<i>Carduelis cannabina</i>)	11.4	24.7
Pulses	BBCH ≥ 50	Small granivorous bird "finch"	Linnet (<i>Carduelis cannabina</i>)	3.4	7.4
Pulses	BBCH 10 - 49	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	10.9	24.0
Pulses	BBCH ≥ 50	Small omnivorous bird "lark"	Woodlark (<i>Lullula arborea</i>)	3.3	7.2

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Pulses	Leaf development BBCH 10-19	medium herbivorous/granivorous bird "pigeon"	Wood pigeon (Columba palumbus)	22.7	55.6
Pulses	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	11.3	26.8
Pulses	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	9.7	25.2
Root & stem vegetables	BBCH 10 - 39	Small granivorous bird "finch"	Linnet (Carduelis cannabina)	11.4	24.7
Root & stem vegetables	BBCH \geq 40	Small granivorous bird "finch"	Linnet (Carduelis cannabina)	3.4	7.4
Root & stem vegetables	BBCH 10 - 39	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0
Root & stem vegetables	BBCH \geq 40	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	3.3	7.2
Root & stem vegetables	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	11.3	26.8
Root & stem vegetables	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	9.7	25.2
Strawberries	BBCH 10 - 39	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0
Strawberries	BBCH \geq 40	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	4.4	9.6
Strawberries	Late (Flowering/ development of fruit/ Maturity of fruit) BBCH 61-89	Frugivorous bird "Starling"	Starling (Sturnus vulgaris)	13.4	27.0
Strawberries	BBCH 10 - 19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	11.3	26.8
Strawberries	BBCH \geq 20	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	9.7	25.2
Sugar beet	late (summer/ autumn) (BBCH 30-49)	Small granivorous bird "finch"	Linnet (Carduelis cannabina)	11.4	24.7
Sugar beet	early (spring) (BBCH 10-19)	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0
Sugar beet	BBCH 10-19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	5.9	10.9
Sugar beet	BBCH 20 - 49	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	2.8	7.7
Sugar beet	BBCH 10-19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	5.9	10.9
Sugar beet	BBCH 20 - 49	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	9.7	25.2
Sunflower	Early Germination/ leaf development) BBCH 00-19	Small omnivorous bird "lark"	Woodlark (Lullula arborea)	10.9	24.0

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Sunflower	Early (Germination/ leaf development) BBCH 00-19	Small insectivorous bird "wagtail"	Yellow wagtail (Motacilla flava)	11.3	26.8
Sunflower	Late (Flowering, seed ripening) BBCH 61-92	Small granivorous/insectivorous bird "bunting"	Yellowhammer (Emberiza citronella)	10.0	21.7
Vineyard	BBCH 10 - 19	Small insectivorous species "Redstart"	Black Redstart (Phoenicurus ochruros)	11.5	27.4
Vineyard	BBCH \geq 20	Small insectivorous species "Redstart"	Black Redstart (Phoenicurus ochruros)	9.9	25.7
Vineyard	BBCH 10 - 19	Small granivorous bird "Finch"	Linnet (Carduelis cannabina)	6.9	14.8
Vineyard	BBCH 20 - 39	Small granivorous bird "Finch"	Linnet (Carduelis cannabina)	5.7	12.4
Vineyard	BBCH \geq 40	Small granivorous bird "Finch"	Linnet (Carduelis cannabina)	3.4	7.4
Vineyard	Ripening	Frugivorous bird "Trush/starling"	Song Thrush (Turdus philomelos)	14.4	28.9
Vineyard	BBCH 10 - 19	Small omnivorous bird "lark"	Wood Lark (Lullula arborea)	6.5	14.4
Vineyard	BBCH 20 - 39	Small omnivorous bird "lark"	Wood Lark (Lullula arborea)	5.4	12.0
Vineyard	BBCH \geq 40	Small omnivorous bird "lark"	Wood Lark (Lullula arborea)	3.3	7.2

Table I. 2. Shortcut values for mammalian generic focal species. The shortcut value based on mean RUDs should be used for reproductive assessments, and the shortcut value based on 90th percentile RUDs should be used for acute assessments.

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Bare soils	BBCH < 10	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	5.7	14.3
Bulbs & onion like crops	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Bulbs & onion like crops	BBCH ≥ 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Bulbs & onion like crops	BBCH ≥ 40	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	43.4	81.9
Bulbs & onion like crops	BBCH 10 - 39	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	7.8	17.2
Bulbs & onion like crops	BBCH ≥ 40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	4.7	10.3
Bush & cane fruit	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Bush & cane fruit	BBCH ≥ 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Bush & cane fruit	BBCH 10-19	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	43.4	81.9
Bush & cane fruit	BBCH 20 - 39	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	36.1	68.2
Bush & cane fruit	BBCH ≥ 40	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	21.7	40.9
Bush & cane fruit	Fruit stage BBCH 71-79 currants	Frugivorous mammal "dormouse"	Garden dormouse (<i>Eliomys quercinus</i>)	9.7	19.4
Bush & cane fruit	BBCH 10-19	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	4.7	10.3
Bush & cane fruit	BBCH 20 - 39	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	3.9	8.6
Bush & cane fruit	BBCH ≥ 40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	2.3	5.2
Cereals	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Cereals	BBCH ≥ 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Cereals	BBCH ≥ 40	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	21.7	40.9
Cereals	Early (shoots)	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	22.3	42.1

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Cereals	BBCH 10-29	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Cereals	BBCH 30 - 39	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	3.9	8.6
Cereals	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Cotton	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Cotton	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Cotton	BBCH 40 - 49	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Cotton	BBCH \geq 50	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	18.1	34.1
Cotton	BBCH 10-49	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Cotton	BBCH \geq 50	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	1.9	4.3
Fruiting vegetables	Fruit stage BBCH 71-89	Frugivorous mammal "rat"	Brown rat (Rattus norvegicus)	25.2	45.2
Fruiting vegetables	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Fruiting vegetables	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Fruiting vegetables	BBCH 10 - 49	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Fruiting vegetables	BBCH \geq 50	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	21.7	40.9
Fruiting vegetables	BBCH 10-49	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Fruiting vegetables	BBCH \geq 50	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Grassland	All season	Large herbivorous mammal "lagomorph"	Brown Hare (Lepus europaeus)	17.3	32.6
Grassland	late	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Grassland	All season	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Grassland	Late season (seed heads)	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	6.6	14.4
Grassland	New sown grass seeds	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	6.6	14.4
Hop	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Hop	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Hop	BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	21.7	40.9

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Hop	BBCH 10-19	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Hop	BBCH 20 - 39	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	3.9	8.6
Hop	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Leafy vegetables	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Leafy vegetables	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Leafy vegetables	BBCH 40-49	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Leafy vegetables	BBCH \geq 50	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	21.7	40.9
Leafy vegetables	All season	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	14.3	35.1
Leafy vegetables	BBCH 10-49	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Leafy vegetables	BBCH \geq 50	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Legume forage	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Legume forage	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Legume forage	BBCH 40 - 49	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Legume forage	BBCH \geq 50	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	21.7	40.9
Legume forage	Leaf development BBCH 21-49	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	14.3	35.1
Legume forage	BBCH 10-49	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Legume forage	BBCH \geq 50	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Maize	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Maize	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Maize	BBCH 10 -29	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Maize	BBCH 30 - 39	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	36.1	68.2
Maize	BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	18.1	34.1
Maize	BBCH 10-29	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Maize	BBCH 30 - 39	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	3.9	8.6
Maize	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	1.9	4.3
Oilseed rape	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	4.2	7.6
Oilseed rape	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Oilseed rape	BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	18.1	34.1
Oilseed rape	All season	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	14.3	35.1
Oilseed rape	BBCH 10-29	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Oilseed rape	BBCH 30 - 39	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Oilseed rape	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	1.9	4.3
Orchards	Application crop directed BBCH <10 or not crop directed	Small insectivorous mammal "shrew"	Common shrew (Sorex araneus)	1.9	5.4
Orchards	Application crop directed BBCH <10 or not crop directed	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	72.3	136.4
Orchards	Application crop directed BBCH 10-19	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	57.8	109.2
Orchards	Application crop directed BBCH 20-40	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	43.4	81.9
Orchards	Application crop directed BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (Microtus arvalis)	21.7	40.9
Orchards	Fruit stage BBCH 71-79 currants	Frugivorous mammal "dormouse"	Garden dormouse (Eliomys quercinus)	22.7	47.9
Orchards	Application crop directed BBCH <10 or not crop directed	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	14.3	35.1
Orchards	Application crop directed BBCH 10-19	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	11.5	28.1
Orchards	Application crop directed BBCH 20-40	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	8.6	21.1
Orchards	Application crop directed BBCH \geq 40	Large herbivorous mammal "lagomorph"	Rabbit (Oryctolagus cuniculus)	4.3	10.5
Orchards	Application crop directed BBCH <10 or not crop directed	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Orchards	Application crop directed BBCH 10-19	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	6.2	13.8
Orchards	Application crop directed BBCH 20-40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	4.7	10.3
Orchards	Application crop directed BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	2.3	5.2
Ornamentals / nursery	Application to plant – exposure to underlying ground	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Ornamentals / nursery	BBCH 40 - 49	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	72.3	136.4
Ornamentals / nursery	BBCH \geq 50	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	36.1	68.2
Ornamentals / nursery	Application crop directed BBCH 10 - 49	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	7.8	17.2
Ornamentals / nursery	Application crop directed BBCH \geq 50	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	3.9	8.6
Potatoes	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Potatoes	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Potatoes	BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	21.7	40.9
Potatoes	BBCH 10 - 40	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	14.3	35.1
Potatoes	BBCH \geq 40	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	4.3	10.5
Potatoes	BBCH 10 - 39	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	7.8	17.2
Potatoes	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	2.3	5.2
Pulses	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Pulses	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Pulses	BBCH 40 - 49	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	72.3	136.4
Pulses	BBCH \geq 50	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	21.7	40.9
Pulses	BBCH 10 - 49	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	14.3	35.1
Pulses	BBCH \geq 50	Large herbivorous mammal	Rabbit (<i>Oryctolagus cuniculus</i>)	4.3	10.5

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
		“lagomorph”			
Pulses	Pre harvest seed BBCH 81-99	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	6.6	14.4
Pulses	BBCH 10 - 49	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Pulses	BBCH \geq 50	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Root & stem vegetables	BBCH 10 - 19	Small insectivorous mammal “shrew”	Common shrew (Sorex araneus)	4.2	7.6
Root & stem vegetables	BBCH \geq 20	Small insectivorous mammal “shrew”	Common shrew (Sorex araneus)	1.9	5.4
Root & stem vegetables	BBCH \geq 40	Small herbivorous mammal “vole”	Common vole (Microtus arvalis)	21.7	40.9
Root & stem vegetables	BBCH 10-39	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Root & stem vegetables	BBCH \geq 40	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	2.3	5.2
Strawberries	BBCH 10 - 19	Small insectivorous mammal “shrew”	Common shrew (Sorex araneus)	4.2	7.6
Strawberries	BBCH \geq 20	Small insectivorous mammal “shrew”	Common shrew (Sorex araneus)	1.9	5.4
Strawberries	BBCH \geq 40	Small herbivorous mammal “vole”	Common vole (Microtus arvalis)	28.9	54.6
Strawberries	BBCH 10-39	Large herbivorous mammal “lagomorph”	Rabbit (Oryctolagus cuniculus)	14.3	35.1
Strawberries	BBCH \geq 40	Large herbivorous mammal “lagomorph”	Rabbit (Oryctolagus cuniculus)	5.7	14.0
Strawberries	BBCH 10-39	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Strawberries	BBCH \geq 40	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	3.1	6.9
Sugar beet	BBCH 10 - 19	Small insectivorous mammal “shrew”	Common shrew (Sorex araneus)	4.2	7.6
Sugar beet	BBCH \geq 20	Small insectivorous mammal “shrew”	Common shrew (Sorex araneus)	1.9	5.4
Sugar beet	BBCH \geq 40	Small herbivorous mammal “vole”	Common vole (Microtus arvalis)	18.1	34.1
Sugar beet	BBCH 10-39	Large herbivorous mammal “lagomorph”	Rabbit (Oryctolagus cuniculus)	14.3	35.1
Sugar beet	BBCH \geq 40	Large herbivorous mammal “lagomorph”	Rabbit (Oryctolagus cuniculus)	3.6	8.8
Sugar beet	BBCH 10-39	Small omnivorous mammal “mouse”	Wood mouse (Apodemus sylvaticus)	7.8	17.2

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Sugar beet	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	1.9	4.3
Sunflower	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Sunflower	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Sunflower	BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	18.1	34.1
Sunflower	BBCH 10-19	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	14.3	35.1
Sunflower	BBCH 20 - 39	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	7.2	17.6
Sunflower	BBCH \geq 40	Large herbivorous mammal "lagomorph"	Rabbit (<i>Oryctolagus cuniculus</i>)	3.6	8.8
Sunflower	BBCH 10-19	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	3.9	8.6
Sunflower	BBCH 20 - 39	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	1.9	4.3
Sunflower	BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (<i>Apodemus sylvaticus</i>)	7.8	17.2
Vineyard	Application ground directed	Large herbivorous mammal "lagomorph"	Brown Hare (<i>Lepus europaeus</i>)	11.1	27.2
Vineyard	BBCH 10-19	Large herbivorous mammal "lagomorph"	Brown Hare (<i>Lepus europaeus</i>)	6.7	16.3
Vineyard	BBCH 20 - 39	Large herbivorous mammal "lagomorph"	Brown Hare (<i>Lepus europaeus</i>)	5.5	13.6
Vineyard	BBCH \geq 40	Large herbivorous mammal "lagomorph"	Brown Hare (<i>Lepus europaeus</i>)	3.3	8.1
Vineyard	BBCH 10 - 19	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	4.2	7.6
Vineyard	BBCH \geq 20	Small insectivorous mammal "shrew"	Common shrew (<i>Sorex araneus</i>)	1.9	5.4
Vineyard	Application ground directed	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	72.3	136.4
Vineyard	Application crop directed BBCH 10 - 19	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	43.4	81.9
Vineyard	Application crop directed BBCH 20 - 39	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	36.1	68.2
Vineyard	Application crop directed BBCH \geq 40	Small herbivorous mammal "vole"	Common vole (<i>Microtus arvalis</i>)	21.7	40.9

Crop	Scenario	Generic focal species	Representative species	Shortcut value for mean RUDs	Shortcut value for 90th percentile RUDs
Vineyard	Application ground directed	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	7.8	17.2
Vineyard	Application crop directed BBCH 10 - 19	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	4.7	10.3
Vineyard	Application crop directed BBCH 20 - 39	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	3.9	8.6
Vineyard	Application crop directed BBCH \geq 40	Small omnivorous mammal "mouse"	Wood mouse (Apodemus sylvaticus)	2.3	5.2

ANNEX II REVIEW QUESTIONNAIRE ON THE EASE OF USE OF THE GUIDANCE DOCUMENT

The Commission recommends that for all dossiers submitted as of 1 July 2010 this Guidance Document should be applied. This Guidance Document should be revised in 2012 taking into account experience from using it. Member States are encouraged to use this questionnaire to provide feedback to EFSA.

1 Have you found the guidance on Tier 1 risk assessments simple to use?

2 If your response was NO, please offer thoughts for improvements.

3 Have you found the higher tier guidance straight-forward to use?

4 If your response was NO, please offer thoughts for improvements.

5 Have you used the EFSA risk assessment tool?

6 If your response was NO, can you please explain why you have chosen not to use it?

7 If your response was YES, have you found it simple to use?

8 If your response was NO, please offer thoughts for improvements.

9 If there are key scientific considerations that are not addressed by the Guidance Document, please provide a short outline.

10 Please present any evidence of bird populations which have been adversely affected by or benefitted from decisions made using the Guidance Document.