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GUIDANCE

Guidance on the Biocidal Products Regulation

Volume III Human Health - Assessment & Evaluation (Parts B+C)

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LEGAL NOTICE

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DOCUMENT HISTORY

Version	Comment	Date
Version 1.0	First edition	December 2013
Version 1.1	Corrigendum covering the following: (i) Added Annex A, a Commission document on Substances of Concern (ii) Reformatting into ECHA corporate style (iii) Editorial revisions such as punctuation, spelling, etc. (iv) Correcting broken hyperlinks (v) Adding hyperlinks to list of abbreviations and section cross references	April 2015
Version 2.0	Update to section 3 Exposure Assessment The section has been fully revised as follows: • updated text on Exposure Assessment • alignment of the guidance with REACH principles/guidance on exposure • editorial revisions such as punctuation, spelling, etc. • removal of the "technical aspects" into a separate document on Biocides Human Health Exposure Estimation Methodology (available on Biocides webpages). • improvement of workflow diagrams	October 2015
Version 2.1	Corrigendum to update the guidance to address Part C Evaluation and to add text and links on "Applicability of Guidance" The text has been revised as follows: • Preface: updated to be in line with the general information in the Part A. • General Introduction: a new paragraph to explain the association of the evaluation and assessment processes. • Preface: to add text and links on "Applicability of Guidance"	February 2017
Version 3.0	Update to add a new Section for guidance from ARTFood Project 2 The text has been revised as follows: • To add a new section 5 • To revise section 3.4.2 to cross refer to this new section.	November 2017
Version 4.0	Update to add a new Section for guidance from ARTFood Project 1 The text has been revised as follows:	Xxxxx 2017

	• To add a new section 6 To revise section 3.4.2 to cross refer to this new section.	

PREFACE

The Guidance on the Biocidal Products Regulation (BPR) is to be applied to applications for active substance approval and product authorisation as submitted from 1 September 2013, the date of application (DoA) of the Biocidal Product Regulation (the BPR).

This document describes the BPR obligations and how to fulfil them.

The scientific guidance provides technical scientific advice on how to fulfil the information requirements set by the BPR (Part A), how to perform the risk assessment and the exposure assessment for the evaluation of the human health and environmental aspects and how to asses and evaluate the efficacy to establish the benefit arising from the use of biocidal products and that it is sufficiently effective (Parts B & C).

In addition to the BPR guidance, the Biocidal Products Directive (BPD) guidance and other related documents are still considered applicable for new submissions under the BPR in the areas where the BPR guidance is under preparation. Furthermore these documents are still valid in relation to the evaluation of applications for active substance approval or applications for product authorization submitted for the purposes of Directive 98/8/EC (BPD) which may be still under evaluation under the Biocidal Products Regulation (BPR)), . Also the Commission has addressed some of the obligations in further detail in the Biocides competent authorities meetings documents which applicants are advised to consult. Please see ECHA Biocides Guidance website for links to these documents: [https://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation].

Applicability of Guidance

Guidance on applicability of new guidance or guidance related documents for active substance approval is given in the published document "*Applicability time of new guidance and guidance-related documents in active substance approval*" available on the BPC Webpage[1] [https://echa.europa.eu/about-us/who-we-are/biocidal-products-committee] and for applicability of guidance for product authorisation, please see the CA-document CA-july2012-doc6.2d (final), available on the ECHA Guidance page [https://echa.europa.eu/documents/10162/23036409/ca-july12-doc_6_2d_final_en.pdf].

[1] Link available under Working Procedures (right column) [https://echa.europa.eu/about-us/who-we-are/biocidal-products-committee]

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This will be updated at the end of the consultation procedure when section 5 is incorporated into the full Volume III.
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Figures

Tables

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NOTES to the reader

References: The references in this document have (in the majority) been carried over from former BPD documents and some of the details are missing. Many of the details have been traced and the references updated but there are some that are still incomplete: this is on-going work and will be further updated at a future update.

Hyperlinks to Abbreviations: Hyperlinks have been added to abbreviations throughout the document and not only on first use; this is because readers may not necessarily read the complete document and may only reference to sections they require at that time.

How to move to the abbreviations list and then back to the text: if you Ctrl+click on a hyperlink to jump to the target location, you can go back to your previous location by pressing **Alt+left arrow** key. For Mac PCs: the equivalent is either **Command+left arrow** in Adobe Reader or **Command+[** (open square bracket) in Preview.

Hyperlinks to Sections: Hyperlinks have been added to text that cross refers to another section of this Guidance document; this is on-going work because of the current update to section 3 and will be completed for a future update.

List of Abbreviations

NOTES to the reader

How to move to the abbreviations list and then back to the text:

If you Ctrl+click on a hyperlink to jump to the target location, you can go back to your previous location by pressing **Alt+left arrow** key.

For Mac PCs: the equivalent is either **Command+left arrow** in Adobe Reader or **Command+[** (open square bracket) in Preview.

Standard term / Abbreviation	Explanation
ADI	Acceptable daily intake
ADME	Absorption, distribution, metabolism, and excretion
AEC	Acceptable Exposure Concentration
AEL	Accepted exposure level
AF	Assessment factor
AMPeakMet	Peak rate of hepatic metabolism
AOEL	Acceptable Operator Exposure Level
APF	Assigned Protection Factors
ARfD	Acute Reference Dose
a.s.	Active substance
ASTM	American Society for Testing and Materials
ATP	Adenosine-tri-phosphate
AUC	Area under the curve
BEAT	Bayesian Exposure Assessment Tool (computerised database of exposure data)
BMD	Benchmark dose
BPC	Biocidal Products Committee (ECHA body)
BPD	Biocidal Products Directive. Directive 98/8/EC of the European Parliament and of the Council on the placing on the market of biocidal products
BPR	Biocidal Products Regulation. Regulation (EU) No 528/2012 of the European Parliament and of the Council concerning the making available on the market and use of biocidal products
b.r.	Biocidal Residue
BTM	Biocides Technical Meeting
bw	Body weight

Standard term / Abbreviation	Explanation
CA	Competent Authority • Evaluating CA (eCA) is the Competent Authority that evaluates the application for an active substance approval or an application for a Union authorisation. • Receiving CA is the Competent Authority that receives an application for a National Authorisation.
CAR	Competent Authority Report, (also known as the assessment report).
Cat	Category
CEFIC	European Chemical Industry Council
CEM	Consumer Exposure Module
C.I.	Confidence interval
CLP (Regulation)	Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of substances and mixtures
C&L	Classification and labelling
ConsExpo	Software enabling estimation of the consumer exposure model
Cmax	Peak plasma concentration
CNS	Central nervous system
CSA	Chemical safety assessment
CSAF	Chemical specific adjustment factors
CVMP	Committee for Medicinal Product for Veterinary Use
CYP	Cytochrome P isoforms
d	Day(s)
DBP	Disinfection By-Product
DEREK	Deductive Estimation of Risk from Existing Knowledge
DG	European Commission Directorate General
DG SANCO	European Commission Directorate-General for Health and Consumers
DIN (TTC, INT)	Deutsches Institut für Normung e.V. (German Institute for Standardisation)
DM	Dry Matter
DMEL	Derived Minimal Effect Level
DNA	Deoxyribonucleic acid
DNEL	Derived No Effect Level

Standard term / Abbreviation	Explanation
DPD	Dangerous Preparations Directive (1999/45/EC)
DRA	Dietary Risk Assessment
DRAWG	Dietary Risk Assessment Working Group
DSD	Dangerous Substance Directive (67/548/EEC)
EBPF	European Biocidal Product Forum
EC	European Communities or European Commission
EC_{50}	Median effective concentration
ECB	European Chemicals Bureau
ECD	Electron Capture Detector
ECETOC (TRA)	European Centre for Ecotoxicology (and Toxicology of Chemicals) (Targeted Risk Assessment)
ECVAM	European Centre for the Validation of Alternative Methods
EEC	European Economic Community
EFSA	European Food Safety Agency
ELISA	Enzyme-linked Immunosorbent Assay
EN	European norm
EPA (DK)	Environmental Protection Agency of Denmark
EPA (USA)	Environmental Protection Agency of the United States of America
EU	European Union + Norway, Iceland and Lichtenstein Please note the BPR applies to the European Economic Area (EEA) and thus all references to the EU in the text should be understood as EEA (EU + Norway, Iceland and Lichtenstein)
EUROPOEM	European Predictive Operator Exposure Model Database Project
FAO	Food and Agriculture Organization
FCA	Freund's Complete Adjuvant
FDA	U.S. Food and Drug Administration
FQPA	Food Quality Protection Act
GI(T)	Gastrointestinal (tract)
GEV	Generic Exposure Value
GLEV	Generic Lowest Exposure Value
GLP	Good laboratory practice
GPMT	Guinea Pig Maximisation Test
GSD	Geometric standard deviation

Standard term / Abbreviation	Explanation
h	Hour(s)
HEEG	Human Exposure Expert Group (under BPD)[2]
HI	Hazard index
HPT	Human Patch Test
HQ	Hazard quotient
HRIPT	Human Repeat-Insult Patch Test
IC_{50}	Median immobilisation concentration or median inhibitory concentration 1 (explained by a footnote if necessary)
ICD	Irritant contact dermatitis
ICRP	International Commission on Radiological Protection
IHCP	Institute for Health and Consumer Protection (DG Joint Research Centre)
ILSI	International Life Sciences Institute
INT	2-p-iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method (please refer to DIN)
IOEL	Indicative occupational exposure level
IPCS	International Programme on Chemical Safety of the World Health Organisation
IR	Infrared
ISO (TC, SC, WG)	International Organisation for Standardisation (Technical Committee, Scientific Committee, Working Group)
ITS	Integrated testing strategy
JECFA	Joint FAO/WHO Expert Committee on Food Additives and Contaminants
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
JRC	Joint Research Centre
k	Rate constant for biodegradation
K	Kelvin
Ka	Acid dissociation coefficient
Km	Michaelis constant, describes the substart concentration at which half the enzyme's active sites are occupied by substrate
K_{ow}	Octanol-water partition coefficient
K_P	Solid-water partitioning coefficient of suspended matter
Kst	Dust explosion constant

[2] Note: Under BPR replaced by the AdHoc Working Group on Human Exposure

Standard term / Abbreviation	Explanation
LC	Langerhans cells
$LD(C)_0$	Lethal dose for 0% of the group of tested animals
$LD(C)_{50}$	Lethal dose for 50% of the group of tested animals
LEL	Lower explosive limit
LEV	Local exhaust ventilation
LLNA	Local lymph node assay
LOAEC	Lowest Observed Adverse Effect Concentration
LOAEL	Lowest Observed Adverse Effect Level
LOC	Limiting oxygen concentration
log P	Octanol/water partition coefficient
LOQ	Limit of quantification
LVET	Low volume eye test
M	Molarity
MAC	Maximum admissible concentration
MCCEM	Multi-Chamber Concentration and Exposure Model
MIT	Minimum ignition temperature
MITI	Ministry of International Trade and Industry (Japan)
MMAD	Mass median aerodynamic diameter
mmHg	Millimeter(s) of mercury, a unit of pressure equal to 0.001316 atmosphere
mN/m	Millinewton(s) per metre, a unit of torque
mol	Mole(s)
MOS	Margin of Safety
MOTA	Manual of Technical Agreements (of the Biocides Technical Meeting)
MRL	Maximum residue level
MS	Mass spectrometry
MSCA	Member State Competent Authority
MTD	Maximum tolerated dose
MW	Molecular Weight
M&K	The guinea pig maximization test of MAGNUSSON and KLIGMAN
NAEL	No Adverse Effect Level
NESIL	Non Expected Sensitisation Induction Level

Standard term / Abbreviation	Explanation
N(L)OAEL	NOAEL and/or LOAEL
nm	Nanometre(s)
No	Number
NOAEC	No observed adverse effect concentration
NOAEL	No observed adverse effect level
NOEC	No observed effect concentration
NOEL	No observed effect level
OC	Operational condition
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational exposure limit
OPPT	Office for Pollution Prevention and Toxics (U.S. Environmental Protection Agency)
OSHA	Occupational Safety and Health Administration (European Agency for Safety and Health at Work)
Pa	Pascal(s)
para.	Paragraph
PBPK	Physiologically based Pharmacokinetic
PEC	Predicted environmental concentration
PHED	Pesticide handler exposure database
pKa	Negative decadic logarithm of the acid dissociation constant (describes how acidic (or not) a given hydrogen atom in a molecule is)
PKPD	Pharmacokinetic/pharmacodynamic
PNEC	Predicted no effect concentration
PPE	Personal Protective Equipment
PPP	Plant Protection Product
PT	Product type
(Q)SAR	(Quantitative) structure activity relationship
QSPR	Quantitative structure-property relationships
r	Correlation coefficient
RA	Risk Assessment
RAC	Committee for Risk Assessment (ECHA body)
$rate_{a.s.}$	Use rate of active substance [kg/ha]
$rate_{metabolite}$	Application rate at which metabolite should be tested [kg/ha]

Standard term / Abbreviation	Explanation
RC	Risk Characterisation
REACH	Regulation (EC) No 1907/2006 on Registration, Evaluation, Authorisation and Restriction of Chemicals
RDT	Repeated dose toxicity
RD_{50}	Respiratory Depression expressed as decrease of respiratory rate by 50%
RD_{10}	Respiratory Depression expressed as decrease of respiratory rate by 10%
rLLNA	Reduced LLNA
RMM	Risk Management Measures
RMS	Rapporteur Member State
RPE	Respiratory Protective Equipment
RT	Respiratory tract
s	Second(s)
SAF	Safety Assessment Factor
SCIES	Screening-Level Consumer Inhalation Exposure Software
SDS	Safety data sheet
SD	Standard deviation
SETAC	Society of Environmental Toxicology and Chemistry
SHEDS	Stochastic Human Exposure and Dose Simulation model
SME	Small and medium-sized enterprise
SMILES	Simplified molecular-input line-entry system
SoC	Substances of concern
SOPs	Standard Operating Procedures developed by the Residential Exposure Assessment Work Group for Residential Exposure Assessments (for the U.S. EPA Office of Pesticide Programs)
STP	Sewage treatment plant
TD	Toxicodynamic
TKTD	Toxicokinetic/toxicodynamic
TLV	Threshold limit value
TMDI	Theoretical maximum daily intake
Test Methods Regulation	Regulation (EC) No 440/2008 laying down test methods pursuant to the REACH Regulation
TK	Toxicokinetic
TG	Technical guideline(s), technical group(s)

Standard term / Abbreviation	Explanation
TGD	Technical Guidance Document
TM	Biocides Technical Meeting, an established subsidiary body responsible for the implementation of the Biocidal Products Directive, together with the European Commission.
TNsG	Technical Notes for Guidance
TTC	Threshold of toxicological concern
UDS	Unscheduled DNA synthesis
Vmax	Maximum velocity, reflects how fast the enzyme can catalyze the reaction
VP	Vapour Pressure
VMP	Veterinary Medicinal Product
w/w	Weight per weight ratio
w/v	Weight per volume ratio
WCCE	Worst Case Consumer Exposure
WHO	World Health Organisation
WoE	Weight of evidence
WPEM	Wall Paint Exposure Assessment Model

Glossary of Terms

Standard term / Abbreviation	Explanation
abuse	is intentional misuse, for example inhaling aerosol propellant - as such, it is not included in exposure estimation.
active substance (a.s.)	is the substance (or microorganism) that has an action on or against harmful organisms (Article 3(1)(c) BPR)..
actual dermal exposure	is the amount of active substance or in-use biocide formulation (biocidal product) that reaches the skin through e.g. (work) clothing or gloves and is available for uptake through the skin.
Aggregate exposure assessment	it refers to the assessment of the total exposure to one substance resulting from more than one exposure path (oral, dermal, inhalation and dietary exposure) and/or from more than one use (uses in all relevant product types and uses in other regulatory frameworks).
application	refers to using the in-use biocide(biocidal product).
biocidal product	is a substance or mixture that consists of, contains or generates one or more active substances and which has a biocidal intention (see full definition at Article 3(1)(a) BPR).
biological monitoring	is the sampling of blood, urine, saliva or exhaled air at suitable times before, during and after the task, and analysing for the substance or a metabolite to determine the body dose. The sampling regime needs expert advice and ethical clearance.

Standard term / Abbreviation	Explanation
bulk samples	are samples of the biocide in use (and where necessary, the concentrate).
bystanders	are those who could be located within or directly adjacent to the area where a biocidal product has been applied; their presence is quite incidental and unrelated to work involving biocides, but whose position might lead them to be exposed for a short period of time (acute exposure); and who take no action to avoid or control exposure.
central tendency	in a distribution is a value that describes best the central value. The central tendency may be used in exposure estimates where well trained operators show practically continuous use.
clothing	can range from minimal (e.g. T-shirt and shorts) through to leisure wear, work clothing and coveralls, to impermeable suits. It includes PPE.
degradation of PPE	a damaging change in one or more physical properties of the protective glove as a result of exposure to a chemical substance
deterministic estimates	are single-value, including worst-case estimates.
dislodgeable residues	are post-application residues that are available for uptake through human contact with substances on surfaces.
empirical (database) model	is a data distribution of exposures derived from site surveys or laboratory simulations, strongly associated with the biocide application task(s). The only inputs are new exposure data to reinforce the model. The outputs are "indicative exposure values" which when modified by pattern of use data, are compared with toxicological endpoint data. This is used in Tier 1 and Tier 2 assessments.
exposure reduction	measures are techniques to reduce risk through substitution of products, controlling the product, its sectors for use, specifying in-use control measures.
exposure data (experimental)	are personal samples (for inhalation and dermal exposure) and each is a data-point. It is unlikely that a sufficiently powerful data set would exist for meaningful statistics to apply to most scenarios.
exposure information	includes the frequency and duration of exposure, the selection of products in preference to others on the market, and the patterns of use.
exposure models	are used to predict exposure from databases, from statistical relationships and through mechanistic calculations. They provide information which, in conjunction with other data, leads to a quantitative estimate of exposure.
exposure via the environment	is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food or water.
external exposure	is the exposure reaching the outside of the animal's body boundary (for example, on the skin, in lungs, in the gastro-intestinal tract). "External exposure" is not adjusted for factors such as dermal absorption, oral absorption or breakdown in the digestive system of the livestock animal or absorption via the livestock animal's respiratory system.
field blank samples	are sampling media that are treated in the same way as monitoring media, without being exposed to the biocide in use.

Standard term / Abbreviation	Explanation
foreseeable non-proper (incorrect) use	is the use of biocidal products not in line with the instructions for use or without the consideration of some or all common and specific technical, operational and personal protective measures (e.g. the over-application or inadequate dilution of a biocide, common spillage scenarios, use without or with non-proper RPE and PPE). Accidents, malfunctions or deliberate misuse are not addressed.
likelihood of exposure	is the expression of probability that exposure will occur at all. It can be quoted to reflect "none detected" values in exposure surveys and studies. See also LoD, LoQ.
in-use biocide	is the product as it is being applied, whether or not diluted by the user, as a paint, a dust, a spray, a solid, a solution, or as a component of a fluid.
industrial users	are those involved in manufacturing, handling and/or packaging of actives or products in industry as well as those using biocidal products in their own processes at industrial setting, for example, manufacturers of timber cladding using wood preservatives or food companies using disinfectants.
ingestion	arises from the swallowing of biocides. Ingestion can also occur through poor hygiene practice (e.g. through dislodging from contaminated skin to food or cigarettes, by hand-mouth contact, or through applying cosmetics).
inhalation exposure	reflects the airborne concentration that is available in the breathing zone. The substance is then available for uptake via the lungs or following mucociliary elevator action from the gastrointestinal tract.
intended use	of a biocidal product means what is supposed to be used according to the manufacturer's specifications, instructions, and other information.
LoD, LoQ - limits of detection and quantitation	are levels, below which the biocide cannot be detected, and cannot be measured accurately, respectively.
mathematical model	is a tool whereby inputs by the user result in a prediction of exposure through calculation. This is used in Tier 1 and Tier 2 assessments.
misuse	foreseeable misuse refers to such use of a biocidal product which is not according to label instructions, which is expected to occur based on experience, monitoring data etc. and which is expected to be perpetrated by a large number of users of the biocidal product.
mixing & loading	handling biocide concentrates, diluting them and where necessary, putting the in-use formulation into the application apparatus.
NOAEL	the no observed adverse effect level.
none-detected	values from exposure studies - see likelihood of exposure, limits of detection.
non-professional applications	where products are for non-professional user (consumer) application, and include examples where people in a workplace are not employed to use biocides (e.g. fly sprays in an office).
non-professional users	are the general public - consumers - .There is an expectation – but little guarantee, that non-professionals will comply with instructions for use of a product. They have no access to controls or formal PPE.
penetration of PPE	that proportion of biocide that by-passes PPE, e.g. by soaking through seams and zips, being drawn in at the neck, cuffs and ankles by the "bellows effect", that gets inside protective gloves by them being donned with contaminated hands.

Standard term / Abbreviation	Explanation
permeation of PPE	the migration of biocide through the PPE barrier, e.g. solvent-based product through latex-based gloves.
personal monitoring	is the sampling of a biocide during its application or mixing and loading, using samplers deployed on the person. See also static monitoring.
personal protective equipment (PPE)	includes head, eye, respiratory (RPE), body, hand and foot protection that is designed to protect the wearer. The basic safety requirements that PPE must satisfy, in order to ensure the health protection and safety of users, are laid down in the Council Directive 89/686/EEC.
phases of activity	are mixing & loading, application, post-application and removal of the biocide.
post-application	covers the scenarios of sampling, maintaining and cleaning and may give rise to secondary exposure.
potential dermal exposure	is the deposition of active substance or biocidal product on the outer surface of clothing and on any bare skin.
preparation or formulation	is the biocidal product as placed on the market; the active substance with its co-formulants, diluents, carrier materials and stabilisers.
primary exposure	is that which occurs to the user (i.e. the person who applies the biocide).
probabilistic (stochastic) modeling	is used to combine data in order to derive fair 'central tendency' and 'realistic worst case' values. It is based on distributions of parameters. See deterministic estimates.
professional users (e.g. employees and the self-employed)	will handle biocidal products within the framework of statutory requirements. They are trained and skilled in the main objectives of their occupation and may have some experience and skill in the use of the PPE if that is necessary for their normal work. Not all professional users will have the knowledge and skills to handle hazardous biocidal products (e.g. incidental use of slimicides, insecticides, irregular disinfections and use of products containing preservatives).
protocols	are detailed descriptions of the work to be undertaken in surveys or studies and the objectives to be achieved.
removal and disposal phase	includes removing exhausted antifoulant coatings, disposing of used preservative fluids and burning treated timber.
Realistic worst case	is the situation where the exposure is estimated using from a range of factors (i.e. duration, amount, exposure controls), where applicable, the ones that would be expected to lead to maximum amount of exposure. The realistic worst case does not include deliberate misuse.
Residents	are those who live or work adjacent to an area that has been treated with a biocidal product; whose presence is quite incidental and unrelated to work involving biocides but whose position might lead them to be exposed; who take no action to avoid or control exposure and who might be in the location for 24 hours per day (longer term exposure).
risk assessment	is the comparison of a predicted human dose from undertaking a task or tasks with appropriate toxicological endpoint values or NOAELs.
scenario	is one or a number of well defined tasks for which exposure can be characterised.
secondary exposure	is that which is not primary. It is characterised through the exposed person having little or no control over their exposure, which may be acute or prolonged. It includes re-entry to treated zones (contact with treated surfaces, inhalation of residual vapours, ingestion of residues).

Standard term / Abbreviation	Explanation
static monitoring	is sampling of background atmospheric concentrations or deposition.
studies	are short laboratory simulations of limited tasks, or workplace based small surveys to indicate a likely exposure pattern.
surrogates or tracers	- e.g. strontium salts, dyes, fluorescent agents - are used in surveys and studies to enable analysts to trace the exposure pattern.
surveys	are extensive measurement of exposure resulting from real biocide application tasks.
task	covers the phases of use of a biocide. It is a unit of operation within one or several scenarios.
Tier 1	is a screening level risk assessment.
Tier 2	is a detailed risk assessment, taking into account patterns of work and risk management measures.
Tier 3	is the output of an individual exposure study, possibly generated as a result of a data requirement for product registration.
trained professional users	probably have specialised knowledge and skill in handling hazardous chemicals. Protective measures as foreseen in the European Communities regulations on safety and health at work (instruction, training, exposure control, PPE) should be observed. Qualification might be documented by the endorsement of management systems for occupational safety and health, by certification to branch-specific standards or by approval through competent authorities. The term specialised professional user has the same definition as trained professional user.
TWA	time weighted average exposure by inhalation.
user sectors	industrial, professional, non-professional and secondary.
ventilation	has several meanings. It may be a control measure in the workplace; it may refer to passive air changes within a building; and it may refer to the human breathing rate. The context should be clear from the text.
visualisation	involves the introduction of a coloured or fluorescent tracer to the biocide in-use formulation for post-exposure quantitation.
work clothing	- work uniform or work wear is a set of clothes worn at work. They are not designed to protect the health and safety of the worker and do not constitute PPE. However, they do protect the wearer to some extent from dermal exposure.

General introduction

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General Principles

1 Effects Assessment - Hazard Identification

2 Effects Assessment - Hazard Characterisation (Dose-Response/Concentration Relationship)

3 Exposure Assessment

4 Risk Characterisation

5. Guidance On Estimating Dietary Risk From Transfer Of Biocidal Active Substances Into Foods – Non-Professional Uses

NOTE FOR CA CONSULTATION

This draft document is an abbreviated version of the full Guidance document and only includes the relevant section (i.e. Section 6 and its appendices) and subject of this update to Volume III Human Health- assessment and evaluation (Parts B+C).

All other sections are out of scope of this update and have been removed: this is to facilitate working with the document as the full guidance document is over 360 pages in length.

The current published full *Guidance on Biocidal Products Regulation: Volume III Human Health Part B Assessment* is available on the ECHA website, at the following link: https://echa.europa.eu/documents/10162/23036412/biocides_guidance_human_health_ra_iii_part_bc_en.pdf/30d53d7d-9723-7db4-357a-ca68739f5094**.**

Please note that at the time of launching this consultation, the updated version 2.0 with the new Section 5 had not been published: this is due to be published in November. If you wish to see this version once published, please go to the ECHA website/BPR guidance webpage [https://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation] and open Volume III Human Health- assessment and evaluation (Parts B+C).

6. Guidance On Estimating Livestock Exposure to Active Substances used in Biocidal Products

6.1 Background

The Dietary Risk Assessment Working Group (DRAWG) was formed in May 2009 under the Biocidal Product Directive (BPD), upon request of the Biocides Technical Meeting, in order to develop guidance for dietary risk assessment (DRA) of biocidal active substances (a.s.). Under the new Biocidal Products Regulation (BPR), the Biocidal Product Committee (BPC) at its meeting in February 2014 (BPC-2) established and agreed upon the mandate of the ad hoc Working Group on the Assessment of Residue Transfer to Food (ARTFood), to continue and finalise the guidance developed by DRAWG.

In this guidance ARTFood has focused its efforts on the external exposure assessment of livestock animals. Guidance detailing how to proceed beyond external exposure estimation has been developed by the CVMP-BTM Working Group[3] and it is referenced in this section as EMA-CVMP guidance "Guideline on risk characterisation and assessment of maximum residue limits (MRL) for biocides" (EMA/CVMP/SWP/90250/2010)[4]. Maximum residue limits (MRLs) on commodities from livestock origin are set by EMA in line with CA-March17-Doc.7.6.c-final[5].

The DRAWG has collected from all EU Member States livestock external exposure estimates performed as part of EU-wide biocidal active substance evaluations. These estimates were evaluated in order to compile available tools, identify gaps and define external exposure scenarios. The results of these evaluations are the basis of the

[3] CVMP: Committee for Medicinal Products for Veterinary Use; BTM: Biocides Technical Meeting. Guideline on risk characterisation and assessment of maximum residue limits (MRL) for biocides.

[4] Guideline on risk characterisation and assessment of maximum residue limits (MRL) for biocides (EMA/CVMP/SWP/90250/2010). [http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/01/WC500181638.pdf]

[5] CA-March17-Doc.7.6.c-final. [https://www.google.fi/search?rls=com.microsoft%3Aen-GB%3AIE-SearchBox&dcr=0&q=CA-March17-Doc.7.6.c-final&oq=CA-March17-Doc.7.6.c-final&gs_l=psy-ab.12...2798.2798.0.5285.1.1.0.0.0.0.54.54.1.1.0....0...1.1.64.psy-ab..0.0.0....0.Wb8um0se6hw]

following text and provide technical guidance that is intended to be used in the context of a step-wise approach.

The method uses a threshold concept for external exposure of food producing animals to identify those substances for which a more detailed evaluation is needed. If the estimated external exposure of a food producing animal to the pharmacologically active substance and/or its toxic degradation products and/or any substance of concern contained in the biocidal product do not exceeds the trigger value (of 4 µg/kg bw), no significant residues are expected in food of animal origin and evaluation do not proceed further, unless the substance shows toxicological concerns. If the external exposure estimation exceeds that trigger value, the assessment moves to the next tier, which would aim at refining the exposure estimate. If after refinement the trigger value is still exceeded, it can be concluded that a more detailed consideration of the potential for residues in edible products is required. The "Guideline on risk characterisation and assessment of maximum residue limits (MRLs) for biocides" (EMA-CVMP guidance), details how to proceed beyond external exposure estimation. According to the EMA-CVMP guidance, an estimation of the worst case consumer exposure (WCCE) is undertaken and compared to the acceptable daily intake (ADI). If the WCCE is lower than 30% of the ADI, and in case where there is no particular concern in relation to the toxicity of the active substance, then an MRL evaluation may not be required. If, on the other hand, it is concluded that WCCE is above 30% of the ADI and in case there is a particular concern in relation to the toxicity of the active substance, then an MRL evaluation may be required.

It should be pointed out that the stepwise approach that serves as a framework for the methodologies presented in this section, is not binding. Applicants and Member States Competent Authorities may choose to skip any of the steps and proceed immediately to the approach detailed in the EMA-CVMP guidance document "Guideline on risk characterisation and assessment of maximum residue limits (MRL) for biocides" Furthermore, the methods described in this section are to be seen as recommendations for performing assessment of biocide transfer into food. Applicants wishing to propose other methods for assessment may do so as long as these other methods are substantiated, well documented and in line with the general principles of this guidance document and the EMA-CVMP guidance.

6.2 Introduction

The principles outlined in the CA-March17-Doc.7.6.c-final should be taken into consideration in order to assess whether the question of residues should be further explored. If it is concluded that the estimation is required, the present guidance document provides the methodology for the estimation of the external exposure of a food producing animal to the biocidal active substance.

Biocidal products are divided into 22 product types (PTs), some of which are used in areas or on objects where food or feed are produced, stored and/or processed. In this way or through direct treatment, biocidal active substances can be carried over into food or feed. In addition, through the use of biocides in animal husbandry, livestock can be exposed leading to residues in the food products obtained from livestock. Five basic groups of intended uses have been identified by way of which livestock animals can be exposed to biocidal active substances:

1. treatment of animal housing (mainly PT 3, 18, 19 and 21);
2. treatment of feedstuff and drinking water or of storage facilities (mainly PT 4, 5 and PT12);
3. treatment of materials that livestock animals may come in contact with (mainly PT 8);
4. direct treatment of livestock animals (mainly PT 3, 18 and 19);
5. treatment of aquaculture (mainly PT3 and PT21).

For each of these groups, possible methods for exposure estimation are discussed in this document.

Other PTs are unlikely to lead to livestock exposure, but this has to be considered on a case-by-case basis. On a general basis, the question on the residue should only be further explored when active substances under the normal conditions of use can lead to livestock exposure.

The possibility of livestock exposure might be considered and be addressed either by an exposure assessment or a waiver in the form of a "Justification for Non-Submission of Data" detailing the reasons for the waiver, which should demonstrate that the transfer of biocidal active substance residues to livestock is unlikely.

For a biocidal a.s. leading to exposure through more than one route (e.g. dietary and dermal), through more than one use (e.g. professional and non-professional), and that is used in more than one PT and/or in more than one regulatory area (e.g. plant protection products, veterinary medicines, food contact materials or food additives), then an aggregate exposure assessment should be conducted. No EU-wide harmonised guidance exists on how to perform aggregate exposure assessment; thus in the absence of such a procedure, no aggregate dietary exposure assessments is proposed in this section until respective guidance has been developed.

6.3 Stepwise approach to risk characterisation

A stepwise approach is proposed to performing evaluation of biocidal products where exposure to livestock can be foreseen.

Tier I focuses on the estimation of external exposure arising from contact of animals with the active substance, or its degradation products, in treated areas. Based on the intended use(s) and modelling approaches, realistic worst-case exposure scenarios are developed and a first tier assessment is carried out. In Tier II, experimental data may be requested to refine the external exposure assessment, for example measurements of relevant residues of the active substance or of its degradation products on the walls in stables. Further steps involve the full dietary risk assessment and possible establishment of an MRL (these steps are described in the EMA-CVMP guidance).

6.3.1 Tier I: initial external exposure estimation

NOTE to the reader:

It is acknowledge that currently the animal intake triggering the submission of animal studies is 0.1 mg/kg DM for the active substances falling under Reg. (EU) No 544/2011 and 0.004 mg/kg bw under Reg. (EU) No 283/2013 (EFSA, Estimation of animal intakes and HR, STMR and MRL calculations for products of animal origin, September 2015. [https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_mrl_guidelines_animal_intake_mrl_2015_en.pdf]. In addition, new figures for feed intake are available (OECD ENV/JM/MONO(2013)8). The section presented here reports outdated figures, which were valid at the time of drafting the document. This section is presented mainly to describe the approach used to derive the external trigger value to be used for the purposes of this guidance document.

A detailed description of the treatment process should identify whether the active substance or its degradation products can be expected to end up in the animal body or food products from these animals. If the estimated external exposure of the animals to the active substance or its degradation products exceeds a pre-defined threshold (trigger value), then this is interpreted as indicating the possible presence of residues in food products from these animals. In this case, Tier II should be followed.

The trigger value to be used is directly derived from the practice of the European Food Safety Agency (EFSA) in the risk assessment of Plant Protection Products (PPP) under Regulation (EC) No 1107/2009.

The rules applied by the European Food Safety Agency (EFSA) to initiate the process of food risk assessment and possible MRL setting in food of animal origin is based on the substance content of the animal feed, which in turn determines the animal's exposure to the substance. The threshold value used is 0.1 mg of substance per kg of feed dry matter (DM). It was decided at TMIII_08 that the threshold value to trigger Tier II and further steps for biocidal livestock exposure assessment should be derived from this value.

Based on standard livestock weights and feed intake, the external exposure values of livestock corresponding to 0.1 mg/kg of feed DM were calculated. The corresponding reference data and calculations have been provided by EFSA. The data on animal weights and feed intake were taken from the DG SANCO Guidelines for the generation of data concerning residues as provided in Annex II part A, section 6 and Annex III, part A, section 8 of Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market (http://ec.europa.eu/food/plant/protection/resources/app-g.pdf , which is available at http://ec.europa.eu/food/plant/protection/resources/publications_en.htm#residues).

The results of the calculations are displayed in the following table[6]:

Table 1: External exposure values

	Chicken	Dairy cattle	Beef cattle	Pig	Model Goat	UK Sheep	UK Turkey
Body weight [kg] -*default**	1.9	550	350	75	70	75	7
Feed (dry matter) intake [kg /day] –*default**	0.12	20	15	3	3	3	0.2
Substance intake [mg/day] at the 0.1 mg/kg trigger value	0.012	2	1.5	0.3	0.3	0.3	0.02
Substance intake [mg/kg bw/ day]	**0.0063**	**0.0036**	**0.0043**	**0.0040**	**0.0043**	**0.0040**	**0.0029**

*please note: the default values have been changed; the current default values are presented in table 1 Appendix 6-1.

The first four columns correspond to the four indicator livestock species described in the SANCO guidance (chicken including laying hens, dairy cattle, beef cattle, pig). The additional three columns (Model goat, UK sheep and UK turkey) give values commonly accepted within EFSA.

As was expected, the values obtained differ between species. However, because the variation range is extremely narrow, because the value of 0.1mg / kg feed DM is already conservative, and because there is no need for absolute precision for an indicator of the need for further refinement, it was proposed to use the median value of **0.004 mg / kg livestock bw** of external exposure over 1 day as the threshold for triggering Tier II assessment and further steps across all livestock species.

Under Regulation (EC) No 1107/2009 the trigger value is used for long-term and acute exposure. For the food risk assessment of biocides, the frequency of biocide application may differ from a daily to a monthly basis. In addition it shall be noted that not only the

[6] Substituting the default body weights from the current guidance document (as listed in Appendix II) for the DG SANCO body weights results in a median substance intake of 0.004 mg/kg bw/d.

duration of exposure but also the delay between the biocide application and animal slaughter determines the residue in edible tissue. The delay after biocide use could correspond to the withdrawal period, defined in Point 9 of Article 1 of Directive 2001/82/EC, as amended: "*The period necessary between the last administration of the veterinary medicinal product to animals, under normal conditions of use and in accordance with the provisions of this Directive, and the production of foodstuffs from such animals, in order to protect public health by ensuring that such foodstuffs do not contain residues in quantities in excess of the maximum residue limits laid down pursuant to Regulation (EEC) No 2377/90*". In the case of an intermittent application, some products, in particular eggs or milk, can be intermittently but significantly contaminated. This is why, in case of intermittent use, the trigger value should be applied to the most acute exposure pattern (over 24 hours) and not to the averaged exposure over time. Where relevant, a more flexible approach to the exposure pattern may be considered at Tier II.

6.3.2 Tier II: refined external exposure estimation

If the estimated external exposure of the animals exceeds the trigger value of 0.004 mg a.s./kg bw/d at Tier I, it is necessary to perform a refined, more realistic external exposure estimation. The need for additional studies for a specific active substance depends to a large extent on the intended use of the biocidal product and is therefore a case-by-case decision involving expert judgement. At this stage, further data should only be related to the refinement of external exposure estimation. Considerations on the bioavailability and distribution of the internal dose, which may be decisive as to the need for setting an MRL, will be made at a later stage. If the estimated external exposure of the animals at Tier II still exceeds the trigger value of 0.004 mg a.s. / kg bw/d, then it is necessary to proceed further applying the approach reported in the EMA-CVMP guidance.

The figure below summarises the overall stepwise approach, and includes steps undertaken by both the national Competent Authorities (CA) and the European Medicines Agency (EMA) as reported in the EMA-CVMP guidance.

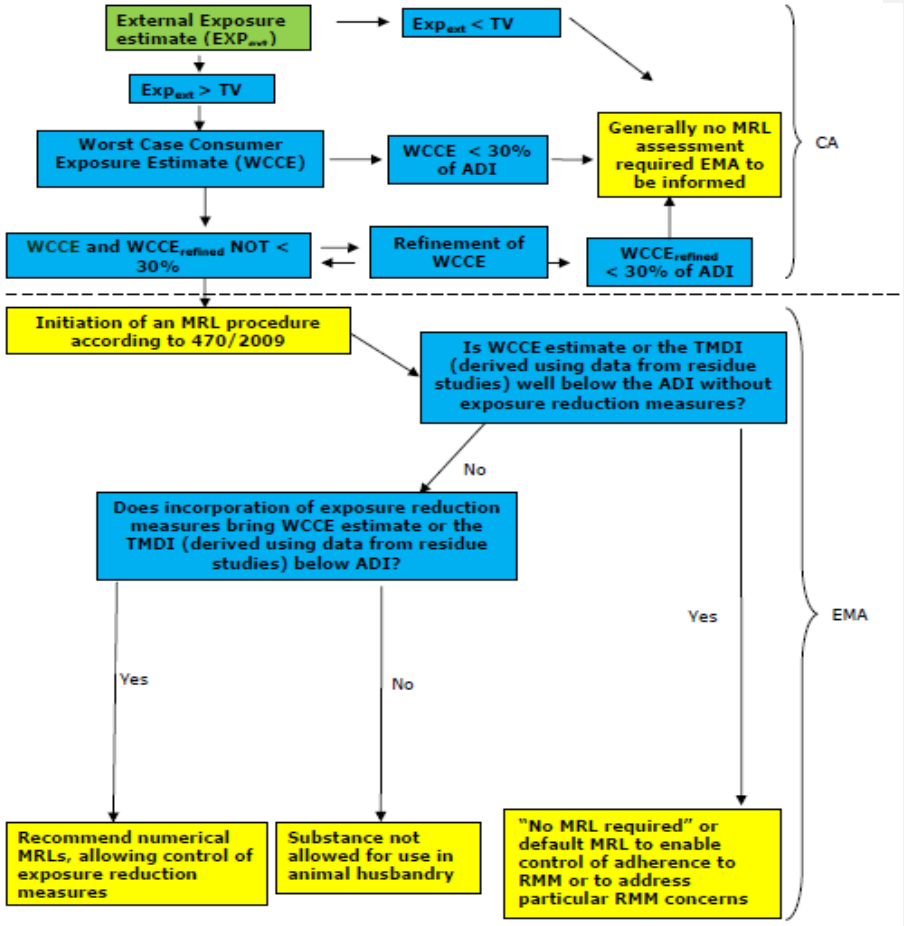

Figure 1: Decision tree summarising the overall approach reported in the EMA-CVMP guidance

Key:

Exp_{ext} = External exposure of the animal
TV = Trigger Value (4 µg/kg/day)
DRA = Dietary Risk Assessment
WCCE = Worst Case Consumer Exposure
TMDI = Theoretical Maximum Daily Intake (based on maximum residue concentrations combined with the standard food basket)
ADI = Acceptable daily intake
WP = Withdrawal period
RMM = risk management measures

6.4 General Considerations

6.4.1 Substances for which this guidance does not apply

Although it is assumed that the exposure of livestock to active substances below the trigger value of 0.004 mg a.s./kg bw/d would lead to insignificant residues in edible animal matrices, a minute exposure of humans still occurs. Thus, the trigger value is not an appropriate approach for substances that exert a non-threshold toxicity effects (such as genotoxic substances) and substances of particular concern (such as substances with reproductive/developmental/neurotoxic actions). For these substances, the approach of the EMA-CVMP guidance must be followed. In cases where an ADI has not been derived yet, another equal toxicological threshold value (e.g. the $AEL_{long\text{-}term}$, which is in many cases in the same order of magnitude as the ADI) can be used for a preliminary assessment of the toxicity of the active substance.

6.4.2 Substances which require particular consideration

Active substances with a potential for accumulation (e.g. substances with a log P_{ow}>3) can also pose a problem even if the estimated exposure is below the trigger value. For active substances that exhibit these characteristics, the Applicant should provide a justification based on absorption, metabolism and elimination data to prove that the active substance and its metabolites are non-accumulating and that the exposure assessment approach described in this guidance can be used for the active substance. Metabolism studies in livestock would be useful as well, if available. If the exposure assessment approach described in this guidance cannot be used, the approach of the EMA-CVMP Guidance must be followed. Data provided in the Applicant's dossier may give an indication of the active substance's potential for bioaccumulation.

Biocidal active substances might be essential nutrients; in such cases, consideration should be given to the relevance of the external trigger value and the percentage of the exceedance of the reference values compared to the dietary reference intake.

In case of the possibility of degradation of the active substance before uptake by animals occurs, the degradation products should be assessed. Degradates of the active substance are identified in the physical chemical sections on photolysis and hydrolysis studies in water and air, as well as in stability studies of the formulation or active substance. Degradation products can be more toxic and/or more persistent than the active substance itself. An exposure assessment, based on the same stepwise approach used for the a.s., should be performed for any degradation products if the toxicity of the parent compound does not cover the toxicity of the degradation product.

Biocidal products may contain formulants that are substances of concern (SoC). The guidance of SoC should be applied (see Annex A of this guidance) and a decision on the relevance of these substances in relation to the risk posed through livestock exposure should be assessed case by case in a proportionate manner.

Commented [SJ4]: CONSULTATION NOTE:
Annex A is available in the current published guidance document:
https://echa.europa.eu/documents/10162/23036412/biocides_guidance_human_health_ra_iii_part_bc_en.pdf/30d53d7d-9723-7db4-357a-ca68739f5094

Feed/water is often stored for a period of time after being treated with a biocide. During this time, degradation of the active substance may occur, resulting in the generation of degradation products accompanied by diminishing residues of the active substance itself. When degradation leads to the generation of other toxic substances, it should be assessed whether the parent reference values cover their toxicity profile. Read-across or QSAR, or other predictive models can be used to conclude on the adequacy of the parent ADI with respect to the degradation products. If the toxicity of the degradation products is not covered by the parent compound, these substances must be included as residues in the exposure calculation. Applicant's data on the fate of the active substance provides information on degradation.

6.4.3 When to perform an exposure assessment

A livestock exposure assessment must be performed whenever the intended use of a biocidal product is such that livestock animals are exposed to the product. This can be the case for biocidal products used in livestock areas or on materials used in livestock areas. Information concerning the intended use can be found in the Applicant's dossier (see Appendix 6-1I). In some cases, however, intended uses in livestock areas are such that livestock exposure is precluded. For products for which this is the case, the biocidal product label must clearly state the restrictions that preclude livestock exposure to the product (including volatilised residues). These restrictions should be practical and feasible. Restrictions which invite foreseeable misuse or that are not practicable, should not be considered in the exposure assessment. For example, a requirement for poultry to be removed from their housing prior to biocide application and then to be returned following application is unlikely to be adhered to. This is because such housing often contains thousands of birds and their removal from and return to the housing would require extensive time and space resources.

In case of treatment of animal housing, a label restriction might be feasible for restricting treatment to areas out of reach of animals (including a specific description of where the product may be used) and removing animals before treatment. In the latter case, a re-entry interval needs to be indicated on the label and calculations or studies need to be performed to show that the re-entry interval is sufficient. In case of wood treatment, a label restriction might be feasible to preclude the use of treated wood in livestock areas. In cases where wood is treated industrially, it might be feasible to require a certain time period wherein the wood may not be traded to allow time for volatilization of substances. In this case, calculations or studies need to be performed to show that the non-trading period is sufficient.

In cases where practical and feasible restrictions on the label clearly preclude animal exposure, there will be no need for an exposure assessment. In these cases, a waiver in the form of a Justification for Non-Submission of Data has to be submitted detailing the reasons for the waiver.

6.4.4 Choice of Animal

Generally, exposure estimates should be performed for all representative livestock species (beef and dairy cattle, pigs, broiler chickens and laying hens; fish in the case of treatment of aquaculture), unless specific conditions apply, such as the product's intended use is limited in a way that only one species (or age group within a species) is exposed. If additional livestock can be identified as representing the worst-case (e.g. sheep in the case of PT18 products), an exposure assessment for this livestock should be performed as well. The representative species are considered representative because consumption of their edible tissues and products lead to highest human consumer exposure when considering long term and acute dietary patterns.

6.5 Tier I - Methods of exposure estimation

Tier I of external exposure assessment encompasses a realistic worst-case exposure estimate based on information on the intended use and on a set of default values. The estimation assumes that the entire amount of biocidal product applied is taken up by animals.

Animals can be exposed to the biocidal active substance by different routes of exposure: inhalation, oral uptake and dermal uptake. For screening, route of exposure is irrelevant as uptake of the entire amount of applied product is assumed regardless of the route of

exposure[7]. In subsequent steps, exposure estimates for the different routes of exposure will differ because of the route-specific parameters applied[8]. Therefore, beyond screening, an estimate should be performed for each relevant[9] route taking into account the fraction of applied product available for each route. The results of the individual estimates are then added up to get the total external exposure value.

A number of parameters influence the exposure of animals. For example, some biocidal products have to be applied when the animals are not present in the stables. To calculate the amount of active substance available for animal's exposure, information about the re-entry period and the volatilisation rate are necessary. When animals are present during application, they are exposed directly to the biocidal product. However, since the target of the biocidal product is the animal housing and not the animal, it can be assumed that animals come in contact only with a fraction of the product. Information on the area of the treated surfaces that can be reached by the animals (e.g. the height of the wall that animal reached corresponds to the height of the animal) or information on how often animals lick surfaces can be used to further refine the estimations. Default values have been collected from other guidance documents and publications that can be used to perform a realistic worst-case exposure calculation (see Appendix 6-1 for values and references).

Many biocidal products are not used daily, but with longer time intervals between applications (weeks to months). Residues remaining from a single application decline over time due to factors such as degradation, volatilisation or uptake by livestock. As a result, livestock is exposed to ever decreasing amounts of residues in the time interval between applications. The exposure assessment methodology described in this guidance does not however differentiate between the day of application and subsequent days. Instead the worst-case is considered which assumes the presence of the highest possible amount of residue, which is the residue present on the days of the application. This assumption is made to ensure that the case in which edible animal matrices are obtained (through slaughter, milking or laying of eggs) directly following exposure is covered.

The Federal Institute for Risk Assessment (BfR) has developed a tool to facilitate the estimation of the livestock exposure to biocidal active substances as described in this guidance document (BfR calculator for estimating external exposure of livestock animals to biocidal active substances: http://www.bfr.bund.de/en/assessment___residue_analytics-54528.html).

Five basic groups of intended uses have been identified and methods for tier I exposure estimation will be described for each of them.

6.5.1 Treatment of Animal Housing

Animal housing includes the facilities in which livestock are reared and kept as well as the vehicles used to transport animals. Biocides may be used to treat any surface in animal housing facilities (including walls, floors, ceilings, window and door frames, troughs, pen enclosures etc.) as well as bedding and manure. If feed and/or drinking water contained

[7] For example, the area available in a stable is multiplied by the application rate of the biocidal product and divided by the number of animals and by body weight to get the total intake per kilogram body weight per day.

[8] For instance, in Example 1.1, the oral uptake of active substance from a wall is calculated using the licking behaviour of a calf. Instead of calculating with the entire amount of active substance available to the animal, only the amount of active substance taken up with the licking scenario is considered. Additional active substance will still be available on the wall for dermal uptake and in the surrounding air for inhalation uptake. The three scenarios have to be added up to arrive at a total exposure estimate.

[9] The assumption that an exposure route is not relevant must always be accompanied by a justification.

in troughs or in storage areas are not removed from the stable prior to biocidal treatment, they can become contaminated with biocides. Animals can be exposed orally (by licking of and chewing treated surfaces, consumption of dead insects, eating straw from the bedding or the floor), dermally (through contact with treated surfaces) and via inhalation (e.g. for volatile substances), for example from use of PT3 and PT18 biocidal products. For an optional initial screening of exposure, the assumption can be made that all of the active substance applied is taken up by animals. This screening can then be refined by performing a more realistic worst case estimation. For example, instead of assuming a complete carry-over of the residue to the animal, the probable contact of the animal with the treated surface or object is taken into account.

When calculating the total amount of product applied to animal housing, the question arises which areas (roof, walls, floor) should be considered. The assumption that only the floor space is treated is reasonable for scatter applications. But in the case of spray and brush applications – in the absence of specific information provided by the Applicant on the biocidal product label –, it should be assumed that walls and ceilings are treated as well. For fogging applications, the entire housing volume must be taken into account. For the estimation of dermal and oral exposure, only those surfaces which can be reached by the livestock provide a source of exposure. For the estimation of exposure via inhalation, all treated surfaces need to be taken into account since the active substance could be volatilised from all surfaces. Whether inhalation is a relevant pathway of exposure depends on the volatility of the active substance at ambient temperature, on the type of formulation used (e.g. dust formulations can contain inhalable particles) as well as on the application method. An inhalation exposure estimation needs to be performed in order to assess the relevance of this route of exposure. For the collection of manure, some stables are designed with special slatted floors. Manure dropped by livestock collects below these slatted floors preventing contact with the animal. In such cases, it is highly unlikely that livestock would be exposed either dermally or orally to biocidal products used for the treatment of manure since the animals do not come in contact with the stored manure. However, if the active substance is volatile then an inhalation exposure assessment would need to be undertaken. The manure to which the biocidal product is applied would be at a relatively high temperature and therefore the volatility of the residues would need to be ideally assessed at such temperatures. In some countries, livestock is not allowed to be kept on slatted floors, and is hence exposed to the manure collecting in pens.

The exposure of livestock via contact with treated bedding depends on the contact period and surface area of animals in contact with bedding material as well as on the type of bedding material and its ability to release residues. It should be kept in mind that manure may be contaminated with biocide residues and subsequently be spread onto agricultural areas, leading to transfer of residues into cultivated crops. Specific data to address this exposure path is usually not provided in the biocide dossier, however applicants may provide useful information if the scenario is considered relevant for the biocidal product use (this scenario is not further discussed in this guidance document).

6.5.1.1 Types of product applications

Fogging applications distribute particles of active substance fairly evenly throughout the air space. The particles settle on the surfaces and are available for oral and dermal uptake. Application with this method does not require an active substance with a high vapour pressure.

Nebulising applications distribute droplets of a liquid that contains solubilised active substance throughout the air space. The particles settle on the surfaces and are available for oral and dermal uptake. Application with this method does not require an active substance with a high vapour pressure.

Spray applications can be used for the treatment of an entire stable or for parts of it. With spraying, aerosols are distributed throughout the air space and settle on surfaces.

Fumigation applications generate gaseous forms of the active substance.

Applications via *vaporizers* allow evaporation of the active substance from impregnated absorbent material at ambient temperature (passive vaporizers) or upon heating (e.g. electric vaporizers).

Brush applications can be used on any surface and are sometimes applied to boards that are subsequently hung up in animal housing.

Granule applications are scattered across the floor. Uptake by livestock animals is mainly oral and possibly dermal.

Dusting powders are applied to horizontal surfaces or in voids. They consist of a low concentration of the active substance mixed with an inert carrier powder and act by contact with the pest.

Bait stations

Some biocidal products are not applied to the animal housing itself, but are contained in bait stations that are put in strategic locations. Examples are products used against termites, flies and rodents. Termite baits are generally installed below ground out in the yard in cylindrical plastic stations or placed indoors over active mud tubes in known areas of termite activity. Considering that the product is enclosed in a container and not exposed to indoor/outdoor conditions, livestock exposure seems to be very limited. However, rodents tend to drag the bait to their nest and may lose bait on their way, providing a source of exposure. Flies may die within reach of animals, providing another source of exposure. To properly address the bait exposure scenario, a detailed explanation on bait placement/frequency/amount of product per bait and robustness of the bait stations to prevent access to the bait by livestock is needed.

6.5.1.2 Route of exposure

Oral exposure

Some livestock animals enjoy licking surfaces or objects in their vicinity. Grown ruminants generally prefer the salt licks provided to them, while calves frequently lick other surfaces and objects (e.g. walls). Pigs do not usually lick walls, but prefer metal objects. Poultry and goats do not engage in this type of behaviour. Through grooming an animal can orally take up a substance that has been transferred to its skin by rubbing against treated surfaces or by aerosol dropping or settling after spray treatment in the vicinity of the animal.

Insecticides (PT 18) are used in animal housing to control flies and other insects. Consumption of insects killed by a biocide provides a source of biocidal exposure. Poultry seek out dead insects intentionally. Other animals only accidentally ingest dead insects (e.g. when they have dropped in the feed). It is not necessary to consider the accidental uptake of insects since the amount of residue ingested in this way is minute. For an exposure calculation, the amount of biocidal product consumed by an insect in 24 hours is multiplied by the number of dead insects consumed by livestock.

Feed remaining in troughs may unintentionally be contaminated if it is present in the treated area during application of a biocide. Due to animal behaviour and feeding practices, this exposure scenario varies between species. Cattle are usually fed twice a day and consume all of the feed given to them in a single sitting. Any leftover feed is removed from the trough prior to the next feeding. Some stables are equipped with computerised systems that calculate the nutrition needs of each animal based on monitoring data. When an animal approaches the feeding station, the appropriate amount of feed is released. For each of these feeding practices, direct contamination of feed is unlikely, however, biocidal residues left in troughs may migrate into the next feed batch. Cattle housing is often equipped with a contraption for holding a bale of hay for the animals to nibble on throughout the day. The hay can be contaminated during a

biocide application and animals can subsequently take up the residues while nibbling on the hay. To avoid contamination with dirt, water is often provided to cattle via dispenser bottles, making biocidal contamination with biocides unlikely. However, other dispenser systems work by releasing water into a trough when the animal pushes a lever. With these systems, water may be contaminated directly or through migration of residues from the trough.

Fattening pigs are at a stage in their lifecycle where their feed consumption is large so as to promote the fattening process. Like cattle, they are usually given feed twice a day and consume all of it at one sitting. Direct contamination of feed is therefore unlikely, however, biocidal residues left in troughs may migrate into the next feed batch. Like cattle, fattening pigs are given water in dispenser bottles or in dispenser troughs.

Feeding practices for poultry differ from those for cattle and pigs. Depending on whether poultry is held in battery cages or allowed to roam across the floor, feed is provided to them on conveyor belts or gutters (cages) or in dispenser bowls (ground). Poultry kept free range with access to the outside feed directly from the ground or from dispenser bowls. Dispenser bowls are equipped with a cylinder mounted on the bowl from where stored feed slides into the bowl as it is being emptied. Providing feed in dispenser bowls, on conveyor belts or in gutters allows poultry to feed throughout the day and some portion of the daily feed and water rations is always exposed to the environment, therefore allowing contamination with biocides.

The label of a biocidal product may indicate that feed, water and troughs are to be covered during biocidal treatment. In this case, contaminated feed/water is generally not a source of exposure as long as the cover is put into place properly (i.e. provides a complete cover) and is impermeable to smoke, small particles and droplets.

For an oral exposure calculation, the following parameters may be needed. Default values for these parameters can be found in Appendix 6-1:

- Maximum area within reach of animal
- Number of animals per stable
- Available wall and floor area per animal in transport vehicles
- Number of animals per compartment in transport vehicles
- Frequency of surface licking
- Surface area of tongue
- Biocidal product consumption by flies
- Number of dead flies consumed
- Exposed feed surface
- Bodyweight

Dermal exposure

Large slaughter animals, e.g. cattle and pigs, frequently rub against surfaces such as walls and pen enclosures. These surfaces are often treated with biocides, providing a source of exposure. Small animals such as poultry and rabbits do not engage in this type of behaviour. Usually, the biocide label requires that animals be removed from the premises to be treated. But in some cases, animals are present when their housing is treated with a biocide. Animals may be exposed to spray applications during treatment or directly after treatment when aerosols drop and settle on the animals' skin or feathering. Animals prefer not to be close of the treatment area and will try to move away. However, since most animal keeping facilities do not allot much room per animal, moving away from the treatment site may not be possible.

For a dermal exposure calculation, the following parameters may be needed. Default values for these parameters can be found in Appendix 6-1:

- Maximum area within reach of animal
- Number of animals per stable
- Available wall and floor area per animal in transport vehicle

- Number of animals per compartment in transport vehicle
- Body surface area in contact with surface
- Bodyweight

Inhalation exposure

Fumigation applications are frequently used to treat animal housing after livestock have been sent to slaughter or been otherwise relocated and before the entry of new livestock. Usually the new livestock are not allowed into the housing until after a specified period of time, when most of the residues have been removed through ventilation. Hence animals are not present during biocidal application. For an exposure calculation, the amount of residue that remains once the new animals are brought into the housing must be determined. Residues from fumigation applications are in the form of small particles and possibly some vapours. Residues from fogging applications in the form of small droplets typically <25µm in diameter are either available for inhalation and/or can settle on surfaces for uptake via the oral and dermal route. Biocidal active substances from aqueous products can also be released into the air and be available for inhalation.

For an inhalation exposure calculation, the following parameters may be needed. Default values for these parameters can be found in Appendix 6-1:

- Housing volume per stable
- Number of animals per stable
- Ventilation rate in stable
- Available volume per animal in transport vehicle
- Number of animals in transport vehicle
- Ventilation rate in transport vehicle
- Alveolar ventilation rate
- Bodyweights

In the following, example calculations are given for estimating initial external exposure (screening and realistic worst-case estimate) following treatment of animal housing. The realistic worst-case estimate is an overestimate as it estimates exposure on the first day of application. As the substance is taken up by animals, less substance would be available for exposure on subsequent days.

6.5.1.3 Examples of Tier I livestock exposure estimation – treatment of animal housing

Example 1.1: Treatment of Animal Housing – Exposure of calves (special case) to spray treatment

Product: Insecticide spray, VP = $2x10^{-7}$ Pa at 20°C, MW = 449.9 g/mol

Intended Use

Used in and around animal housing. Spray application in areas where flies congregate or settle, such as floors, walls, ceilings and around doors and windows. 1 application every 6 weeks to 4 months at 25 mg as/m^2. No animals are present during treatment.

Exposure Estimation

The calf was chosen as the representative animal. While grown cattle prefer licking salt licks provided in stables, calves are less choosy and like to lick other objects as well. In the following calculations, default values from Appendix 6-1 are used.

Screening (route of exposure irrelevant):

Application rate = 25 mg a.s./m^2

Area treated (walls+floor) = 330 m^2

Number of animals per stable = 80

Body weight of calf = 200 kg

25 mg a.s./m^2 x 330 m^2 ÷ 80 ÷ 200 kg

= 0.5156 mg a.s./kg bw/d

Realistic worst-case estimate:

Oral exposure through licking of surface:

For calves, exposure from consumption of dead flies is considered not relevant compared to exposure from licking surfaces.

Emission factor for spraying (fraction emitted to the treated surface during surface treatment by spraying, see Table 54 item #18) = 0.85

Tongue surface area: 0.008 m^2

Licks per day: 10

Body weight: 200 kg

25 mg a.s./m^2 x 0.85 x 0.008 m^2 x 10 ÷ 200 kg

= 0.0085 mg a.s./kg bw/d

Oral exposure through uptake of contaminated feed:

It is assumed as a worst-case that troughs are not covered during biocidal treatment and that all residues contained on the bottom and sides of the trough migrate into the next feed batch that is given after biocidal treatment. It follows that all of the residue contained in the trough is taken up by the animal.

Emission factor for spraying (fraction emitted to the floor during surface treatment by spraying, see Table 54 item #18) = 0.11

Exposed feed surface = 0.5m^2

Body weight: 200 kg

Amount of active substance contained in trough:

25 mg a.s./m^2 x 0.11 x 0.5 m^2 = 1.375 mg a.s.

Exposure of animal:

1.375 mg a.s. ÷ 200 kg

= 0.0069 mg a.s./kg bw/d

Dermal exposure through rubbing against surfaces:

Rubbing against surfaces is considered the relevant path of dermal uptake for calves. It is assumed that all active substance has settled on surfaces and that animals are not exposed to the spray during application. The exposure estimate covers dermal uptake as well as oral intake from grooming.

Emission factor for spraying (fraction emitted to the treated surface during surface treatment by spraying, see Table 54 item#18) = 0.85

Body surface area in contact with surface = 0.87 m^2

Body weight: 200 kg

25 mg a.s./m^2 x 0.85 x 0.87 m^2 ÷ 200 kg

= 0.0924 mg as/kg bw/d

Inhalation exposure:

It is assumed that the animal is exposed to air containing the active substance at its saturated vapour concentration (SVC). This represents a worst-case as the active substance cannot achieve a higher concentration in the air.

SVC =

$$\frac{\text{vapour pressure x molecular weight}}{\text{gas constant x temperature in degrees Kelvin}}$$

$$\frac{2\times10^{-7}\text{ Pa at }20^{o}\text{C x }449.9\text{ g/mol}}{8.31451\text{ J/K mol x }293^{o}\text{K (equivalent to }20^{o}\text{C)}}$$

$$= 3.6935\times10^{-8}\text{ g a.s./m}^3$$

$$= 3.6935\times10^{-5}\text{ mg a.s./m}^3$$

Alveolar ventilation rate = 25 m^3/d

Body weight = 200 kg

$$3.6935\times10^{-5}\text{ mg a.s./m}^3 \times 25\text{ m}^3\text{/d} \div 200\text{ kg}$$

$$= 4.6169\times10^{-6}\text{ mg a.s./kg bw/d}$$

Total exposure:

oral exposure (licking) + oral exposure (feed) + dermal exposure + inhalation exposure

$$= 0.0085 + 0.0069 + 0.0924 + 4.6169\times10^{-6}$$

$$= 0.1078\text{ mg a.s./kg bw/d}$$

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement option:

- measurement of the amount of residue on surfaces
- measurement of the amount of residue in the air
- measurement of the residue level in feed after contact with the treated trough

For a complete exposure assessment, the calculation needs to be repeated for beef and dairy cattle, pigs, broiler chickens and laying hens.

***Note**: Because this is an example of a spray application, residues were adjusted to account for the fraction emitted to the treated surface during surface treatment by spraying. This adjustment does not apply to other types of applications.*

Example 1.2: Treatment of Animal Housing – Exposure of laying hens from spray treatment

Product: Insecticide, VP = 2.1×10^{-8} Pa at 20°C, MW = 434.3 g/mol

Intended Use

Use in animal housing for combating flies. The product contains 0.8 g a.s./L and is applied with a low pressure sprayer to walls, ceilings and window frames in strips of 1-2 m width with a maximum application rate of 40 mg as/m^2 every 21 days in the months of April to October.

Exposure Estimation

The exposure is estimated for laying hens. In the following calculations, default values from Appendix 6-1 are used.

Screening (route of exposure irrelevant):

Wall and roof area per stable = 2030 m^2

Number of animals = 10000

Body weight = 1.9 kg

40 mg a.s./m^2 x 2030 m^2 ÷ 10000 ÷ 1.9 kg

= 4.2737 mg a.s./kg bw/d

Realistic worst-case estimate:

Oral exposure through ingestion of flies:

Chickens do not lick walls, but they seek out dead flies for consumption.

Fly consumption = 10 flies/d

Consumption of biocidal product (spray deposit) by flies = 3.5 mg biocidal product/d

Concentration of a.s. in biocidal product = 0.8 g/L (assuming product density of 1, this is equal to 0.0008 mg a.s./mg biocidal product)

a.s. consumption by flies = 0.0028 mg a.s./fly/d

10 flies/d x 0.0028 mg a.s./fly ÷ 1.9 kg

= 0.0147 mg a.s./kg bw/d

Oral exposure through uptake of contaminated feed:

Body weight: 1.9 kg

Exposed feed surface = 0.01m^2

Emission factor for spraying (fraction of spray product emitted to floor during surface treatment, see Table 54 item #18) = 0.11

Amount of active substance contained in trough:

40 mg a.s./m^2 x 0.11 x 0.01m^2 = 0.0440 mg a.s.

Exposure of animal:

0.0440 mg a.s. ÷ 1.9 kg

= 0.0232 mg a.s./kg bw/d

Dermal exposure through spray treatment:

Poultry does not rub against walls. But dermal exposure can occur from spray hitting poultry during treatment. The exposure estimate includes dermal uptake as well as oral intake from grooming.

Treated area = wall area = 600 m^2

Number of animals = 10000

Body weight of hen = 1.9 kg

% of spray hitting hens = fraction emitted to floor during surface treatment (0.11) (see Table 54 item #18) x 50% (assuming that 50% of the floor is covered by hens) = 0.055 = 5.5%

40 mg a.s./m^2 x 600 m^2 x 5.5% ÷ 10000 ÷ 1.9 kg

= 0.0695 mg a.s./kg bw/d

Inhalation exposure:

It is assumed that the animal is exposed to air containing the active substance at its saturated vapour concentration (SVC). This represents a worst-case as the active substance cannot achieve a higher concentration in the air.

SVC =

$$\frac{\text{vapour pressure x molecular weight}}{\text{gas constant x temperature in degrees Kelvin}}$$

$$\frac{2.1\times10^{-8}\ \text{Pa at } 20^{o}\text{C} \times 434.3\ \text{g/mol}}{8.31451\ \text{J/K mol} \times 293^{o}\text{K (equivalent to } 20^{o}\text{C)}}$$

$$= 3.7437\times10^{-9}\ \text{g a.s./m}^3$$

$$= 3.7437\times10^{-6}\ \text{mg a.s./m}^3$$

Alveolar ventilation rate = 0.2 m^3/d

Body weight = 1.9 kg

$$3.7437\times10^{-6}\ \text{mg a.s./m}^3 \times 0.2\ \text{m}^3\text{/d} \div 1.9\ \text{kg}$$

$$= 3.9408\times10^{-7}\ \text{mg a.s./kg bw/d}$$

Total exposure:

oral exposure (flies) + oral exposure (feed) + dermal exposure + inhalation =

$$0.0147 + 0.0232 + 0.0695 + 3.9408\times10^{-7}$$

$$= 0.1074\ \text{mg a.s./kg bw/d}$$

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement options:

- measurement of amount of residues on surfaces
- measurement of residues on the feathering and skin of poultry
- measurement of concentration of active substance in/on flies
- alternatively, the LD_{50} of the active substance for flies can be used to determine the active substance concentration in/on flies
- measurement of the residue level in feed

For a complete exposure assessment, the calculation needs to be repeated for beef and dairy cattle, pigs and broiler chickens. Exposure from consumption of dead flies should not be included for beef and dairy cattle and pigs.

***Note**: Because this is an example of a spray applications, residues were adjusted to account for the fraction emitted to floor during surface treatment. This adjustment does not apply to other types of applications.*

Example 1.3: Treatment of Animal Housing – Exposure of a dairy cow from a fogging treatment

Product: Disinfectant, VP = 1.58×10^{-4} Pa, MW = 297.18 g/mol

Intended Use

Used indoors by professional users for the disinfection of hatcheries, stables and other infected animal-breeding facilities and materials. Animals are not present during treatment and may not re-enter the premises for 4 hours after treatment. Up to 12 spray, smoke or nebulizer treatments at a rate of 0.005 – 0.1 g a.s./m^3 are intended over the course of a year.

Exposure Estimation

The exposure is estimated for dairy cattle. In the following calculations, default values from Appendix 6-1 are used.

Screening (route of exposure irrelevant):

Housing volume per stable = 9630 m^3

Number of animals per stable = 100

Body weight of dairy cow = 650 kg

9630 m^3 x 100 mg a.s./m^3 ÷ 100 ÷ 650 kg

= 14.8154 mg a.s./kg bw/d

Realistic worst-case estimate:

***NOTE**: For the calculation of oral and dermal uptake, the fraction of residue that has not volatilised, but has settled on surfaces must be calculated. A calculation method has not been agreed, so that the residue amount in the following exposure calculations was set to an arbitrary value of 0.01 mg/m^2 for illustrative purposes only. A value for the fraction of residue that has settled on surfaces must be provided by the Applicant.*

Oral exposure through ingestion of residues:

Exposure from consumption of dead flies is considered not relevant compared to exposure from uptake via food.

Exposure from oral uptake from surfaces is considered not relevant, because grown cattle do not have a habit of licking surfaces.

Oral exposure through uptake of contaminated feed:

It is assumed as a worst case that troughs are not covered during biocide treatment and that all residues contained on the bottom and sides of the trough migrate into the next feed batch that is given after biocide treatment. It follows that all of the residue contained in the trough is taken up by the animal.

Body weight: 650 kg

Exposed feed surface = 2.9 m^2

Amount of active substance contained in trough:

0.01 mg a.s./m^2 x 2.9 m^2 = 0.029 mg a.s.

Exposure of animal:

0.029 mg a.s. ÷ 650 kg

= 0.00004mg a.s./kg bw/d

Dermal exposure through rubbing on surfaces:

Rubbing against surfaces is considered the relevant path of dermal uptake for cows. The exposure estimate includes dermal uptake as well as oral intake from grooming.

Body weight: 650 kg

Body surface area in contact with surface = 1.68 m^2

Total area rubbed = Surface area of skin in contact with surfaces

0.01 mg a.s./m^2 x 1.68 m^2 ÷ 650 kg

= 0.00003 mg a.s./kg bw/d

Inhalation exposure of dairy cow from a fogging treatment

Due to the waiting period of 4 hours, the air concentration at the time of re-entry was calculated with ConsExpo using the following values:

Emission duration: 1 min (This is the time during which application occurs. It is set at the arbitrary value of 1 minute, since it is not relevant for the purpose of this calculation.)

Treated area = housing volume = 9630 m^3

Product amount: housing volume x application rate (100 mg a.s./m^3) = 963 g

Vapour pressure: 1.58x10^{-4} Pa

Molecular Weight: 297.18 g/mol

Temperature: 25 °C

Ventilation rate: 0.9/h

Air concentration at the time of re-entry = 0.0190 mg a.s./m^3

Body weight of dairy cow = 650 kg

Alveolar ventilation rate of dairy cow = 62 m^3/d

0.0190 mg a.s./m^3 x 62 m^3/d ÷ 650 kg

= 0.0018 mg a.s./kg bw/d

Total exposure:

oral exposure + dermal exposure + inhalation exposure

= 0.00004+ 0.00003 + 0.00181

= 0.0019 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is not exceeded. No significant residues are expected in food from dairy cattle. Dietary risk assessment can be stopped for dairy cattle.

Possible Tier II refinement options (in case the trigger value would have been exceeded)

- measurement of amount of residues on surfaces
- measurement of amount of residues in the air
- measurement of amount of residues in feed

For a complete exposure assessment, the calculation needs to be repeated for beef cattle, pigs, broiler chickens and laying hens.

Example 1.4: Treatment of Transport Vehicles – Exposure of pigs from a liquid treatment

Product: Disinfectant

Intended Use

The product is used for the disinfection of transport vehicles. Surfaces and materials need to be cleaned thoroughly with water and detergent, and any detergent needs to be rinsed of with clean water. Excess water needs to be removed before disinfection. For disinfection, 390 mg a.s./m^2 are applied and enough liquid is used so that surfaces (floors, walls) stay wet during the treatment period. The minimum treatment period is 5 minutes.

Exposure Estimation

The pig was chosen as the representative animal. In the following calculations, default values from Appendix 6-1 are used.

Screening (route of exposure irrelevant):

Body weight: 100 kg

Available wall+floor area per animal = 1 m^2

390 mg a.s./m^2 x 1 m^2 ÷ 100 kg

= 3.9 mg a.s./kg bw/d

Realistic worst-case estimate:

Oral exposure:

Exposure from oral uptake from walls is considered not relevant, because pigs do not have a habit of licking walls. They do however enjoy licking metal bars such as the ones separating compartments in a transport vehicle.

Body weight: 100 kg

Tongue surface area: 0.008 m^2

Licks per transport period: 10

390 mg a.s./m^2 x 0.008 m^2 x 10 ÷ 100 kg

= 0.3120 mg a.s./kg bw/d

Dermal exposure through rubbing on surfaces:

Rubbing against surfaces is considered the relevant path of dermal uptake for pigs. The exposure estimate includes dermal uptake as well as oral intake from grooming.

Body weight: 100 kg

Body surface area in contact with surface = 0.45 m^2

Total area rubbed = Surface area of skin in contact with surfaces

390 mg a.s./m^2 x 0.45 m^2 ÷ 100 kg

= 1.7550 mg a.s./kg bw/d

Inhalation exposure:

Exposure to vapours is not considered relevant since the active substance does not volatilise.

Total exposure:

oral exposure + dermal exposure + inhalation exposure

= 0.3120 + 1.7550 + 0

= 2.0670 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement options:

- measurement of amount of residue remaining on surfaces
- data on the efficiency of the rinsing

For a complete exposure assessment, the calculation needs to be repeated for beef and dairy cattle, broiler chickens and laying hens.

6.5.2 Treatment of Drinking Water or of Storage Facilities for Feed and Drinking Water

Biocidal products of PT 5 are used for the direct treatment of drinking water. Other types of biocidal products are used for the treatment of feed/water storage facilities, piping systems for the transport of feed/water, feed/water troughs (PT4) or packaging materials for feedstuff (PT12). When feed or water is treated through direct application, the assumption can be made that all of the active substance applied is carried over into the feed/water. When storage facilities, piping systems, troughs and packaging materials are treated, a realistic worst case estimate must factor in the amount of residue that migrates from the treated surface into the feed/water (e.g. based on the fat solubility of the active substance compared to the type of feed). In such a scenario, the outer layers of a feed batch will contain the bulk of the biocide residue while the core will be residue-free. Feed will be mixed during release from storage silos and during filling of troughs. Animals might not be exposed to residues from exposed feed on a daily basis and residue burden will be higher on some days than on others. An exposure assessment involving exposed feed/water should therefore be based on the assumption that residues migrating from treated surfaces to feed are evenly distributed throughout the feed batch.

Feed/water is often stored for a period of time after being treated with a biocide. During this time, degradation of the active substance may occur, resulting in the generation of degradation products accompanied by diminishing residues of the active substance itself. In the case of non-toxic degradation products, a degradation factor can be included in the Tier II exposure calculation. But when degradation leads to the generation of other toxic substances, it should be assessed whether the parent reference values cover their toxicity profile. Read-across or QSAR, or other predictive models can be used to conclude on the adequacy of the parent ADI with respect to the degradation products. If the toxicity of the degradation products is not covered by the parent compound, these substances must be included as residues in the exposure calculation. Applicant's data on the fate of the active substance provides information on degradation

For an oral exposure calculation, the following parameters may be needed. Default values for these parameters can be found in Appendix 6-1:

- Feed/drinking water intake
- Size and holding capacity of feed silos
- Size of packaging material
- Volume of feed/water contained in storage tank, trough or packaging material or moving through piping system
- Exposed feed surface
- Bodyweight

6.5.2.1 Examples of tier I livestock exposure estimation – treatment of drinking water or storage facilities

Example 2.1: Treatment of Drinking Water

Product: Disinfectant

Intended Use

The product is added to drinking water for livestock animals at a rate of 5 mg a.s./L.

Exposure Estimation

The exposure is estimated for a broiler chicken. In the following calculations, default values from Appendix 6-1 are used.

Water consumption = 0.25 L/d

Body weight = 1.7 kg

Screening:

0.25 L/d x 5 mg a.s./L ÷ 1.7 kg

= 0.7353 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance .

Possible Tier II refinement option:

- measurement of amount of residues in water

For a complete exposure assessment, the calculation needs to be repeated for beef and dairy cattle, pigs and laying hens.

Example 2.2: Treatment of a Feed Storage Facility

Product: Disinfectant

Intended Use

The product is used for the disinfection of feed storage tanks. Tanks are treated once a day with an application rate of 100 mg a.s./m^3. Tanks are filled completely with the disinfectant solution and are later drained.

***NOTE**: Due to the variety of available sizes of feed silos, a default value cannot be established. Instead, a range of sizes is provided in Appendix 6-1. Exposure calculations must be performed for all sizes. In case of exceedance of the trigger value for only a few smaller sizes, expert judgement is used to decide whether Tier II estimates are necessary.*

Exposure Estimation

In the following calculations, default values from Appendix 6-1 are used.

First, the concentration of the active substance in the feed is calculated. Disinfectants are designed to have short-term efficacy, so the desired effect will have been achieved by the time the tank is filled again with feed. It can be assumed then that the migration rate of the active substance into the feed is large, e.g. 100%. Taking a tank with a volume of 13.56 m^3 and a holding capacity of 5.7 tons, we have:

100 mg a.s./m^3 x 13.56 m^3 ÷ 5700 kg feed = 0.2379 mg a.s./kg feed

To calculate the exposure of the animal, in this case a fattening pig:

Feed consumption = 3 kg/d

Body weight = 100 kg

Screening:

3 kg feed/d x 0.2379 mg a.s./kg feed ÷ 100 kg

= 0.0071 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement options:

- measurement of amount of residues on silo surface
- measurement of amount of residues in feed.
- biocidal product (in-use solution) left after draining the container:assumption of film thickness: 20 µm (default value based on expert judgement)

For a complete exposure assessment, the calculation needs to be repeated for beef and dairy cattle, broiler chickens and laying hens for the range of silo sizes given in Appendix 6-1.

Example 2.3 Treatment of Paper/Cardboard used for Packaging Feed

Product: slimicide for paperpulp

Intended use

The active substance is used as slimicide in process water and for equipment in and on which slimes may be formed (e.g. during paperpulp processing). The continuous background concentration is 2.5 mg a.s./L. The principal residue will not decompose and may migrate into the food with which the treated paper comes into contact.

Exposure estimation

In the following calculations, default values from Appendix 6-1 are used.

Feedstuffs which are packaged in paper or cardboard which was treated during manufacture with a slimicide may contain biocidal residues as a result of migration from the packaging material into feed.

The amount of active substance present in the paper or cardboard is calculated as follows:

The ESD recommends to perform risk assessment in the papermaking industry with the RIVM/FEI-scenario.

The ESD assumes that 90% of the a.s. is lost in waste water and 10% remains in the paper.

A paper mill produces 5000 m^3 waste water per day.

Active concentration in water = 2.5 mg/L = 2.5 g/m^3 (see intended uses)

Active substance lost by waste water is 5000 m^3 x 2.5 g/m^3 = 12500 g = 12.5 kg/day

The amount of active substance remaining in dry paper is 12.5 kg/day x 0.1 ÷ 0.9 = 1.3889 kg/day

A paper mill produces 200 t/d.

Dry paper contains 1.3889 ÷ 200000 = 6.94 10^{-6} kg as/kg paper = 6.94 mg as/kg paper.

The amount of active substance present in feedstuffs is calculated as follows:

A worst case estimate of the quantity of active substance which may migrate onto packaged feed is made based on the assumption that all of the active substance which remain in the paper from the processing will migrate into feed. According to the EU Notes for Guidance for Food Contact Materials prepared by the European Food Safety Authority

(updated June 2006), the migration of a substance from a packaging material to food with which it is in contact can be estimated with the assumption that 1 kg of feed is in contact with 600 cm^2 of food packaging (i.e. 1670 mg feed/cm^2).

Dry paper weighs 600 g/m^2 (= 60 mg/cm^2)

Dry paper contains 6.94 mg as/kg paper (= 6.940x10^{-6} mg a.s./mg paper).

1 cm^2 of paper contains: 6.940x10^{-6} x 60 = 4.17x 10^{-4} mg as/cm^2.

1 kg feed is wrapped in 600 cm^2 paper = 1670 mg feed/cm^2.

Therefore, the amount of active substance per kg of feed is: 4.17x 10^{-4} ÷ 1670 = 2.5x 10^{-7} mg as/ mg feed = 0.25 mg as/kg feed.

Livestock exposure:

The exposure is calculated for beef cattle.

Feed consumption = 20 kg

Body weight = 500 kg

Screening:

The screening is based on the assumption that all of the feed the animal consumes comes packaged in treated paper/cardboard.

20 kg feed/d x 0.25 mg a.s./kg feed ÷ 500 kg =

0.01 mg a.s./kg bw/d

Realistic worst-case estimate:

Instead of assuming that 100% of the livestock feed is packaged in treated paper/cardboard, a more realistic assumption is made, e.g. 10% of feed is packaged in treated paper/cardboard.

10% x 20 kg feed/d x 0.25 mg/kg feed ÷ 500 kg

= 0.001 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is not exceeded. No significant residues of the active substance in food of animal origin occur. Risk assessment can be stopped.

Possible Step 2 refinement options (in case the trigger value would have been exceeded):

- measurement of the actual active substance concentration in the packaging material
- determination of the active substance migration from paper into feed
- measurement of the actual active substance concentration in feed

For a complete exposure assessment, the calculation needs to be repeated for dairy cattle, pigs, broiler chickens and laying hens.

6.5.3 Treatment of materials that livestock animals may come into contact with.

Materials are treated with biocidal products to protect them from decay. Treated materials can be formed into structures that livestock animals have access to (e.g. wooden fence posts around paddocks), and may become part of animal housing and transport vehicles. In addition, existing structures may be treated with biocides. By chewing on (e.g. horses, rabbits, goats), rubbing against (large slaughter animals) or licking (e.g. ruminants) the treated materials, animals can take up residues of the biocidal product. In addition, volatile substances being released from the treated material

may be inhaled. Only a fraction of the application amount will be available to animals and can be quantified by the amount of material an animal comes into contact with and the amount of residue that can be extracted from the material.

For an exposure calculation, the following parameters may be needed. Default values for these parameters can be found in Appendix 6-1:

- Frequency of surface licking
- Amount of wood consumed
- Residue extraction from wood
- Body surface in contact with surface
- Alveolar ventilation rate
- Bodyweight

6.5.3.1 Examples of livestock exposure estimation –treatment of materials that livestock animals may come into contact with.

Example 3.1: Treatment of Materials – Exposure of horses to treated wood

Product: Wood protection product, VP = $1x10^{-4}$ Pa at 20°C, MW = 349.9 g/mol

Intended Use

Wood (used for edgings of stall in a horse stable) is treated with the biocidal product by vacuum pressure impregnation. The active substance concentration in the biocidal product is 0.5% w/w. Following treatment, the maximal concentration of active substance in the wood is 250 g/m^3.

Exposure Estimation

The treated wood is incorporated into edgings of the horse stall. Livestock animals can be exposed orally by chewing on the wood. Here the exposure is estimated for a horse. In the following calculations, default values from Appendix 6-1 are used.

Maximum absorption of biocidal product into treated wood = 50 L/m^3

Amount of active substance in the outer 1 cm layer of wood = 50 L/m^3 x 0.5% = 250 g a.s./m^3

Wood consumption: $1.9x10^{-5}$ m^3/d (value based on one study, not a confirmed default value)

Body weight: 400 kg

Realistic worst-case estimate:

Oral exposure:

250 g a.s./m^3 x $1.9x10^{-5}$ m^3/d ÷ 400 kg

= $1.1875x10^{-5}$ g a.s./kg bw/d

Dermal exposure:

Thickness of surface layer of the wooden wall representing the amount of substance per square meter = 0.05 mm

Amount of active substance per square meter: 250 g a.s./m^3 x $0.05x10^{-3}$ m = 12.5 mg a.s./m^2

Body surface area in contact with surface = 1.62 m^2

12.5 mg a.s./m^2 x 1.62 m^2 ÷ 400 kg

= 0.0506 mg a.s./kg bw/d

Inhalation exposure:

It is assumed that the animal is exposed to air containing the active substance at its saturated vapour concentration (SVC). This represents a worst-case as the active substance cannot achieve a higher concentration in the air.

SVC =

vapour pressure x molecular weight

gas constant x temperature in degrees Kelvin

$1x10^{-4}$ Pa at 20°C x 349.9 g/mol

8.31451 J/K mol x 293°K (equivalent to 20°C)

$= 1.44x10^{-5}$ g a.s./m^3

= 0.0144 mg a.s./m^3

Alveolar ventilation rate = 43 m^3/d

Body weight = 400 kg

0.0144 mg a.s./m^3 x 43 m^3/d ÷ 400 kg

= 0.0015 mg a.s./kg bw/d

Total exposure:

oral exposure + dermal exposure + inhalation exposure

$1.1875x10^{-2}$ + 0.0506 + 0.0015

= 0.0639 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement options:

- measurement of the amount of wood chewed by animals.
- measurement of the release rate of active substance from wood (if applicable, consideration of the period between wood treatment and the actual use of wood)
- information on evaporation of substance from treated wood
- transfer coefficient from a treated surface from Biocides Human Health Exposure Methodology[10] (page 171) might be applicable

For a complete exposure assessment, the calculation needs to be repeated for beef and dairy cattle, pigs, and goats.

6.5.4 Direct Treatment of Animals

Biocidal products used for the direct treatment of livestock are intended for general disinfection purposes or for repelling insects (flies, mosquitos, midges, ticks etc). They are to be distinguished from veterinary medicinal products, which are intended to prevent or treat disease. For example, the disinfection of teats is considered a biocidal use while treatment of teats for the prevention on mastitis is a veterinary medicinal use. The use classification of products containing active substances with lethal effects on external parasites to be used on animals will depend on the intended use and/or demonstrated claims for the product

[10] Available on ECHA BPR ad hoc Working Group – Human Exposure webpage https://echa.europa.eu/about-us/who-we-are/biocidal-products-committee/working-groups/human-exposure .

(https://circabc.europa.eu/sd/a/51ca9945-167d-411f-9763-92e634af9e1c/Biocides-2002-01%20-%20Borderline%20with%20%28veterinary%29%20medicinal%20products.pdf).

6.5.4.1 Teat disinfection

In the following example, the external exposure of dairy cows is estimated following treatment with a biocidal teat dip product. Teat dips can contaminate milk in two ways, indirectly via dermal uptake of the product by the dairy cow and subsequent partitioning of residues into milk, and directly by being washed into the milk during milking. A teat dip is a local treatment restricted to the udder of the dairy cow, and teat dip residues absorbed by the skin of the udder may potentially mainly be deposited in the tissue where the milk collects. In view of this, it has been considered to set a local trigger value for teat dips. However, residues taken up dermally by the animal can also enter the systemic circulation and be distributed throughout the animal. In addition, no numerical data are currently available on which to base a local trigger value. Hence residues from teat dips that are dermally taken up by the animal are compared to the trigger value of 0.004 mg as/kg bw in livestock (see calculation A in the example below). For residues that go directly into the milk (no dermal uptake assumed), a worst case consumer exposure (WCCE) should be calculated and compared to the ADI (see calculation B in the example below). It should be noted that the WCCE is exceptionally provided here, as normally the evaluation of the WCCE is described in the EMA-CVMP guidance.

The following parameters are needed (default values for these parameters can be found in Appendix 6-1, otherwise use data provided by the applicant):

- Number of daily milkings: default value is 2/day;
- Volume of product applied to teats per cow and milking: default values are 10 mL for dipping, 20 mL for spraying, 2.5 mL for foams;
- Fraction of applied product remaining on teats: The Emission Scenario Document for PT3 products highlights that the amount of the disinfectant remaining on teats depends on the viscosity of the solution and indicates to use 0.5 of the fraction of disinfectant remaining on teats as a worst case. The value is presented as a conservative value;
- Bodyweight of the dairy cow: default value: 650 kg bw;
- Daily milk yield of the dairy cow: default value: 20 L/day.

Three different cases can be distinguished depending on the intended use:

1. Pre-milking teat disinfection: Perform calculation A and B
2. Post-milking teat disinfection: Perform calculation A and B
3. Both pre- and post-milking teat disinfection: Perform calculations A and B twice (i.e. once for pre-milking teat dip and once for post-milking teat dip).

When no information on dermal absorption through teat skin is available, the WCCE for calculation A and B, is the maximum WCCE from either A or B. When information on dermal absorption through teat skin is available, the WCCE for A and B is the sum of WCCEs.

Calculation A assumes that the fraction of the biocidal product that remains on the teats is carried over into the animal (i.e. no residues will directly enter the milk because of contamination). With this assumption, residues can be expected in milk and/or tissues after some hours or days after application depending on the ADME rate of the animal for this compound.

Calculation B assumes that the fraction of the biocidal product that remains on the teats is carried over directly into the milk (i.e. all residues appear in the milk after milking). With this assumption, no biocidal product is taken up by the animal (i.e. the route of dermal uptake can be ignored) and residues in tissues are not expected; no biocidal product is lost in the milking process because of wiping or other handling procedures.

NOTE to the reader:

It should be highlighted that for the aim of this guidance document, (i.e. to estimate whether further information is needed and an MRL procedure should be started), the EMA food basket should be applied. The daily milk consumption in the EMA food basket is 1.5L/day. The food basket is mainly reflecting the dietary pattern of adults, which differs from the children's pattern. This difference is not fully covered by the food basket, but the EMA considered that the system in place for the establishment of MRLs for milk is adequate also for children (EMEA/CVMP/391/02-FINAL-corrigendum November 2002). In case consumer exposure to an active substance is performed **only** with the aim of the estimation of the dietary risk assessment and the MRL status of this active substance is not to be established, other EU agreed consumption figures might be applied to consider the different daily milk intake of the toddler and children, as milk is a relevant commodity for both toddler and children. Data from EFSA food consumption database or EFSA PRIMo model can be used for this purpose.

Example 4.1: Direct Treatment of Animals –Teat disinfection through dipping

Product: Disinfectant

Intended Use

The product is used for the disinfection of teats on dairy cows and is used twice daily before and after each milking. Prior to the next milking, teats are cleaned with a detergent. For each teat disinfection, 10 mL product with an active substance concentration of 2000 ppm (C_prod = 2 mg a.s./mL) are used per animal per treatment. The fraction of product remaining on teats is 0.5 of the fraction applied on the teats (according to ESD for PT3).

Exposure estimation

In the following calculations, default values from Appendix 6-1 are used.

Screening:

n= Number of milkings per day = 2 milkings/day

V_prod = Product volume on teats per milking: 10 mL/milking for 4 teats (default value only applies in case no volume is specified on the product label);

f_prod = The fraction of product remaining on teats is 0.5 of the fraction applied on the teats.

bw = Body weight of the dairy cow = 650 kg bw

V_milk = daily milk yield of the dairy cow = 20 L/day

Screening calculation A

Dermal exposure via teat dips (assuming 100% dermal absorption, a product concentration of 2 mg a.s./mL and 0% degradation of the active substance):

$$n \times (V_{prod} \times f_{prod} \times C_{prod}) / bw$$

$$2 \text{ milkings/day} \times (10 \text{ mL/milking} \times 0.5 \times 2 \text{ mg a.s./mL}) \div 650 \text{ kg bw}$$

$$= 0.031 \text{ mg a.s./kg bw/d}$$

→ The trigger value of 0.004 mg a.s./kg bw/d for livestock is exceeded. Proceed with a refined exposure assessment based on Tier II data.

In case of pre- and post-milking teat disinfection, this calculation needs to be performed twice (i.e. once for pre-milking teat disinfection and once for post-milking teat disinfection). V_prod, f_prod and C_prod could be different.

Screening calculation B

Estimated residues in milk through contamination during milking (assuming 0% dermal absorption, an product concentration of 2 mg a.s./mL, and assuming 0% degradation of the active substance):

n x (V_prod x f_prod x C_prod) / V_milk

2 milkings/day x (10 mL/milking x 0.5 x 2 mg a.s./mL) ÷ 20 L/day

= 1 mg a.s./L

The estimated residues in milk cannot be compared to the trigger value of 0.004 mg a.s./kg bw/d for livestock, because such trigger value is related to the external exposure of the livestock (see the section "Tier I: initial external exposure estimation" for further information).

The worst case consumer exposure (WWCE) should be calculated applying EMA standard food basket:

WCCE = amount a.s. transferred into milk * I_{milk} ÷ bw human

Amount a.s. transferred into milk = amount of the active substance transferred into milk as estimated in the first step of the calculation B.

I_{milk} = daily milk consumption (from EMA food basket: 1.5 L/day).

Bw_human = default body weight for adult (60 kg bw).

WCCE= (1 mg a.s./L*1.5 L)/60 kg bw

WCCE=0.025 mg a.s./kg bw/d

→ If WCCE is above 30% of the ADI, proceed with a refined exposure assessment based on Tier II data.

In case of pre- and post-milking teat disinfection, this calculation needs to be performed twice (i.e. once for pre-milking teat dip and once for post-milking teat dip). V_prod, and C_prod could be different.

Combining calculations A and B

WCCE calculation for calculation A:

I_{milk} = daily milk consumption (from EMA food basket: 1.5 L/day = 1.5 kg/day)

$I_{tissues}$ = daily edible tissue consumption (from EMA food basket: 0.5 kg tissues made up of 0.300 kg of muscle, 0.100 kg of liver, 0.050 kg of kidney and 0.050 kg of fat)

WCCE = amount a.s. transferred into milk and edible tissues * ($I_{tissues}$ + I_{milk}) ÷ bw human

WCCE= 0.031 mg a.s./kg bw/d * (0.5 kg + 1.5 kg) ÷ 60 kg bw= 0.001 mg a.s./kg bw/d

WCCE calculation for A= 0.001 mg a.s./kg bw/d

WCCE calculation for B= 0.025 mg a.s./kg bw/d

When no information on dermal absorption through teat skin is available, the WCCE for calculation A and B, is the maximum WCCE from either A or B. So in this case the WCCE = 0.025 mg/kg as/day, based on calculation B (0% dermal absorption).

For pre- and post-milking disinfections, it means the maximum contribution from pre-milking (A or B) needs to be added to the maximum contribution from post-milking (A or B).

If the overall WCCE is above 30% of the ADI, proceed with a refined exposure assessment based on Tier II data or proceed with the approach described in the EMA-CVMP guidance.

Both calculation (A and B) need to be conducted. Ideally calculation A and B should be corrected for % dermal absorption (see Tier II refinements below) i.e. the portion of the residue absorbed in the animal cannot be found in the milk through direct contamination.

Dermal absorption:

When information on dermal absorption through teat skin is available, the WCCE for A and B is the sum of WCCEs based on the formula D x WCCE (calc A) + (1-D) x WCCE (calc B), where D is dermally absorbed fraction. For example if a dermal absorption (D) of 20% was found for teat skin, the sum of WCCE would be calculated as:

Sum of WCCEs from calculation A and B

$WCCE_{calculation\ A}$ + $WCCE_{calculation\ B}$

= 0.2 x 0.001 mg a.s./kg bw/d + (1-0.2) x 0.025 mg a.s./kg bw/d = 0.020 mg a.s./kg bw/d

For pre- and post-milking applications, calculation A consists of two contributions and calculation B consist of two contributions.

Possible Tier II refinement option:

Dermal absorption is likely to be between 0 and 100% and part of the residue may evaporate or be wiped off in the milking process and therefore Tier II refinement options are encouraged:

- Pre milking products are normally less viscous compared to the post-milking products and the teat is cleaned before milking. Therefore, if information is available, consideration could be given in reducing the fraction of the product (f_prod) that remains on the teat (for calculation A and B).

- Measurement of the amount of residues in the milk at various time-points after application, to determine the likely residue levels in milk (to get an indication whether both calculations A and B are needed and to refine the WCCE from milk). Measurement of residues in the milk just after the treatment shows the direct contamination of the milk. With a continuous teat treatment over the days, the active substance might be absorbed and absorption may reach a plateau. After some days of the treatment, the measured residues correspond to the amount from direct milk contamination and the plateau of the absorption. The measurement of the amount of residues in milk at the plateau of the absorption can be used directly in the WCCE.

- Measurement of the amount of residue remaining on teats in the time period between cleaning after teat-dip application and milking. Ideally, measurement of residues on the teats should be performed just after the application and after the cleaning to estimate the fraction of the product wiped off, which is not available for absorption or direct milk contamination.

- Dermal absorption of the residue through teat skin to determine the amount of residue available for systemic circulation within the animal (this refinement option is relevant for calculation A and B). Calculation A needs to be multiplied by D and calculation B needs to be multiplied by (1-D), where D is a fraction between 0-1 representing the amount available for dermal absorption.

Conclusion:

If one result (from calculation A or B or A+B) exceeds the trigger value or the 30% of the ADI respectively, further refinement can be performed based on additional data. In case after refinement the 30% for the ADI is still exceeded, further evaluation of the substance by the CVMP is required.

6.5.4.2 Foot/Hoof Disinfection

Animals walk through disinfection baths at least twice daily when they exit and enter the stable/milking parlour. Dairy cows walk through six times because they are milked twice a day and let out to graze. The bath is set up at the entrance of the stable or the milking parlour. Although the disinfectant is meant for hooves only, contact with the skin should always be assumed. The depth of the level of disinfectant in the bath will often be above the hoof and splashing will occur as the animals walk through the bath. Some hoof disinfectant baths consist of foam rather than liquid formulations. Foam formulations contain volatile components available for inhalation and exposure to foam formulations lasts longer as foam adheres to legs.

Example 4.1: Direct treatment of Animals – Exposure via hoof disinfectant baths

***NOTE**: An example product for this use has not been submitted at EU-level. The following calculations are based on a hypothetical product with a hypothetical application scenario.*

Product: Disinfectant

Intended Use

The formulation is filled into shallow tubs which animals walk through as they enter or exit their stable /milking parlour. Each tub contains 375 L foam with an active substance concentration of 100 mg/L. A single tub is sufficient for 100 walk-through events.

Exposure estimation

The exposure is calculated for a dairy cow. In the following calculations, default values from Appendix 6-1 are used.

Screening:

(calculated for 1 walk-through event of a single cow)

Number of animals per stable: 100; in case the hoof disinfection is performed on dairy cows from or to the milking parlour, a number of 82 cows should be considered unless a different information is provided by the applicant (See footnote of the Table 2, Animal housing, for further information). In this specific example, it is indicated that a single tub is sufficient for 100 walk-through events bath, therefore 100 cows are considered.

Bodyweight: 650 kg

(375 L product x 100 mg a.s./L product) ÷ 100 animals/stable ÷ 650 kg bw/animal

= 0.5769 mg a.s./kg bw

Realistic worst-case estimate:

Oral exposure:

Oral exposure is not considered relevant, since cattle do not lick or groom their hoofs

(calculated for 2 daily walk-through events of a single cow).

Dermal exposure from walking through the bath:

Daily passes through the tub = 2

Exposed skin/hoof area = 1590 cm^2

Layer of product absorbed = 0.01 cm

Body weight = 650 kg

To calculate the product amount in contact with one hoof/skin:

0.01 cm x 1590 cm^2 = 15.9 cm^3 = 0.0159 L

If 1 L product contains 100 mg a.s., then 0.0159 L product contains 1.59 mg a.s.

Assuming each hoof steps into the hoof bath once at each pass through the bath, then the amount of a.s. each animal comes into contact with during one pass equals -2 x 1.59 mg a.s. = 3.18 mg a.s.

3.18 mg a.s. x 2 daily passes ÷ 650 kg

= 0.0098 mg as/kg bw/d

Inhalation exposure from breathing in vapours released from the formulation:

Inhalation exposure is considered to be negligible. Exposure is transient as livestock traverses the hoof disinfection bath within a matter of seconds, and vapours do not diffuse in significant amounts beyond the entrance/exit area.

Total exposure:

dermal exposure

= 0.0098 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement option:

- measurement of the amount of residue on hoofs and legs

6.5.4.3 Insecticides and Repellents

The products included in this category are products with repellent and/or insecticidal activity (PT 18 and 19) that are not classified as veterinary drugs. Examples of such products are collars, neckties, ear tags, dips, skin and bath treatments and products used to control fish parasites.

Example 4.2: Direct Treatment of Animals – Exposure via fly ear tags

Product: Fly treatment

Intended Use

The product is supplied as ear tags for cattle and has a biocidal effect against flies. Up to two ear tags are attached to each animal, and tags are effective for one whole fly season. Each ear tag contains 935 mg active substance, which is released gradually onto the surface of the tag throughout the season. Through body movements, the lipophilic active substance is transferred onto the hairs of the animal's coat. From there it is dispersed all over the animal, giving protection to the entire body. The release rate of the active substance to the surface of the tag depends on the amount that is removed from the tag. For the purpose of this exposure calculation, an instant release rate is assumed.

Exposure estimation

In the following calculations, default values from Appendix 6-1 are used.

Residues can be taken up by the animal through dermal absorption and through grooming. Calculation of dermal uptake assuming 100% absorption covers all paths of exposure.

Body weight = 500 kg

Dose rate 935 mg a.s. x 2 ear tags/animal = 1870 mg as/d

Screening:

1870 mg a.s./d ÷ 500 kg

= 3.7400 mg a.s./kg bw/d

→ The trigger value of 0.004 mg a.s./kg bw/d is exceeded. Proceed with a refined exposure assessment based on Tier II data or proceed with the EMA-CVMP guidance.

Possible Tier II refinement options:

- measurement of the amount of residue on the animal's skin
- release rate of the ear tags

For a complete exposure assessment, the calculation needs to be repeated for dairy cattle.

6.5.5 Treatment of Aquaculture

The available literature on parameters needed for the exposure assessment of fish is scarce, and reliable default values cannot be established. Consequently, for fish, Step 1 exposure assessment must be skipped unless the Applicant can provide a well justified exposure calculation model. Future development of an assessment model for fish would be useful. The following paragraphs provide some general information on the exposure of fish.

Biocidal products such as disinfectants and antifoulants are used for the protection of structures (e.g. control of growth and settlement of fouling organisms in fish tanks, on fishnets etc.) and for water hygiene in aquaculture. Fish can be exposed orally, dermally and through respiration via the gills. In the case of water treatment in fish enclosures, residues are evenly distributed throughout the water and fish are exposed via all pathways.

The treatment of structures usually occurs on dry land. After the treated objects have been put into the water the active substance of the biocidal product is normally only slowly released in order to maintain its desired effect of the biocidal product. The released substances are diluted in the surrounding water and are available for uptake by fish. Exposure to the fraction remaining on the treated structure can also occur, in particular when fish come into frequent contact with the treated structure.

6.6 Tier II - Principles for exposure estimation

NOTE to the reader:

In this section principles for exposure estimation are laid down. Due to the complexity of Tier II exposure estimations, a comprehensive description of methods for all possible scenarios is not feasible. It should be noted that a Tier II refinement does not necessarily involve performing new studies. Any reliable existing data and/or information that is suitable for refinement purposes can be used. The principles outlined below can be used to help design Tier II trials and build suitable models to estimate exposure from the obtained data on a case-by-case basis.

When the first step of external exposure assessment results in the exceedance of the trigger value of 0.004 mg/kg bw/day, the exposure estimate can be refined in a second tier assessment.

Within Tier I, a realistic worst-case estimate of exposure is given. In Tier II, a further refinement of the estimation of external exposure is performed based on specific data provided by the Applicant related to the active substance and its actual intended use. This may include data already provided by the Applicant, such as information on substance degradation. The Applicant may also submit additional studies providing data for refinement.

Examples for Tier II studies include:

- Studies to allow the identification and quantification of the available active substance or of its degradation products in the treated area (treated surfaces, materials, objects, air, water or feed, the animal itself) at the time animals are

exposed (e.g. if animals are not present during treatment, degradation or volatilisation of the active substance may occur before animals have the opportunity to take it up). When taking into account the degradation rate of an active substance, it has to be considered that degradation products may be more toxic and more persistent than the active substance itself, and an exposure assessment based on the residues of the active substance as well as the toxic degradation products has to be performed using the same step-wise approach as for the a.s. Data on abiotic degradation (hydrolysis, photolysis) can be found in the environmental part of the dossier. Measurement of the concentration of active substance on insects or determination of the LD_{50} for insects can be used in place of the active substance concentration in/on insects.

- Studies to allow the quantification of the dislodgeable fraction, (i.e. the amount of active substance that can be removed from the treated surface), of the active substance or of its degradation products from the treated area (e.g. wiping tests mimicking licking/rubbing behaviour of animals). The biocidal product must remain available at the application site for being effective. It can therefore be assumed that only a fraction of the residue on treated surfaces (the dislodgeable fraction) is available to the animal. Experimental values of the dislodgeable fraction can be used in the calculation. When the product is applied as granules, dislodgeability is not an issue, because granules do not stick to surfaces. For ear tags, the release rate can be determined.
- Studies characterising the effectiveness of a required rinsing step or a justification proving the effectiveness of rinsing based on scientific data or information (e.g. water solubility of the active substance);
- Measurement of the release rate of active substance from treated wood to allow determination of residues remaining after a certain time period (e.g. after a withdrawal period);
- Measurement of the release rate of active substance from e.g. ear tags;
- Studies of exposure patterns linked, for instance, to the behaviour of the exposed animals (e.g. amount of wood chewed).

Tier II can be omitted in favour of proceeding directly to the next phase of risk assessment as detailed in the EMA-CVMP guidance.

6.6.1 Principles for design of Tier II trials

The following section outline some principles that should be taken into consideration when performing tier II trials:

- **Relevant residue**: Before obtaining data, the composition of the relevant residue has to be defined. The relevant residue consists of all toxicologically relevant substances (active substance and possibly degradation products) that remain on treated areas as a result of the use of the biocide in question. Radiolabelled studies on the fate of the active substance (i.e. degradation into toxicologically relevant compounds, formation of reaction products) as well as data on the reactivity of the active substance would provide the necessary information;
- **Analytical method:** A valid analytical method is needed in order to perform measurements. All compounds that comprise the relevant residue (this may include the active substance and toxicologically relevant metabolites, degradation products, by-products and excipients) have to be accounted for;
- **Time frame:** To define a time frame for the trial, the degradation rate/reaction rate as well as the label instructions can be taken into account. When degradation/reaction occurs, a minimum time frame of 2x the half-life might be appropriate. The conditions of degradation/reaction compared to the conditions in

the treated area must be considered. If no degradation/reaction occurs, the frequency of application according to label instructions can serve as a guide;

- **Number of trials:** Measurements should be performed at various time points to adequately capture the degradation of the active substance throughout the treatment period;
- **Site selection, site requirements:** Trials should be performed under realistic circumstances (e.g. in an actual stable) or under conditions reflecting realistic circumstances. The material treated and the application rate must reflect the intended use of the biocidal product;
- **Application of biocidal product:** Trials should be performed using the highest proposed rate of application and using the formulation in question. In cases where multiple applications are intended, this should be reflected in the residue trial;
- **Sampling:** Sampling should occur under as realistic circumstances as possible. Since residue levels will vary within the treated area or in the treated feed/water, several samples have to be obtained. Conditions and time period of storage should be considered as well. For example, for feed stored in treated tanks, samples from the feed layer in direct contact with the tank surface and samples from the inner layers of feed would be obtained and the results averaged. Where no single type of feed is specified, several types of feed need to be tested in order to identify the critical case. For example, for water stored in treated tanks, samples should be taken at various time points to account for the maximum period the water is stored within the treated tank.

Data obtained from the studies are used to make refined exposure estimate(s) for an appropriate time period (e.g. day 1, day 2 etc.) and subsequently each exposure estimate is compared to the trigger value. In cases where the trigger value is exceeded only for the initial exposure period (e.g. only day 1 and 2) management options may be considered. Where the trigger value is exceeded for a longer time period then dietary risk assessment has to proceed to follow the approach detailed in the EMA-CVMP guidance.

Appendix 6-1: Default Value Working Tables

Table 2: Animal Size and Physiology

(for references and explanations see Table 55)

Animal Species	**Body weight (kg)**	**Animal height (cm)** Height to withers or shoulder/ height to top of head/ maximum reaching height	**Body surface area (m^2)** calculated from default bw	**Body surface area in contact with surface (m^2)** (30% of total body surface area)	**Alveolar ventilation rate (l/h)** resting AVR calculated from default bw, (to account for activity use a correction factor of 3)	**Alveolar ventilation rate (m^3/d)** resting AVR calculated from default bw, (to account for activity use a correction factor of 3)	**Feed intake (kg dry matter/day)** based on default bw	**Drinking water intake (l/d)** based on default bw
Beef cattle	500	145/161/177	4.8	1.44	2110	51	12	50
Dairy cattle	650	145/161/177	5.6	1.68	2589	62	25	115
Calf	200	116/129/142	2.9	0.87	1032	25	8	20
Fattening pig	100	77/-/92	1.5	0.45	601	14	3	10
Breeding pig	260	110/-/125	2.8	0.84	1267	30	6	15
Sheep	75	65/72/79	1.5	0.45	480	12	2.5	10
Lamb	40	61/67/73	1.0	0.30	294	7	1.7	5
Slaughter goat (=goat kids)	13	43/57/200	0.5	0.15	122	3	0.5	1.3
Lactating goat	70	76/100/200	1.5	0.45	455	11	2.8	7
Broiler chicken~~s~~	1.7	-/25/-	0.05	0.015	8.2	0.2	0.12	0.25
Laying hen	1.9	-/25/-	0.05	0.015	8.9	0.2	0.13	0.25
Turkey	7	-/34/-	0.3	0.090	23	0.6	0.5	1.0
Horse	400	158/196/234	5.4	1.62	1773	43	16	40

Rabbit	2.5	-/0.3/-	0.20	0.060	34	0.9	0.25	0.5

Table 3: Animal Housing

(for references and explanations see Table 55)

Animal Species	**Number of animals per stable**	**Floor area per stable (m^2)**	**Wall and floor area per stable (m^2)**	**Housing volume per stable (m^3)**	**Floor area per animal (m^2)**	**Maximum area (wall) within reach of animal (m^2)** considering max reaching height (No of compartment walls considered)	**Maximum area within reach of animal (wall+floor) (m^2)** considering max reaching height (No of compartment walls considered)	**Exposed feed surface per animal (m^2)** in case of direct treatment of troughs	**Exposed feed surface per animal (m^2)** in case of treatment of surfaces surrounding troughs	**Ventilation rate housing (m^3/h)** per 500 kg live weight	**Ventilation rate housing (m^3/h)** per animal	**Ventilation rate housing (1/h)** air exchanges per hour
Beef cattle	125	370	1000	3063	2.96	10.8 (3)	13.7 (3)	2.6	0.7	Winter min 50 Summer max 333	Winter min 50 Summer max 333	Winter min 2 Summer max 13.6
Dairy cattle	100*	1170	1670	9630	11.7	21.4 (3)	33.1 (3)	6.6	2.9	Winter min 67 Summer max 417	Winter min 87 Summer max 542	Winter min 0.9 Summer max 5.6
Calf	80	160	330	590	2.0	8.5 (4)	10.5 (4)	2.0	0.5	Winter min 75 Summer max 500	Winter min 30 Summer max 200	Winter min 4.1 Summer max 27.1
Fattening pig	400	600	970	2110	1.5	4.0 (3)	5.5 (3)	1.2	0.4	Winter min 50 Summer	Winter min 10 Summer	Winter min 1.9 Summer

										max 500	max 100	max 19.0
Breeding pig										Winter min 100	Winter min 52	
- individual housing	132	560	910	1960	4.2	9.1 (3)	13.4 (3)	2.4	1.1	Summer max 1000	Summer max 520	Winter min 3.5 Summer max 35,0
- group housing	132	710	1160	2480	5.4	10.3 (3)	15.7 (3)	2.8	1.3			Winter min 2.8 Summer max 27.7
Broiler chickens										Winter min 278	Winter min 0.9	
- free range, litter floor	20000	1110	1600	4170	0.056	-	-	-		Summer max 1853	Summer max 6.3	Winter min 4.3 Summer max 30.2
- parent broiler chickens, free range (grating floor)	7000	390	600	1458	0.056	-	-	-				Winter min 4.3 Summer max 30.2
- parent broiler chickens in rearing, free range	9000	500	750	1880	0.056	-	-	-				Winter min 4.3 Summer max 30.2

(grating floor)												
Laying hen **- battery** **- free range (litter floor)** **- Free range (grating floor)**	21000 10000 20000	750 1430 1270	1100 2030 1822	2810 5360 4780	0.036 0.14 0.064	- - -	- - -	- - -	0.01	Winter min 175 Summer max 2000	Winter min 0.7 Summer max 7.6	Winter min 5.2 Summer max 56.8 Winter min 1.3 Summer max 14.2 Winter min 2.9 Summer max 31.8
Rabbit	5 per cage	0.24 per cage	0.84 per cage	0.072 per cage	0.048	0.27 (4)	0.32 (4)					

* **Please, note** that for the purposes of the human exposure estimation, the number of the dairy cows that are milked daily corresponds to 82. According the ESD for PT3, the default value for a dairy cow herd side is 100 animals. Dairy cows are regularly milked twice per day. The lactation period for dairy cows is normally 270 lactating period of 300 days, 82 milk producing cows are milked per day, from a herd of a 100 dairy cows.

From Recommendation number 13 of the ad hoc WG Human exposure [https://echa.europa.eu/documents/10162/21664016/recommendation_13_teat_disinfection_en.pdf/fbeb394b-e74b-685d-c231-5e3a530e311c].

Table 4: Animal Transport

(for references and explanations see Table 55)

Animal Species	Time spent in transport vehicles (h) transport + resting period + transport	TRUCK No of floors/No of compartments per floor/No of animals per compartment Default truck of 7.0m x 2.5 m	COMPARTMENT Length (m)/ Width (m)/ relevant height (m)	Required floor area per animal during transport (m^2)	Available wall+floor area per animal (m^2) within a compartment	Available volume per animal (m^3) within a truck of 7.0m x 2.5 m	Ventilation rate
Beef cattle	14+1+14	1/2/6	3.5/2.5/1.8	1.35	5.1	2.6	Forced ventilation systems 60 m^3/h/kN loading capacity (with 1000 kg = 9.80665 kN) and a temperature between 5-30°C
Dairy cattle	14+1+14	1/2/5	3.5/2.5/1.8	1.61	6.1	3.2	
Calf	14+1+14	2/2/11	3.5/2.5/1.5	0.73	2.4	1.2	
Fattening pig	24	3/2/20	3.5/2.5/1.0	0.43	1.0	0.4	
Breeding pig	24	2/2/10	3.5/2.5/1.3	0.80	2.4	1.1	
Sheep (with wool)	14+1+14	2/2/18	3.5/2.5/0.8	0.47	1.0	0.4	
Lamb	9+1+9	3/2/35	3.5/2.5/0.8	0.25	0.5	0.2	
Slaughter goat (=goat kids)	9+1+9	3/2/62	3.5/2.5/1.0	0.14	0.3	0.1	
Lactating goat	14+1+14	2/2/16	3.5/2.5/1.5	0.53	1.7	0.8	
Broiler chickens	24	8/12/53	1.17/1.25/0.27	0.0272	0.052	0.0074	
Laying hen	24	7/40/14	0.88/0.5/0.27	0.0304	0.085	0.0084	
Turkey	24	6/6/39	1.17/2.5/0.40	0.0735	0.15	0.030	
Horse	24	1/2/5	3.5/2.5/2.4	1.75	7.5	4.2	

Default values for transport crates for rabbits can be found in an EFSA document at http://www.efsa.europa.eu/en/efsajournal/doc/1966.pdf .

Table 5: Miscellaneous Values and Calculations

	Animal Species	Description	Default	Background Information Remarks	References
1	Dairy cattle	Daily milkings	• 2 milkings/day	• Number of milkings per day may be more frequent, e.g. 3 times per day for high production cows. • For reasons of consistency EMA prefers the number of 2 milkings a day in their evaluations.	EMA Guidance Document: Note for Guidance for the Determination of Withdrawal Periods for Milk; EMEA/CVMP/473/98-FINAL http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004496.pdf • Information given by MS
2	Dairy cattle	Volume of teat dip	• For dipping 10ml/cow/milking • For spraying 20ml/cow/milking • For foams 2-2.5 ml/cow/milking	• In most cases the volume to be applied will be given by Applicant (instruction for use). In all other cases the default value based on information from ES and FR will be applied.	Information provided by ES and FR Pauline Brightling, Graeme A. Mein, Jakob Malmo, Diane P. Ryan. TN07 Lactation, pp. 43. Countdown Downunder: Farm Guidelines for Mastitis Control, ISBN 0 642 37362 0
3	Calf	Surface area of tongue	0.008 m^2		• Information provided by SE
4	Calf	Frequency of surface licking	10 licks per day	• Pen licking frequencies in the studies provided were 2-30 per day and are highly dependent on the calf`s environment • In the studies, licking frequency was not defined. Thus, the question arose whether a licking frequency is a single lick or a distinct period of time during which an animal engages in licking behaviour. When a calf engages in a licking incident, it might not lick widely across a large surface, but basically lick repeatedly at the same general spot on a surface. So, for our calculation it	• Verga M, Pavesi M, Cerutti F, Behaviour and performance of veal calves under different stabling conditions. Ann. Zootech., 1984, 34 (3), 247 – 256 • Boe K.E., Andersen I.L., Early weaning of calves – how does it affect the behaviour?, pp 604 – 610, in livestock environment VI: Proceedings of the 6th international symposium. 2001 ASAE Number 701P0201. ISBN: 1892769212 • Phillips C.J.C., The effects of Forage Provision and Group Size on the Behaviour of Calves. J. Dairy Sci. 2004, 87: 1380 – 1388. • Margerison J.K., Preston T.R., Berry N., Phillips C.J.C,

				would not make a difference, whether the calf licks once at the same spot or several times during one licking incidence. In the calculation we assume anyway that the entire amount of a.s. on the licked spot is taken up by the animal, so whether this happens with one lick or several is inconsequential.	Cross-sucking and other oral behaviours in calves, and their relation to cow suckling and food provision. Applied Animal Behaviour Science, 2003, 80 (4), 277-286. doi:10.1016/S0168-1591(02)00231-9. ISSN: 0168-1591
5	Cattle	Volume of tub for hoof disinfection	375 l	Defaults as given in the ESD: For the disinfection of animals' feet, basins filled with biocides are used. The volume of the bathing device can vary between 375 l and 675 l. In order to cover a worst case, a tub content of 375 l is assumed, which is replaced after 100 walk-through events. For a stable with 100 dairy cows which are milked twice a day, four tub fillings per day are needed.	ESD for Product Type 3: Emission scenarios for veterinary hygiene biocidal products (JRC Scientific and Technical Reports, 2011); EUR 25116 EN – 2011; JRC 67706; doi:10.2788/29747. http://echa.europa.eu/es/guidance-documents/guidance-on-biocides-legislation/emission-scenario-documents
6	Cattle	Daily passes through hoof disinfection tub	Dairy cow: 2	Hooves of dairy cows are regularly disinfected. Cows walk through tubs containing the disinfection solution on their way from or to the milking parlour. As the default number of daily milking event is 2, the daily passes through the hood disinfection tub is set at 2 accordingly.	ESD for Product Type 3: Emission scenarios for veterinary hygiene biocidal products (JRC Scientific and Technical Reports, 2011); EUR 25116 EN – 2011; JRC 67706; doi:10.2788/29747.http://echa.europa.eu/es/guidance-documents/guidance-on-biocides-legislation/emission-scenario-documents
7	Cattle	Number of ear tags per animal	2		
8	Pig	Surface area of tongue	0.008 m^2		Information provided by DE
9	Pig	Frequency of surface licking	10 licks per day	Due to unavailability of literature, the value was adopted from the information on calves.	
1	Chicken	Number of	• 10 dead	• Educated guess by DRAWG	

0		dead flies consumed by chicken	flies per chicken per day	• For evaluation it should be calculated how many flies a chicken must eat in order to reach the trigger value of 0.004 mg/kg. To evaluate the result of this calculation a default value of 10 flies per chicken and day was considered reasonable based on expert judgement. Based on information on stable dimensions in the ESD for veterinary hygiene biocidal products this would refer to about 70 flies/m^2 (10000 laying hen on litter floor, total floor area 1430 m^2) or 180 flies/m^2 (20000 broiler chickens on litter floor, total floor area 1110 m^2).	
11	Chicken	Biocidal product consumption by flies	• Average body weight of fly: 10-12 mg • Sucrose intake 2.5-3.5 mg per fly per day	• Flies cover all other insects that may possibly be the target of biocidal products. • It appears that biocidal product uptake for 24 hours seems a realistic scenario. • It is reasonable to assume that daily biocidal product intake by the fly does not exceed daily sucrose intake.	• T. Michael Cooper, Robin J. Mockett, Barbara H. Sohal, Rajindar S. Sohal, and William C. Orr, Effect of caloric restriction on life span of the housefly, Musca domestica. The FASEB Journal express article10.1096/fj.03-1464fje. Published online August 19, 2004. http://www.fasebj.org/content/early/2004/10/02/fj.03-1464fje.full.pdf
12	Chicken	Floor area covered by animals	• 50%	• See also Example 1.2	
13	Horse, goat, rabbit	Amount of wood consumed	• Horse: no default set • Rabbit <1.25 g/d • Goat: no default set	• Horses: Stereotypic behaviour of wood chewing develops at a higher rate in horses kept in barns and stables, however horses generally do not swallow the wood.. • Rabbit: <0.5% of the total feed intake (considering default feed intake this is < 1.25 g per day) Normal browsing behaviour of goats includes oral investigation of everything in their environment. Goats chew on pen partitions or other structures made of wood; they will chew on almost everything if the goat considers it	• Horse Broom D.M. and Fraser, A.F., Domestic animal behaviour and welfare, 4th Edition, CAB International, Cambridge, UK, 2007; ISBN-13: 978-1845932879; p. 236 mentions 'wood consumption by wood chewer (horse) of 0.5 kg of wood per day from edges of stalls' but this figure is not supported by experimental data. Wood chewing by stabled horses: diurnal pattern and effects of exercise. W.E. Krak, H.W. Gonyou and L.M.Lawrence; J. Anim. Sci.; 1991, 69, p. 1053-1058. Highest reported values in the study are $1.9x10^{-5}$ m^3 and 9.8 g per day (the results are not consistent).

				palatable.	• Rabbit: Jordan, D; Gorjanc, G; Kermauner, A; Stuhec, I., Wooden Sticks as Environmental Enrichment: Effect on Fattening and Carcass Traits of Individually Housed Growing Rabbits; World Rabbit Science, 2008,16 (4):237-243, • Goat Papachristou, T.G.; Dziba, L.E.; Provenza, F.D. ,Foraging ecology of goats and sheep on wooded rangelands, Small Ruminant Research 59 (2005) , n.2-3, 141–156 Mary C. Smith & David M. Sherman, Goat medicine, 2nd Ed., 2009 Blackwell Publishing, USA. ISBN:978-0-781-79643-9
14	/	Extraction from wood	• 100%	• Option for refinement if sufficiently justified	
15	/	Maximum absorption of biocidal product into treated wood	• Treatment with double vacuum pressure: 50L/m^3 (amount in outer 1 cm layer of wood) • Treatment by dipping: 0.05 L/m^2 (amount in outer 1 cm layer of wood)		Biocides Human Health Exposure Methodology, Wood preservatives, Page 47: "In vacuum-pressure processes, wood absorbs 150 litres of preservative solution per m^3. In double vacuum processes, wood absorbs 10 to 50 litres of preservative solution per m^3. In pressure processes, wood absorbs around 300 litres per m^3. For dipping etc., wood appears to absorb 0.2 litres per 4 m^2 fence panel." https://echa.europa.eu/es/about-us/who-we-are/biocidal-products-committee/working-groups/human-exposure
16	/	Density of wood	0.4 g/cm^3		Technical Agreements for Biocides (TAB) version 1.2 (Dec 2016)
17	/	Conversion of amount of active substance	• Thickness of layer "representing" one	• rough conversion calculation based on the assumption that a layer of 0.05 mm thickness is negligible and represents the amount of substance per square meter	

		per cubic meter to a.s. per square meter	square meter: 0.05 mm	$c_{square} = c_{cubic} \times Th_{layer}$ C_{cubic}: Amount of substance per cubic meter of wood (mg/m^3) c_{square} Amount of substance per square meter of wooden wall (mg/m^2) Th_{layer} Thickness of layer "representing" one square meter (m)	
18	/	Emission factors for spraying	• Fraction emitted to floor during air space spray treatment: 0.96 • Fraction emitted to floor during surface treatment by spraying: 0.11 • Fraction emitted to the treated surface during surface treatment by spraying: 0.85		• OECD Series on Emission Scenario Documents Number 18; Emission Scenario Document for insecticides, acaricides and products to control other arthropods for household and professional uses, ENV/JM/MONO(2008)14, 17th July 2008 Table 3.3.-5 Review of the different emission factors for unspecified mode of spraying,
1	/	Dislodgeabl	• 100%	• Option for refinement if sufficiently justified	≠

9		e residue			
20	/	Amount of product hitting animals during treatment	Values to be applied in the formulas: • Available from description of intended use • Available from Tables 1, 2 and 3 • Thickness of layer of product in contact with skin (default 0.01 cm in TNsG on Human Exposure)	• For inhalation exposure apply equations given in the TNsG on human exposure: $C_{inh} = \frac{Q_{prod} \times Fc_{prod}}{V_{room}}$ $A_{inh} = \frac{F_{resp} \times C_{inh} \times Q_{inh} \times T_{contact}}{BW} \times N_{event}$ C_{inh} Average concentration in inhaled air (mg/m^3) Q_{prod} Amount of undiluted product used (mg) Fc_{prod} Weight fraction of active substance in the product V_{room} Volume of the room (m^3) A_{inh} Amount of active substance inhaled/respired (mg/kg bw/d) F_{resp} Inhalable or respirable fraction of product (default 1) Q_{inh} Ventilation rate of –animal (m^3/hour) $T_{contact}$ Duration of exposure (hours) BW body weight (kg) N_{event} Number of events (usually per day) • For dermal exposure also equations are available in the TNsG on Human Exposure: $C_{der} = \frac{C_{Prod}}{D} = \frac{Q_{Prod} \times Fc_{Prod}}{V_{Prod} \times D}$ $A_{der} = C_{der} \times V_{appl} = C_{der} \times TH_{der} \times AREA_{der}$	Biocides Human Health Exposure Methodology https://echa.europa.eu/es/about-us/who-we-are/biocidal-products-committee/working-groups/human-exposure • OECD Emission Scenario Document for insecticides, acaricides and products to control other arthropods for household and professional uses, Table 3.3.-5, ENV/JM/MONO(2008)14, 17th July 2008

				C_{der} Average skin concentration of active substance in product on skin (mg/cm^3) C_{Prod} Average concentration of substance in undiluted product D Dilution factor (if dilution results in 1% dilution the D is 1/0.01 = 100, default is 1) Q_{Prod} Amount of undiluted product used (mg) Fc_{Prod} Weight fraction of active substance in the product V_{Prod} Volume of undiluted product (cm^3) A_{der} Amount of active substance on skin (mg, mg/event, mg/d, mg/kg) V_{appl} Applied volume of product in contact with skin (cm^3) TH_{der} Thickness of layer of product in contact with skin (cm) $AREA_{der}$ Surface area of exposed skin • During fumigations the applicator and presumably also livestock animals will not be present during application. (see OECD ESD for insecticides, acaricides …)	
21	/	Volatilisation rate	Values to be applied in the formulas: • vp and mw available from dossier	• Saturated vapour concentration model calculates exposure to an active substance volatilised from the treated surfaces. It includes the worst-case assumption that the livestock would be exposed to air containing the active substance at the active substance`s saturated vapour concentration at a specific ambient temperature for 24 hours. Further assumptions: no air changes,	• Saturated vapour concentration HEEG Opinion 13: Assessment of inhalation exposure of volatilised biocide active substance http://echa.europa.eu/documents/10162/19680902/heeg_opinion_13_volatilised_inhalation_exposure_en.pdf

			• Gas constant R=8.31451 J/K*mol • Ambient temperature 298 K (=25°C)	absorption via inhalation 100%: $SVC = \frac{mw[\text{g/mol}] \cdot vp[\text{Pa}]}{R[\text{J mol}^{-1}\ \text{K}^{-1}] \cdot T[\text{K}]} = 0.41 \cdot mw \cdot vp$ [mg/m³] *SVC* Saturated vapour concentration (mg as/m³) *vp* Vapour pressure of active substance (Pa) *mw* Molecular weight (g/mol) *R* Gas constant (J/K*mol) *T* Ambient temperature (K)	• Additional formulas for more refined calculations of air concentrations of an active substance can be found in ConsExpo RIVM report 320104004/2005. ConsExpo 4.0 Consumer Exposure and Uptake Models Program Manual J.E. Delmaar, M.V.D.Z. Park, J.G.M. van Engelen (http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp.)
22	/	Skin area exposed to hoof bath		Dairy cow: 1590 cm² The exposed skin area is estimated from the depth of the hoof bath, the height to which splashing occurs and the diameter of the hoof. Height to which splashing occurs = 30 cm Diameter of hoof = 15 cm To calculate the area of exposed hoof/skin, we assume hoof and leg to be of cylindrical shape: 2πrh + πr² = (2π x 7.5cm x 30 cm) + π x (7.5 cm)² = 1413 + 177 = 1590 cm²	Diameter of hoof confirmed by DE veterinary expert
23	/	Thickness of the layer of disinfectant on hoof/skin		0.01 cm, this values is the estimated thickness of the layer of the product for calculation of the human dermal exposure.	ConsExpo 4.1 Consumer Exposure and Uptake Model s and related Cleaning products Fact Sheet (RIVM report 320104003/2006) HEAdhoc recommendation no.13, Exposure Assessmenr of Teat Disinfection Products for Veterinary Hygiene (PT3)

		that could be absorbed			https://echa.europa.eu/documents/10162/21664016/recommendation_13_teat_disinfection_en.pdf/fbeb394b-e74b-685d-c231-5e3a530e311c
24	/	Feed silo sizes and holding capacities		Volume capacity Diameter Height Holding 13.56 m^3 2.55 m 4.30 m 5.7 tons 26.62 m^3 2.55 m 7.80 m 16.0 tons 18.00 m^3 2.30 m 6.95 m 10.8 tons 7.3 m^3 2.00 m 4.85 m 8.3 tons	Information obtained from feed silo suppliers.
25	/	Migration rate to feed	100%	Option for refinement if sufficiently justified	
26	/	Slimicides: loss of a.s. with waste water during paper production	90%	• Default value taken from RIVM/FEI scenario • See also Example 2.4 • As a worst case is it is considered that 10% of the a.s. remains in the paper	Supplement to the methodology for risk evaluation of biocides, Harmonisation of Environmental Emission Scenarios for Slimicides (product type 12), European Commision DG ENV / RIVM, September 2003 Reference 4L1784.A0/R0009/FBA/TL/Nijm http://echa.europa.eu/documents/10162/16908203/pt12_slimicides_en.pdf
27	/	paper mill waste water	5000 m^3	See also Example 2.4	Supplement to the methodology for risk evaluation of biocides, Harmonisation of Environmental Emission Scenarios for Slimicides (product type 12), European Commision DG ENV / RIVM, September 2003 Reference 4L1784.A0/R0009/FBA/TL/Nijm pp. 27, Table 4.1 http://echa.europa.eu/documents/10162/16908203/pt12_slimicides_en.pdf
28					
29	/	daily paper production per mill	200 t/d	See also Example 2.4	Supplement to the methodology for risk evaluation of biocides, Harmonisation of Environmental Emission Scenarios for Slimicides (product type 12), European

					Commision DG ENV / RIVM, September 2003, Reference 4L1784.A0/R0009/FBA/TL/Nijm pp. 51 average is 200 tonnes of paper per day http://echa.europa.eu/documents/10162/16908203/pt12_slimicides_en.pdf
30	/	dry paper weight	600 g/m^2	See also Example 2.4	Supplement to the methodology for risk evaluation of biocides. Emission scenario document for biocides used in paper coating and finishing (Product type 6, 7 & 9). INERIS –DRC-01-25582-ECOT-CTi/VMi-nº01DR0183.doc pp. 3: grammage (i.e. the weight in grams of one square meter of paper) is 25-300 g.m^{-2} for papers 170 – 600 g.m^{-2} for paperboards https://echa.europa.eu/documents/10162/16908203/pt6_pt7_pt9_paper_coating_and_finishing_en.pdf
31	/	packaging surface in contact with 1 kg feed	600 cm^2	See also Example 2.4	EU Notes for Guidance for Food Contact Materials prepared by the European Food Safety Authority Updated on 30/07/2008 http://www.efsa.europa.eu/de/search/doc/21r.pdf A = is area of the food contact material in cm², conventionally set at 600 cm².(pp. 91)
32	/	Fraction of feed (that was packaged in treated cardboard/ paper) consumed by animals	10%	See also Example 2.4	Expert judgement

1
2

Table 6: References and Explanations

No.	Description	Default Values	Background Information Remarks	References
1	**Body weight**	See Table 1	• Relevant body weights are those at slaughter for meat-producing animals and those during milk and egg production. • In EU only young goats are slaughtered. Information on slaughter weights for goats were available from MS: 8-10 kg and 13 kg (NL), 8-12 kg (IT), 13-18 kg (EL). • For lactating goat the value of 70 kg is commonly accepted by EFSA. • For horses the age of slaughter exhibits a range as horses are slaughtered at young and older ages. To account for this, an average slaughter weight for horses was chosen. • For rabbits the slaughter weight in the EU ranges from 1.8 to 3.2 kg, an average value was chosen as default value.	• Beef and dairy cattle, sheep, lamb, breeding and fattening pig, broiler chicken, laying hen, turkey: OECD guidance document on overview of residue chemistry studies, Annex 4, ENV/JM/MONO(2009)31, July 28th 2009 • Calf: Council Regulation (EC) No 1/2005 of 22 December 2004 on the protection of animals during transport and related operations and amending Directive~~s~~ 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97 • Goat: Information provided by MS • Goat kids: Information provided by MS • Horse: Revised guideline on environmental impact assessment for VMPs in support of VICH guidelines GL6 and GL 38, EMEA/CVMP/ERA/418282/2005-Rev.1 • Rabbit: Opinion of the EFSA AHAW Panel, The Impact of the current housing and husbandry systems on the health and welfare of farmed domestic rabbits, Annex to the EFSA Journal (2005) 267, 1-31
2	**Animal height**	See Table 1	• The height of animals is highly variable between breeds of one species. The default values for animal height were estimated based on species commonly kept as food producing species. • Height to withers: The withers is the ridge between the shoulder blades of a four-legged animal. In many species it is the tallest point of the body, and in horses and dogs it is the standard place to measure the animal's height. • For the height to top of head the distance head to withers was estimated and added to the height to the withers. This was not done for pigs as their head is lower than their shoulders or back. • The maximum reaching height considers stretching of animals. For cattle, sheep and horses this has been calculated as the height to the withers plus twice the distance head to withers. For pigs this was calculated	• Cattle, pig, sheep, goat, horse: http://www.ansi.okstate.edu/breeds/cattle/ (visited April 30, 2015) • Pig: Council Regulation (EC) No 1/2005 of 22 December 2004 on the protection of animals during transport and related operations and amending Directives 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97 • Goat: British goat society www.allgoats.com and Information provided by MS • Poultry: Code of Recommendations and Minimum Standards for the Welfare of Animals Transported within New Zealand. Animal Welfare Advisory Committee, Ministry of Agriculture and Fisheries, Wellington, New Zealand. Code of Animal Welfare No. 15. ISBN 0-478-07372-0, ISSN 1171-090X, November 1994 and Amendments to this document from June 1996 • Rabbit: Opinion of the EFSA AHAW Panel, The Impact of the current housing and husbandry systems on the health and

			as the height to the back plus the extra head allowance of 15 cm given in Council Regulation (EC) No 1/2005. For goat the maximum reaching height includes standing on its hind legs, based on information provided by MS this was estimated to be 2m. • For poultry animal height is not needed, for calculations for transport vehicles values from New Zealand reference were applied.	welfare of farmed domestic rabbits, Annex to the EFSA Journal (2005) 267, 1-31
3	**Body surface area** **(BSA)**	See Table 1	Mathematical formulas relating external surface area BSA to total body weight (W) or eviscerated body weight (E): • Pig: BSA (cm^2)= 734 x $W^{0.656}$ • Cattle: BSA (m^2)= 0.14 x $W^{0.57}$ • Sheep: BSA (m^2)= 0.085 x $W^{0.67}$ • Chicken: BSA (cm^2)= 0.67 x E + 536 • Duck: BSA (cm^2)= 0.66 x E + 583 • • Turkey >7 kg: BSA (cm^2)= 0.10 x E + 3025 (applied for default BSA) • All mammals: BSA (m^2)= 0.11 x $W^{0.65}$	Pig: Grommers F.J. et al (1970), Swine-Floor Contact Area as a Function of Body Weight and Posture, J. Anim Sci 31: 1232-1234. https://www.animalsciencepublications.org/publications/jas/pdfs/31/6/JAN0310061232 (visited April 30, 2015) • Cattle, sheep, : Berman, A. (2003), Effects of Body Surface Area Estimates on Predicted Energy requirements and heat Stress, J. Dairy Sci. 86: 3605-3610, http://jds.fass.org/cgi/reprint/86/11/3605 • Chicken, duck, turkey: Thomas (1978), Observations of the relationship between the surface area and weight of eviscerated carcases of chicken, ducks and turkeys, J. Fd.Technol 13:81-86, http://www3.interscience.wiley.com/cgi-bin/fulltext/120060846/PDFSTART (visited April 30, 2015) • All mammals (applied for horse, rabbit): US EPA USEPA (US Environmental Protection Agency). 1993. Wildlife Exposure Factors Handbook. EPA/600/R-93/187. Office of Research and Development, Washington, DC, USA
4	**Body surface area in contact with surface**	30% of total body surface area See Table 1 for values considering the default body	For a fully relaxed pig lying flat on the side 6-16% of total body surface area is in contact with the floor (Grommers et al.). For all animal species a default value of 30% of total body surface area was estimated from the available pig data. This should comprise the fact that animals may lie on both sides.	• Grommers F.J. et al (1970), Swine-Floor Contact Area as a Function of Body Weight and Posture, J. Anim Sci 31: 1232-1234. • EFSA Scientific Report Q-2006-028 (2007), Scientific Report on animal health and welfare aspects of different housing and husbandry systems for adult breeding boars, pregnant, farrowing sows and unweaned piglets, http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178655708740.htm (visited April 30, 2015)

		weight.		
5	**Alveolar ventilation rate (AVR)**	See Table 1 for values considering the default body weight.	A scaling approach for calculation of alveolar ventilation rates in farm animals is proposed. From the listed references the following formulae have been deduced: Resting AVR • Mammals: AVR (ml/mn) = 276 x $bw^{0.78}$ • Birds: AVR (ml/mn) = 92.3 x $bw^{0.735}$ To account for activity, a correction factor of 3 is suggested to arrive at the non-resting alveolar ventilation rate.	• Calder, W. A. (1984). Size, Function and Life History. Harvard University Press, Cambridge, Mass. • Stahl, W. R. (1967). Scaling of respiratory variables in mammals. Am. J. Physiol. 22:453–460. • Lasiewski, R.C., and W.A. Calder. 1971. A preliminary allometric analysis of respiratory variables in resting birds. Resp. Phys. 11:152-166. • Bech C, Johansen K, Maloiy GMO. 1979. Ventilation and expired gas composition in the flamingo (Phoenicopterus ruber) during normal respiration and panting. Physiological Zoology 52(3):313-328. • Dawson, T. J. and Needham, A. D. (1981). Cardiovascular characteristics of two resting marsupials: an insight into the cardio-respiratory allometry of marsupials. J. Comp. Physiol. 145, 95-100. • Brown, R. P., Delp, M. D., Lindstedt, S. L., Rhomberg, L. R., and Beliles, R. P. (1997). Physiological parameter values for physiologically based pharmacokinetic models. Toxicol. Ind. Health 13:407–484. • National Greenhouse Gas Inventory Committee (2007). Australian Methodology for the Estimation of Greenhouse Gas Emissions and Sinks 2006: Agriculture. Department of Climate Change, Australia. ISBN: 978-1-921297-91-5. Glazier DS (2008). Effects of metabolic level on the body size scaling of metabolic rate in birds and mammals. Proc. R. Soc. B 275: 1405–1410. • Weibel ER, Bacigalupe LD, Schmitt B, Hoppeler H (2004). Allometric scaling of maximal metabolic rate in mammals: muscle aerobic capacity as determinant factor. Respiratory Physiology & Neurobiology 140:115–132
6	**Feed intake**	See Table 1 for values considering the default body	Various sources for feed intake of livestock animals are available. The feed intake relates to body weight (and age) of the animals. The ratio dry matter feed intake/body weight gives a stable value and these values are applied as default values: Ruminants and horses: 4% of body weight	• OECD GUIDANCE DOCUMENT ON RESIDUES IN LIVESTOCK, Series on Pesticides No. 73 ENV/JM/MONO(2013)8 • EU Commission guidance document 7031/VI/95 rev. 4, July 22nd 1996, page 4 • Turkey: Nutrient Requirements of Poultry, Subcommittee on Poultry Nutrition, National Research Council, 8th and 9th revised edition, 1984 and 1994, National Academy Press,

		weight.	Pigs: 3% of body weight Poultry (except turkey): 7% of body weight Turkey: 5% of body weight Rabbit: 10% of body weight These values were confirmed by study data available to MS from evaluations of various substances. (Please note that defaults given in the OECD and EU Commission guidance documents (see references) may deviate from the proposed default values agreed by DRAWG for this document.)	Washington, DC • Rabbit: Opinion of the EFSA AHAW Panel, The Impact of the current housing and husbandry systems on the health and welfare of farmed domestic rabbits, Annex to the EFSA Journal (2005) 267, 1-31
7	**Drinking water intake**	See Table 1 for values considering the default body weight.	• For beef cattle, calf, fattening pig, horses and goat default drinking water intake corresponding to 10% of body weight. According to Regulation (EC) No. 1/2005 the minimal water supply during transport should be 10% of animal live weight. • For dairy cattle, breeding pigs, sheep and lamb values as reported in the references were chosen. • For poultry consumption data for animals at age of common slaughter time were chosen • For rabbits the ratio between feed intake and water consumption is about 1:2.	• Dairy cattle, breeding pig, sheep, lamb: Ontario Ministry of Agriculture Food & Rural Affairs, http://www.omafra.gov.on.ca/english/engineer/facts/07-023.htm (visited April 30, 2015) • Chicken, turkey USDA National Agricultural Library http://www.nal.usda.gov/ (visited April 30, 2015) Ontario Ministry of Agriculture Food & Rural Affairs http://www.omafra.gov.on.ca/english/engineer/facts/07-023.htm (visited April 30, 2015) • Beef cattle, calf, slaughter goat, lactating goat, horse: Council Regulation (EC) No 1/2005 of 22 December 2004 on the protection of animals during transport and related operations and amending Directives 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97 • Rabbit: Opinion of the EFSA AHAW Panel, The Impact of the current housing and husbandry systems on the health and welfare of farmed domestic rabbits, Annex to the EFSA Journal (2005) 267, 1-31
8	**Number of animals per stable**	See Table 2	• For rabbits information for cages not for complete stable: 5 rabbits per cage of0.6 m length, 0.4 m width and 0.3 m height.	• Beef and dairy cattle, calf, breeding and fattening pig, broiler chicken, laying hen: OECD Emission Scenario Document for Insecticides for Stables and Manure Storage Systems, ENV/JM/MONO(2006)4, January 25th 2006, table 5.2 • Rabbit: Opinion of the EFSA AHAW Panel, The Impact of the

				current housing and husbandry systems on the health and welfare of farmed domestic rabbits, Annex to the EFSA Journal (2005) 267, 1-31
9	**Floor area per stable**	See Table 2	See Table 5, line 8	See Table 5, line 8
10	**Wall and roof area per stable**	See Table 2	See Table 5, line 8	See Table 5, line 8
11	**Housing volume per stable**	See Table 2	See Table 5, line 8	See Table 5, line 8
12	**Floor area per animal**	See Table 2	Calculated from default values: "floor area per stable" divided by "number of animals per stable"	/
13	**Maximum area within reach of animal**	See Table 2	Calculated from floor area A per animal and maximum reaching height H of animal: • Assuming each animal is kept in a rectangular pen of area A with one side x and another side 2x, pen side x is calculated as $x = \frac{\sqrt{A}}{\sqrt{2}}$ • For the maximum wall area W within reach of an animal it was considered that the animal is standing in a pen with solid walls. The relevant height of the wall is the maximal reaching height H of the animal. For pigs and cattle the wall in the back was not included: $W = 5x \times H$ For horses and calves all four walls were included:	/

			$W = 6x \times H$ For poultry and sheep this parameter is not given as default value. • The overall maximum area within reach of animal (wall+floor) is the sum of floor area plus wall area per animal.	
14	**Exposed feed surface in a trough**	see Table 2	**For cattle and pigs**, the exposed feed surface in a trough equals the inner surface area of a trough. Troughs are empty and uncovered during biocidal treatment. It is assumed that all residues contained on the bottom and the sides of the trough migrate into the next feed batch placed into the troughs after biocidal treatment. In case of direct treatment of troughs, the entire inner surface area of the trough contains residues in the amount of the application rate. In case of treatment of surrounding surfaces, residues equal the amount that drops to the floor (= bottom of trough). Therefore, the exposed feed surface equals the surface area of the bottom of the trough. **For poultry**, the exposed feed surface equals the surface area of the bottom (=top) of the trough. Troughs are filled during biocidal treatment, and the top layer of the feed batch is contaminated directly. To calculate the surface areas, the following assumptions are made: All animals: • Troughs are designed to stretch across the entire width (w) of an animal's pen enclosure. • The depth of a trough is assumed to equal ¼ of the length (¼ l) of an animal's pen enclosure. Cattle and pigs:	

			• Each pen enclosure is assumed to have short sides of length x (width w of animal pen) and long sides of length 2x (length l of animal pen). x can be calculated using the value for the available floor area per animal (A) (for values see Table 2) • The height (h) of a trough is assumed to be 50 cm for cattle and 30 cm for pigs. Poultry: • Each battery cage is assumed to be square-shaped with sides x and to house one chicken. x can be calculated using the value for the available floor area per animal (see Table 2) <u>Calculation of Exposed feed surface FS_{exp} for direct treatment of trough</u> $FS_{\exp} = 0.25A + 2(w \times h + 0.25l \times h)$ $= 0.25A + 3h\frac{\sqrt{A}}{\sqrt{2}}$ <u>Calculation of Exposed feed surface FS_{exp} for treatment of surrounding surfaces</u>: FS_{exp} = w*¼l = ¼ A	
15	**Ventilation of animal housing**	see Table 2 for values considering default body weights or default dimensions of animal	• Default values are based on the publication Seedorf et al. that reports recommendations and actual measurements for livestock buildings in Northern Europe. This reflects the worst-case scenario compared to Southern Europe where ventilation rates would be higher due to hot climate. • The ventilation rate per 500 kg live weight as reported in the publication. • The ventilation rate per animal was calculated based on default body weights. • The air exchanges per hour were calculated based on	• SEEDORF, J., ET AL. (1998): A survey of ventilation rates in livestock buildings in northern Europe. J. agric. Engng Res. 70, 39 – 47

		housing	default dimensions of animal housing.	
16	**Time spent in transport vehicles**	See Table 3	• EC transport requirements are different for short (< 8 hrs) and long (> 8 hrs) journeys. Since the maximum time is spent in a vehicle during long distance transports (> 8 hrs), these seem most relevant for worst case biocide exposure assessment.	• Council Regulation (EC) No 1/2005 of 22 December 2004 on the protection of animals during transport and related operations and amending Directives 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97
17	**Model truck for animal transport**	See Table 3	• Assumed size of model truck for animal transport: 7.0m x 2.5m	• Information obtained from various livestock transport companies
18	**Compartments for animal transport**	See Table 3	• Length and width of compartments were calculated for a model truck of 7.0 m x 2.5 m. • Relevant compartment height was estimated based on information obtained from livestock transporters and recommendations for minimal compartment heights during transport by SCAH, EFSA Panel AHAW and New Zealand Animal Welfare Advisory Committee. • No of animals per compartment was calculated as $n = \frac{l \times b}{f}$ and rounded down to the nearest integer l internal length of a compartment (m) b internal width of a compartment (m) f required floor area per animal during transport (m^2) n number of animals in a compartment	• Information obtained from various livestock transport companies • SCAH report on "The welfare of animals during transport (details for horses, pigs, sheep and cattle)", March 11th 2002, https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scah_out71_en.pdf • EFSA Panel AHAW Scientific Opinion related to the Welfare of Animals during Transport, EFSA Journal 2004; 44, 1-36 • EFSA Panel AHAW Scientific Opinion Concerning the Welfare of Animals during Transport, EFSA Journal 2011; 9(1): 1966 • Code of Recommendations and Minimum Standards for the Welfare of Animals Transported within New Zealand. Animal Welfare Advisory Committee, Ministry of Agriculture and Fisheries, Wellington, New Zealand. Code of Animal Welfare No. 15. ISBN 0-478-07372-0, ISSN 1171-090X, November 1994 and Amendments to this document from June 1996
19	**Required floor area per animal during transport**	See Table 3	• Default values (A) as given in Regulation (EC) No 1/2005 or calculated based on default body weights (bw) applying formulas given in the SCAH report. Cattle, calf, lamb $A = 0.021\ bw^{0.67}$ Pigs	• Council Regulation (EC) No 1/2005 of 22 December 2004 on the protection of animals during transport and related operations and amending Directives 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97 • SCAH report on "The welfare of animals during transport (details for horses, pigs, sheep and cattle)", March 11th 2002, https://ec.europa.eu/food/sites/food/files/safety/docs/sci-

			A = 0.0192 $bw^{0.67}$ Lactating goat A = 0.031 $bw^{0.67}$ Sheep, slaughter goat A = 0.026 $bw^{0.67}$ Chicken A = 0.016 bw Turkey A = 0.0105 bw Horse See Council Regulation No 1/2005	com_scah_out71_en.pdf (visited April 30, 2015) • EFSA Panel AHAW Scientific Opinion related to the Welfare of Animals during Transport, EFSA Journal 2004; 44, 1-36 • EFSA Panel AHAW Scientific Opinion Concerning the Welfare of Animals during Transport, EFSA Journal 2011; 9(1): 1966
20	**Available wall+floor area per animal during transport**	See Table 3	• Default values calculated from length, width and relevant compartment height. $wf = \frac{F+W}{n}$ $= \frac{(l \times b) + 2(l \times r) + 2(b \times r)}{n}$ wf available wall+floor area in a compartment (m^2/animal) l internal length of a compartment (m) b internal width of a compartment (m) r relevant compartment height (m) F available floor area in a compartment (m^2) W available wall area in a compartment (m^2)	/

			n number of animals in a compartment Animals have only access to the walls and floors of their compartment. Available wall areas are calculated based on the assumption that the surface area is solid. This is generally not the case. Walls for larger livestock have metal bars. Therefore surface areas for walls are overestimated. However, since floors have ribbed surfaces, surfaces areas for floors are underestimated. Poultry are kept in cages. Surface areas (wall, floor) are overestimated.	
21	**Available volume per animal during transport**	See Table 3	• Default values calculated as $v = \frac{V}{N}$ $= \frac{L \times B \times H}{N}$ $= \frac{7.0m \times 2.5m \times (c \times h)}{c \times d \times n}$ v available volume per animal (m^3) V available volume in a truck (m^3) n number of animals in a compartment (default see table 3) N total number of animals in a truck c number of floors in a truck (default see table 3) d number of compartments per floor (default see table 3) L internal truck length (m) (default 7.0 m) B internal truck width (m) (default 2.5 m)	/

			R internal truck height (m) l internal compartment length (m) b internal compartment width (m) h internal compartment height (m) • Very worst-case calculation Division of the truck floor in compartments does not influence the available volume in a truck, but may influence the maximum number of animals within a truck.	
22	**Ventilation during transport**	See Table 3	Forced ventilation systems are required for very long transport duration (e.g. 14 hrs transport – 1hr rest – 14 hrs transport -24 hrs rest).	• Council Regulation (EC) No 1/2005 of 22 December 2004 on the protection of animals during transport and related operations and amending Directives 64/432/EEC and 93/119/EC and Regulation (EC) No 1255/97

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Appendix 6-2: Information provided by the Applicant and from other Regulatory Areas

Table 7: Information to be provided by the Applicant

Information relating to the intended use
- target animals - application method - frequency of treatments - application rate - re-entry period if animals are not present during treatment - concentration of active substance in product and in in-use product (e.g. in the spray formulation) - detailed description of areas to be treated (e.g. floors, walls, specified equipment, spot treatment) - product formulation It should be clearly specified in the intended use description provided by the Applicant whether every treatment is performed with the same application rate or if refresher treatments subsequent to the initial treatment are applied at a different rate.
Information relating to the active substance
- physico-chemical properties - degradation/volatilisation rate (environmental part of the dossier)

Table 8: Information on risk assessment from other regulatory areas

PPP	
EU Pesticide database	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN
RMS Assessment Reports submitted for the EU peer review of active substances used in plant protection products	http://dar.efsa.europa.eu/dar-web/provision
JMPR Reports	http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmpr/jmpr-rep/en/
VMP	
EMEA Summary Reports/ Summary Opinions	http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/ vet_mrl_search.jsp&mid=WC0b01ac058006488e
JECFA Reports	http://apps.who.int/food-additives-contaminants-jecfa-database/search.aspx
Food and feed additives	
EFSA: Evaluations of the Panel on food additives and nutrient sources added to food (ANS)	http://www.efsa.europa.eu/en/applications/foodingredients/regulationsandguidance
EFSA: Evaluations of the Panel on food contact materials, enzymes, flavourings and	http://www.efsa.europa.eu/en/applications/foodcontactmaterials/regulationsandguidance

processing aids (CEF)	
EFSA: Evaluations of the FEEDAP Panel (Additives and products or substances used in animal feed)	http://www.efsa.europa.eu/en/applications/feedadditives/regulationsandguidance
JECFA Reports	http://apps.who.int/food-additives-contaminants-jecfa-database/search.aspx

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References:

NOTE FOR CA CONSULTATION

The references have been deleted.. If any new references are added, these will be incorporated into the main list of references at the end of the consultation.

Annex A: Substances of Concern – Proposed Human Health (Toxicology) Assessment Scheme for Authorisation of Biocidal Products

NOTE FOR CA CONSULTATION

Annex A is available in the current published guidance document:
https://echa.europa.eu/documents/10162/23036412/biocides_guidance_human_health_ra_iii_part_bc_en.pdf/30d53d7d-9723-7db4-357a-ca68739f5094

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