



Australian Government

**Australian Pesticides and
Veterinary Medicines Authority**



Acute reference doses (ARfD) for agricultural and veterinary chemicals used in food producing crops or animals

Edition 1/2024

Current as of 31 March 2024

© Australian Pesticides and Veterinary Medicines Authority 2024

ISSN 1446-1412 (electronic)

This work is copyright. You may download, display, print and reproduce the whole or part of this work in unaltered form for your own personal use or, if you are part of an organisation, for internal use within your organisation, but only if you or your organisation do not use the reproduction for any commercial purpose and retain this copyright notice and all disclaimer notices as part of that reproduction. Apart from rights to use as permitted by the *Copyright Act 1968* or allowed by this copyright notice, all other rights are reserved and you are not allowed to reproduce the whole or any part of this work in any way (electronic or otherwise) without first being given the specific written permission from the Commonwealth to do so.

This document includes some recommendations made by the Office of Chemical Safety (OCS).

Comments and enquiries regarding copyright:

Assistant Director, Communications
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262
Sydney NSW 2001 Australia

Telephone: +61 2 6770 2300

Email: communications@apvma.gov.au.

This publication is available from the [APVMA website](#).

Contents

Introduction	1
ARfD list	2

List of tables

Table 1: ARfD list	2
--------------------	---

Introduction

The Acute reference doses for agricultural and veterinary chemicals (ARfD list) provides a tabulation of acute reference doses (ARfDs; in units of mg/kg bodyweight) for each agricultural or veterinary (agvet) chemical listed.

The **'Study' column** provides information about the pivotal study, including type, the NOAEL (no-observed-adverse-effect level) and the critical toxicological endpoint. For some agvet chemicals, longer-term rather than acute dosing studies have been used to establish the ARfD. In these cases, the NOAEL was selected on the basis of toxicological effects observed after the first dose.

The **'Comments' column** may:

1. provide additional information about its applicability to the general population
2. advise that an ARfD is not necessary
3. indicate that the ARfD has been adopted from that established by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR).

The **'Date' column** indicates when particular ARfDs were established.

ARfD list

Table 1: ARfD list

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
A					
Abamectin (sum of abamectin + 8,9-Z Isomer)	0.002	0.25	6 August 2018	Based on the overall NOAEL of 0.25 mg/kg bw/d for clinical signs in dogs (mydriasis) observed in the first week of treatment at 0.5 mg/kg bw/d.	<p>A total uncertainty factor of 100 has been applied. The ARfD also applies to the 8,9-Z isomer of avermectin B_{1a} and 24-hydroxymethyl abamectin.</p> <p>The 24-hydroxymethyl metabolite of abamectin is regarded as having no greater toxicity than the parent molecule.</p>
Acephate	0.1	≥ 1.2	2005	Single dose study in humans. No inhibition of erythrocyte acetylcholinesterase activity was reported in either sex at any dose. No clinically significant changes were seen in vital signs or on electrocardiography, haematology, clinical chemistry, urine analysis or physical examination. The NOAEL was 1.2 mg/kg bw, the highest dose tested.	<p>The critical toxicological effect of acephate is the inhibition of acetylcholinesterase activity in the nervous system, an effect that is dependent on C_{max} rather than on the area under the curve (AUC).</p> <p>Data on inhibition in vitro indicate that human brain acetylcholinesterase is slightly less sensitive to inhibition by acephate than is rat brain acetylcholinesterase. Well conducted toxicokinetics studies, available for both rats and humans, show that there is no significant difference between the 2 species; in particular, C_{max} values have the same relationship to administered dose in the 2 species, and acephate is rapidly absorbed and eliminated in both species.</p>

3 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
					<p>Data for rats in vivo indicate that inhibition of brain acetylcholinesterase activity occurs at lower doses than those required for a similar level of inhibition of erythrocyte acetylcholinesterase activity.</p> <p>Data for dogs and monkeys in vivo indicate that brain and erythrocyte acetylcholinesterase activities are nearly equally inhibited at any given dose, and do not show the difference seen in rats, which might thus be rat-specific.</p> <p>Well-conducted single – and repeated-dose studies in humans clearly demonstrated a dose where no inhibition of blood cholinesterase activities occurred. Data from animals in vivo do not show sex differences in inhibition of acetylcholinesterase activity or clinical signs.</p> <p>Since there is no interspecies extrapolation, an overall safety factor of 10 was used.</p>
Acequinocyl	0.08	8	13 January 2021	Rat mechanistic studies; single oral dose produced effects on blood coagulation (increases in prothrombin and activated partial thromboplastin time) at higher doses.	
Acetamiprid	0.1	10	27 July 2001	Single dose gavage neurotoxicity rat study; a NOAEL of 10 mg/kg bw was based on reductions in locomotor activity at the next higher dose.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Acibenzolar-S-methyl	0.01	10 [LOAEL]	23 April 2002	Developmental rat study; based on haemorrhagic discharge in dams at LOAEL of 10 mg/kg bw/d.	
Aclonifen			24 November 2020		ARfD considered to be unnecessary due to its low acute toxicity, the lack of evidence for any acute neurotoxicity and the absence of any other toxicologically relevant effect that might be attributable to a single dose.
Afidopyropen	0.3	30	27 November 2017	Developmental rabbit studies; an overall NOAEL of 30 to 32 mg/kg bw/d was based on inappetence observed at the next higher dose.	ARfD for afidopyropen applies to the general population.
Aldicarb	0.001	0.01	15 December 1999	Human acute study; a NOAEL of 0.01 mg/kg bw was based on significant and dose-related RBC AChE inhibition at the next higher dose.	
Ametoctradin			1 February 2012		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Amicarbazone	0.1	10	9 June 2006	Acute neurotoxicity study; a NOAEL of 10 mg/kg bw was based on clinical signs of neurotoxicity at the next higher dose.	
Aminocyclopyrachlor			09 September 2022		ARfD considered to be unnecessary due to its low acute toxicity, the lack of evidence for any acute neurotoxicity and the absence

5 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
					of any other toxicologically relevant effect that might be attributable to a single dose.
Aminopyralid			10 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Amisulbrom			14 June 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Atrazine			5 December 2000		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Aureobasidium pullulans			21 February 2017		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Azafenidin	0.016	16	4 July 2001	Developmental rat study; a NOAEL of 16 mg/kg bw/d was based on increased incidence of resorptions (predominantly early) at the next higher dose.	ARfD for azafenidin only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Azimsulfuron			10 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Azinphos-methyl	0.075	0.75	5 December 2000	Acute human study; a NOAEL of 0.75 mg/kg bw was based on the	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				absence of RBC ChE inhibition or clinical signs.	
Azoxystrobin			21 April 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
B					
Bacillus amyloliquefaciens			9 May 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Bacillus licheniformis			9 May 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Bacillus sphaericus strain 2362			9 May 2003		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Bacillus subtilis (see Bacillus amyloliquefaciens)					
Bacillus thuringiensis			6 September 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally

7 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
					occurring background levels of the organism.
Bacillus thuringiensis subsp. thuringiensis serotype 1 (strain MPPL 002)			28 August 2003		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Beauveria bassiana			8 August 2017		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Bentazone			21 April 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Benzovindiflupyr	0.1	10	23 July 2018	Clinical observations, (decreased locomotor activity at 1 hour post-dosing and reduced forelimb grip strength in females at 1 hour post-dosing).	
Benzylpenicillin procaine			10 October 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Bicyclopyrone	0.01	1	10 January 2017	Developmental rabbit study; a NOAEL of 1 mg/kg bw/d was based on increased incidence of urogenital	ARfD for bicyclopyrone only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				malformations along with skeletal variations at the next higher dose.	
Bifenazate			10 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Bitertanol			21 April 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Bixafen	0.2	20	18 January 2016	Developmental rat study; a NOAEL of 20 mg/kg bw/d was based on reduced body weight gain in dams and foetuses at the next higher dose.	
Bixlozone			06 April 2020		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity or neurological effects after a single dose..
Boscalid			10 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Broflanilide			15 September 2023		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Bromide			10 October 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

9 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Bromoxynil	0.05	5	07 May 2021	Developmental rat study; a NOAEL of 5 mg/kg bw/d was based on reduced numbers of live fetuses, foetal weight, increased late uterine deaths and decreased maternal body weight, along with microphthalmia and minor skeletal variations at maternotoxic doses.	The ARfD applies to bromoxynil and its esters, expressed as bromoxynil phenol equivalents. ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Bupivacaine			17 February 2017		There was insufficient information to establish an ARfD, however, based on its proposed pattern of use the dietary intake is likely to be low.
Buprofezin	0.5	50	31 October 2006	Developmental rabbit study; a NOAEL of 50 mg/kg bw/d was based on bodyweight loss at the next higher dose.	
Butafenacil			19 November 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
C					
Captan	0.1	10	18 May 2007	Developmental rabbit study; a NOAEL of 10 mg/kg bw/d was based on reduced maternal body weight and increased skeletal variations in fetuses at the next higher dose.	ARfD for captan only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Carbaryl	0.01	1	13 December 2002	Subchronic neurotoxicity rat study; a NOAEL of 1 mg/kg bw/d was based	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				on behavioural indications of autonomic neurotoxicity and reduced brain, plasma and RBC ChE activity at the next higher dose.	
Carbendazim	0.05	50 [LOAEL]	15 February 2011	Special acute study in male rats; based on significant testicular and efferent ductal alterations at 50 mg/kg bw, the lowest dose tested.	The ARfD is also supported by an acute in vivo genotoxicity study, with increased frequencies of micronuclei were observed in spermatids at a LOAEL of 50 mg/kg bw.
Carbetamide	0.3	30	1 October 2020	90-day and 1-year dog studies; a NOAEL of 30 mg/kg bw/d was based on the observation of clinical signs of neurotoxicity including unsteady gait, drowsiness and tremor which were manifest early in the studies and may occur after acute exposures.	
Ceftiofur (as free acids and salts)			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Cephalexin			22 November 2000		ARfD is considered to be unnecessary; therapeutic dose for adults ranges between 1 to 4 g/day.
Cetrimide			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Chlorantraniliprole			9 May 2008		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

11 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Chlorfenvinphos	0.02	1.9	5 December 2000	14-day mouse study; a NOAEL of 1.9 mg/kg bw/d was based on inhibition of RBC ChE activity at the next higher dose.	
Chlormequat	0.07	7.5	23 June 2005	2-year dietary dog study; a NOAEL of 7.5 mg/kg bw/d was based on excessive salivation and muscle weakness observed after a single dose.	
Chloropicrin			16 January 2014		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Chlorpyrifos	0.03	1	June 2019	Based on the no observed effect level of 1 mg/kg bw for inhibition of erythrocyte (acetyl) cholinesterase human males and incorporates a total uncertainty factor of 30.	Selected NOAEL is sufficiently protective against inhibition of brain cholinesterase and other effects of chlorpyrifos. (APVMA Reconsideration of chlorpyrifos - Toxicology update - June 2019)
Chlorpyrifos-methyl	0.03	1	13 July 2023	Based on the no observed effect level of 1 mg chlorpyrifos/kg bw for inhibition of erythrocyte (acetyl) cholinesterase human males and incorporates a total uncertainty factor of 30.	Based on read-across from chlorpyrifos due to a lack of chlorpyrifos-methyl specific data.
Cinmethylin	0.3	30	20 August 2003	Developmental rat study; a NOAEL of 30 mg/kg bw/d was based on clinical signs (excess salivation and urine	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				stained abdominal fur) at the next higher dose.	
Clethodim			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Clofentezine			31 December 2019		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Clitoria ternatea			23 November 2015		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
d-Cloprostenol			21 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Cloquintocet acid			5 July 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Clothianidin	0.2	25	1 August 2003	Acute neurotoxicity mouse study; a NOAEL of 25 mg/kg bw was based on clinical signs (reduced spontaneous activity) at the next higher dose.	

13 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Codling Moth Granulosis Virus			25 November 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Cyantraniliprole			21 January 2013		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Cyazofamid			6 June 2013		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Cyclaniliprole			29 February 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Cyflufenamid			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Cyflumetofen			31 January 2022		ARfD is considered to be unnecessary due to its low oral toxicity and the absence of any neurological effects or developmental toxicity after a single dose.
Cyhalofop-butyl			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
γ -Cyhalothrin (purified 1R, 3R, α S isomer)	0.01	0.5	31 October 2023	Combined NOAEL	A combined NOAEL was derived from the \pm λ -cyhalothrin acute neurotoxicity study in rats and neurotoxicity in repeat-dose studies with cyhalothrin and λ -cyhalothrin in dogs treated orally, in which the first week of dosing and typically within a few hours after each dose (consistent with a C_{\max} driven effect). A total uncertainty factor of 25 was used because \pm λ -cyhalothrin is rapidly absorbed and excreted and its neurotoxic effects are C_{\max} dependent. A relative potency factor of 2 for γ -cyhalothrin compared with \pm λ -cyhalothrin has been applied.
\pm λ -cyhalothrin (combination of the 1S, 3S, α R and 1R, 3R, α S isomers)	0.02	0.5	31 October 2023	Combined NOAEL	A combined NOAEL was derived from the \pm λ -cyhalothrin acute neurotoxicity study in rats and neurotoxicity in repeat-dose studies with cyhalothrin and λ -cyhalothrin in dogs treated orally, in which the first week of dosing and typically within a few hours after each dose (consistent with a C_{\max} driven effect). A total uncertainty factor of 25 was used because \pm λ -cyhalothrin is rapidly absorbed and excreted and its neurotoxic effects are C_{\max} dependent.
β -Cypermethrin	0.05	4.7	19 March 2002	3-month feeding dog study; a NOAEL of 4.7 mg/kg bw/d was based on clinical signs (whole body tremors, head nodding, 'lip-licking', subduedness, ataxia, agitation and a	

15 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				high-stepping gait) at the next higher dose.	
D					
Decoquate			4 June 2013		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Derquantel	0.01	1	27 May 2011	Acute neurotoxicity dog study; a NOAEL of 1 mg/kg bw was based on clinical signs (mydriasis, ptosis, dry eyes) at the next higher dose.	
Dexamethasone			10 October 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Diazinon	0.01	0.2	20 December 2002	Acute dose human volunteer study; a NOAEL of 0.2 mg/kg bw was based on RBC ChE inhibition at the next higher dose.	
2,6 dichlorobenzamide (BAM)	0.13	12.5	14 February 2023	8-day oral (gavage) toxicity study oral (gavage) toxicity study in rats; a NOAEL of 12.5 mg/kg bw/d was based on the occurrence of adverse clinical signs (impaired righting reflex, miosis, hypothermia, moderate analgesia and rapid but	An important plant metabolite common to dichlobenil and fluopicolide. ARfD for 2,6 dichlorobenzamide (BAM) applies to the general population.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				shallow breathing) at the next higher dose.	
2,4-dichlorophenoxyacetic acid (2,4-D)	0.8	75	12 September 2006	Acute neurotoxicity rat study; a NOAEL of 75 mg/kg bw was based on gait/coordination effects and decreased motor activity at the next higher dose.	
Dichlorprop-P			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Dichlorvos	0.1	1	6 April 2004	Single oral dose human volunteer study; a NOAEL of 1 mg/kg bw was based on the absence of any reduction in RBC ChE activity at 1 mg/kg bw, the only dose tested.	
Diclazuril			7 October 2021		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any neurological effects or developmental toxicity after a single dose.
Difethialone	0.0005	0.48 [LOAEL]	17 April 2007	Acute oral rat study; a LOAEL of 0.48 mg/kg bw was based on death.	
Diflufenican			May 2020		ARfD considered to be unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose
Dimethenamid-P	0.25	25	12 August 03	Developmental rat study; a NOAEL of 25 mg/kg bw/d was based on signs of	ARfD for dimethenamid-P only applies to women of child-bearing age. An ARfD for

17 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				toxicity in the foetus (reduced bodyweight and incomplete ossification) at the next higher dose.	the general population is considered to be unnecessary. Note: Dimethenamid-P, the S-isomer, and its racemic mixture have equivalent toxicity at similar dose levels.
Dimethoate	0.02	0.2	23 November 2010	Human volunteer study; a NOAEL of 0.2 mg/kg bw/d was based on ChE inhibition in whole blood at the next higher dose.	
Dimethomorph			17 April 2020		ARfD considered unnecessary due to its low oral toxicity and the absence of any neurological effects or developmental toxicity after a single dose
Dimpropyridaz			19 December 2022		ARfD considered unnecessary due to its level acute oral toxicity, lack of acute neurotoxicity, lack of effects on reproduction and development and lack or any effect that would likely occur following a single exposure event.
Dinotefuran	1.25	125	10 August 2015	Developmental rabbit study; a NOAEL of 125 mg/kg bw/d was based on reduced body weight gain at the next higher dose.	
Diphenylamine			21 April 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose. (JMPR–98).

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Diquat ion	0.8	75	15 July 2019	Acute neurotoxicity rat study; a NOAEL of 75 mg/kg bw was based on clinical signs, inappetence and reduced bodyweight gain at the next higher dose.	Consistent with WHO JMPR 2013. To convert from the mass of diquat ion to the mass of diquat dibromide multiply by a factor of 1.867.
Diuron			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Doramectin	0.02	1.5	14 October 2002	Developmental rabbit study; a NOAEL of 1.5 mg/kg bw/d was based on maternal toxicity with major malformations (cleft palate, phocomelia, syndactyly and coelosomia) observed in fetuses at 3 mg/kg bw/d and delayed ossification observed at 1.5 and 3 mg/kg bw/d.	ARfD for doramectin only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
E					
Emamectin benzoate	0.03	5	11 December 2018	Based on acute neurotoxicity in rats (tremors, irritability) at 10 mg/kg bw. Neurobehavioral effects were accompanied by serious histopathological observations of neuronal degeneration in brain and spinal cord as well as effects on sciatic nerves at 25 mg/kg bw.	JMPR 2011. Uncertainty factors applied were 10 for interspecies uncertainties, 10 for intraspecies uncertainties and 2 for severity of effect due to the serious neuropathological effects at 25 mg/kg bw.
Enterococcus faecium			4 September 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are

19 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
					unlikely to be distinguishable from naturally occurring background levels of the organism.
Epoxiconazole	0.2	20	16 April 2002	Developmental rabbit study; a NOAEL of 20 mg/kg bw/d was based on increased incidence of resorptions at the next higher dose.	ARfD for epoxiconazole only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Eprinomectin	0.2	1.5	31 January 2018	Human clinical trial; absence of any effects at the highest tested dose of 1.5 mg/kg bw.	ARfD was based on a clinical trial with ivermectin using a 'read across' approach due to the structural similarity and pharmacokinetic similarities of the 2 avermectin analogues.
Esfenvalerate	0.02	1.75	31 January 2018	Acute neurotoxicity rat study; a NOAEL of 1.75 mg/kg bw was based on clinical signs of neurotoxicity (tremors) at the next higher dose.	
Ethametsulfuron-methyl			17 January 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Ethoxyquin	0.5	50	21 February 2000	Acute oral (capsule) dog study; a NOAEL of 50 mg/kg bw for effects on the hepatic biliary system and clinical signs at the next higher dose.	ARfD for ethoxyquin is based on JMPR evaluation (2005). The ARfD which is applicable for the general population includes 3 residues (MEQ, DHMEQ and DHEQ).
Ethoxysulfuron			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Ethyl formate			26 November 2003		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Etofenprox	1	100	4 December 2017	Developmental rabbit studies; an overall NOAEL of 100 mg/kg bw/d in 2 studies was based on reduced maternal bodyweight and food consumption immediately after dosing and an increased incidence of post-implantation loss at the next higher dose. (JMPR 2011, EFSA 2009)	ARfD for etofenprox only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Etoxazole			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Eugenol			19 August 2020		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
F					
Fenamiphos	0.003	0.25	7 November 2005	Acute oral dog study; a NOAEL of 0.25 mg/kg bw was based on inhibition of RBC ChE activity at the next higher dose.	
Fenbuconazole			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

21 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Fenhexamid			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Fenitrothion	0.03	0.33	5 December 2000	Acute single dose human volunteer study; a NOAEL of 0.33 mg/kg bw was based on the absence of any inhibition of plasma and RBC ChE activity at the highest tested dose.	
Fenpropidin	0.07	7	20 July 2023	Rat developmental neurotoxicity study; a NOAEL of 7 mg/kg bw/d based on decreased female brain weight on PND 72 at the next higher dose. This is supported by a NOAEL of 10 mg/kg bw/d in a rabbit prenatal developmental toxicity study due to the occurrence of decreased male body weight and increased fetal (litter) incidence of malformations (persistent truncus arteriosus, severely malaligned sternbrae) in the presence of substantial maternotoxicity at the next higher dose.	
Fenpyrazamine	0.8	80	15 February 2017	Acute neurotoxicity rat study; a NOAEL of 80 mg/kg bw was based on a reduction in motor activity and number of rearings at the next higher dose.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Fenpyroximate	0.005	0.5	13 June 2023	1-year capsule fed dog study; a NOAEL of 0.5 mg/kg bw/d was based on the occurrence of bradycardia at the next higher dose.	The electrocardiographic effects of fenpyroximate may potentially occur following acute exposure.
Fipronil	0.03	2.5	23 February 2024	Two acute oral neurotoxicity rat studies; a NOAEL of 2.5 mg/kg bw was based on reduced footsplay at the next higher dose, as well as pharmacological studies in mice with a NOAEL of 3 mg/kg bw/d	This is a group ARfD value which includes fipronil, fipronil amide, desulfinyl fipronil, fipronil sulphide and fipronil sulphone.
Flazasulfuron			26 September 2011		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Flonicamid			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Florasulam			26 May 2009		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Florfenicol			4 January 2001		ARfD considered unnecessary due to its low oral toxicity after a single dose; structural analogs of florfenicol have a long history of therapeutic use without acute effects.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Florpyrauxifen-benzyl			8 August 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Florylpicoxamid			16 February 2022		ARfD considered to be unnecessary on the basis of its low acute toxicity, the lack of evidence for any acute neurotoxicity and the absence of any other toxicologically relevant effect that might be attributable to a single dose.
Fluazaindolizine	1.3	125	1 September 2022	Acute oral neurotoxicity rat study; a NOAEL of 125 mg/kg bw was based on inappetence and bodyweight loss at the next higher dose.	This ARfD applies to fluazaindolizine and its metabolites namely IN-A5760, IN-F4106, IN-QEK31, IN-QZY47, IN-TMQ01, IN-UJV12 or IN-UNS90, expressed as fluazaindolizine.
Flubendiamide			14 December 2007		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Fludioxonil			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Fluensulfone	0.15	16.2	12 June 2014	2-Gen reproduction study; a NOAEL of 16.2 mg/kg bw/d based on post-natal loss of pups at the next higher dose.	ARfD for fluensulfone applies to the general population.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Flufenoxuron			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Flumethrin			4 September 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Flumiclorac pentyl			8 December 2004		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Flumioxazin	0.1	10	26 February 2021	Oral rat development study; a NOAEL of 10 mg/kg bw/d based on an increased incidence of cardiovascular abnormalities at the next highest dose.	ARfD for flumioxazin only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Flunixin meglumine	0.02	2	1 August 2002	6-week rat study; a NOAEL of 2 mg/kg bw/d was based clinical signs (reduced activity) at the next higher dose.	
Fluopyram	0.5	50	6 July 2015	Acute neurotoxicity rat study; a NOAEL of 50 mg/kg bw was based on slightly lower motor and locomotor activity at the next higher dose.	
Fluoxapiprolin			23 May 2022		ARfD considered unnecessary, based on the absence of any toxic effects in laboratory animals observed after a single dose.

25 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Flupyradifurone	0.35	35	11 August 2015	Acute neurotoxicity rat study; a NOAEL of 35 mg/kg bw was based on increased incidences of piloerection and increased incidences of pupil dilation at the next higher dose.	
Fluralaner			31 May 2018	ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.	
Flutolanil			28 August 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Fluxapyroxad			20 March 2020		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Fomesafen	1	100	29 March 2021	Rat acute neurotoxicity study; a NOAEL of 100 mg/kg bw based on potential acute neurotoxicity at the next higher dose.	
G					
Gamma-Cyhalothrin				See γ -Cyhalothrin	
Geraniol			19 August 2020		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Glufosinate ammonium			28 August 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Glyphosate			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
H					
Halauxifen-methyl			17 September 2014		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Halofuginone	0.0003	0.025	16 June 2006	Developmental rabbit study; a NOAEL of 0.025 mg/kg bw/d was based on reduced body weight gain and food consumption, mortality and abortions at the next higher dose.	ARfD for halofuginone only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Halsulfuron-methyl	0.5	50	4 February 2022	Developmental rabbit study; a NOAEL of 50 mg/kg bw/d was based on increased number of resorptions (total and per dam and increased post-implantation loss) at the next higher dose.	ARfD for halosulfuron-methyl only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Hexaflumuron			31 August 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Hexythiazox			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
I					
Imazalil	0.05	5	29 January 2007	Developmental rabbit study; a NOAEL of 0.05 mg/kg bw/d was based on increased number of resorptions and a reduced number of live pups at the next higher dose.	ARfD for imazalil only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Imazapic			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Imazapyr			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Imazethapyr			2 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Indaziflam	0.08	7.5	12 May 2023	3-month gavage dog study; a NOAEL of 7.5 mg/kg bw/d was based on degenerative lesions in the spinal cord and sciatic nerve at the next higher dose of 15 mg/kg bw/d.	For dietary risk, indaziflam is the sum of indaziflam and 6-[(1R)-1-fluoroethyl]-1,3,5-triazine-2,4-diamine (=indaziflam-triazinediamine), expressed as indaziflam.
Indoxacarb (S-Isomer) + R-Isomer	0.1	12.5	30 May 2008	Acute neurotoxicity rat study; a NOAEL of 12.5 mg/kg bw was based	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				on reduced bodyweight gain and food consumption at the next higher dose.	
Inpyrfluxam	0.3	30	26 May 2023	Acute neurotoxicity study in rats; a NOAEL of 30 mg/kg bw was based on reduced motor activity (no neuropathology correlates) and body temperature at the next higher dose.	Inpyrfluxam is expressed as inpyrfluxam and gly-CH ₂ OH-S-2840.
Ipconazole			18 January 2010		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Ipflufenquin	1.2	125	10 March 2023	Acute neurotoxicity study in rats; a NOAEL of 125 mg/kg bw was based on the reduction in body temperature and the motor activity ambulation and fine movement observed at the next higher dose.	
Isocycloseram	0.08	7.5	18 November 2021	Developmental rat study; a NOAEL of 7.5 mg/kg bw/d was based on an increased incidence of bifid sternum, which might be attributable to a single exposure at the next higher dose.	
Isofetamid	3	300	9 March 2017	Developmental rabbit study; a NOAEL of 300 mg/kg bw/d is based on reduced maternal bodyweight gain early in gestation at the next higher dose.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Isopyrazam	0.3	30	24 May 2016	Rat acute neurotoxicity study; a NOAEL of 30 mg/kg bw was based on clinical signs of toxicity (weak appearance and decreased activity).	
Isotianil					ARfD considered to be unnecessary due to its low acute toxicity, the lack of evidence for any acute neurotoxicity and the absence of any other toxicologically relevant effect that might be attributable to a single dose.
Isoxaflutole			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Ivermectin	0.2	1.5	31 January 2018	Human clinical trial; absence of any effects at the highest tested dose of 1.5 mg/kg bw.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
K					
Kaolin			5 September 2022		ARfD considered to be unnecessary due to the absence of any systemic exposure following oral, dermal or inhalation exposure. Calcined kaolin is insoluble in all aqueous and organic solvents that are physiologically relevant.
Ketoprofen	0.001	0.1	8 December 2000	Acute pharmacological rabbit study; a NOAEL of 0.1 mg/kg bw was based on inhibition of platelet aggregation at the next higher dose.	
Kresoxim-methyl			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
L					
Lactobacillus acidophilus			4 September 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Lactobacillus brevis			4 September 2002		ARfD unnecessary. Naturally occurring organism – from naturally occurring background levels of the organism.
Lactobacillus casei			4 September 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are

31 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
					unlikely to be distinguishable from naturally occurring background levels of the organism.
Lactobacillus plantarum			4 September 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Lambda-Cyhalothrin				See ± λ-Cyhalothrin	
Lasalocid			19 April 2021		ARfD considered to be unnecessary due to the absence of any neurological effects or development toxicity after a single dose.
Lignocaine hydrochloride monohydrate	0.03		13 June 2023	Human oral pharmaceutical product	Considered to be adequately protective against both local and systemic effects. The point of departure was derived from a short-term human oral over the counter pharmaceutical product. A total UF of 32 was used ($10^{0.5}$ for extrapolation from a LOAEL (pharmaceutical effect) to NOAEL and 10 for intraspecies variability).
d-limonene			04 May 2021		ARfD unnecessary. Naturally occurring compound that is also a food additive - residues from its use are unlikely to be distinguishable from naturally occurring background levels.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Lufenuron			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
M					
Maldison	1.5	15	12 April 2005	Acute oral human study; a NOAEL of 15 mg/kg bw was based on inhibition of RBC and plasma ChE activity at the higher dose.	
Mancozeb	0.3	30	17 February 2023	Developmental rabbit study: a NOAEL of 30 mg/kg bw/d was based on deaths, clinical signs of toxicity and an increased number of abortions observed at the next higher dose.	ARfD for mancozeb only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Mandestrobin			30 March 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Mandipropamid			9 April 2010		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Mecoprop	0.5	50	17 January 2001	Developmental rat study; a NOAEL of 50 mg/kg bw/d was based on embryoletality and foetotoxicity (lower bodyweight and shorter CR length) at the next higher dose.	ARfD for mecoprop only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Mecoprop-p (salts and esters)	0.5	50	25 August 2021	Developmental rat study; a NOAEL of 50 mg/kg bw/d was based on embryoletality and foetotoxicity (lower bodyweight and shorter CR length) at the next higher dose.	ARfD for mecoprop-p only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary. Mecoprop-P (salts and esters) is defined as: The sum of mecoprop-P ((S)-2-(4-chloro-o-tolyloxy)propionic acid), HMCPP ((2S)-2-[4-chloro-2-(hydroxymethyl)phenoxy]propanoic acid; free and conjugated), CCPP (2-[(1S)-1-carboxyethoxy]-5-chlorobenzoic acid) and 4-glucosyl-MPP ((2S)-2-[4-(D-glucopyranosyloxy)-2-methylphenoxy]propanoic acid) expressed as mecoprop-P free acid.
Mefentrifluconazole			27 November 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Melaleuca Oil	10	1000	12 August 2010	Based on an in vivo micronucleus study in mice using a default safety factor of 100.	
Meloxicam	0.004	0.04	4 August 2004	Human clinical trial; a pharmacological NOAEL of 0.04 mg/kg bw/d was based on increased blood pressure, pulse rate and ECG at higher doses.	
Mesosulfuron-methyl			18 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Mesotrione			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Metalaxyl			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Metamitron	0.1	10	4 December 2017	Developmental rat study; a NOAEL of 10 mg/kg bw/d was based on the observation that acute CNS effects, in particular sedation and lower transient body temperature, occurred at doses in excess of 10 mg/kg bw/d. The only identified NOAEL of 10 mg/kg bw/d in the toxicological database was observed in a rat developmental study for reduced bodyweight gain. This NOAEL was selected as the basis of the numerical ARfD (EFSA, 2008).	ARfD for metmitron applies to the general population.
Metazachlor			15 July 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Metcamifen	0.3	30	21 July 2020	Developmental rabbit study; a NOAEL of 30 mg/kg bw/d was based on increased incidence of skeletal and cartilage variants of the vertebrae and ribs, which might be	ARfD for metcamifen only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.

35 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				attributable to a single exposure to metcamifen at higher doses.	
Methamidophos	0.003	0.3	30 January 2004	Acute neurotoxicity rat study; a NOAEL of 0.3 mg/kg bw was based on plasma, RBC and brain ChE inhibition at the next higher dose.	
Methidathion	0.01	1	31 May 2004	Acute neurotoxicity rat study; a NOAEL of 1 mg/kg bw was based on RBC and brain ChE inhibition at the next higher dose.	
Methiocarb	0.005	0.5	4 December 2017	Developmental rat study; a NOAEL of 0.5 mg/kg bw/d was based on clinical signs (muscle fasciculation's) at the next higher dose.	ARfD for methiocarb applies to the general population.
Methomyl	0.02	0.1(H)	5 March 2007	Acute (capsule) human toxicity study; a NOAEL 0.1 mg/kg bw was based on erythrocyte ChE inhibition at the next higher dose.	Source; JMPR 2001.
Methoprene			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Methoxyfenozide			12 January 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
1-Methylcyclopropene			13 December 2023		The establishment of an ARfD for a gas is not appropriate since oral ingestion is not the likely mode of entry into the body.
Metobromuron	0.25	25	20 June 2022	Ten-day rat toxicity study; a NOAEL of 25 mg/kg bw/d was based on an elevated number of blood reticulocytes at the next higher dose.	
Metrafenone			13 April 2010		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Metribuzin			18 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Mevinphos	0.003	0.025	5 December 2000	28-day human volunteer study; a NOAEL of 0.025 mg/kg bw/d was based on inhibition of RBC ChE activity and clinical signs at the next higher dose.	
Milbemectin	0.06	6	29 April 2005	Developmental rat study; a NOAEL of 6 mg/kg bw/d was based on reduced maternal bodyweight gain at the next higher dose.	ARfD for milbemectin only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Molinate	0.002	1.8 [LOAEL]	25 February 2022	Rat development neurotoxicity study; a LOAEL of 1.8 mg/kg bw/d based on the lowest relevant point of departure.	A total safety factor of 1000 is applied (10 for extrapolation from the LOAEL to the NOAEL, 10 for interspecies extrapolation and 10 for intraspecies extrapolation).

37 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Monepantel			31 August 2009		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Moxidectin	0.01	1	28 March 2002	28-day dietary dog study and developmental rabbit study; a NOAEL of 1 mg/kg bw/d was based on neurotoxicity at the next higher dose (in dogs); and maternal toxicity (reduced weight gain) at the next higher dose (in rabbits).	
N					
Nicarbazin			19 April 2021		ARfD considered to be unnecessary due to the absence of any neurological effects or developmental toxicity after a single dose.
Niclosamide			20 September 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Novaluron			17 January 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Nuclear polyhedrosis virus of <i>helicoverpa armigera</i> occlusion bodies			17 December 2003		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
O					
Omethoate	0.003	0.25	20 October 2005	Acute neurotoxicity rat study; a NOAEL of 0.25 mg/kg bw was based on plasma ChE inhibition at the next higher dose.	
O-phenylphenol (see 2-phenylphenol)					
Oxathiapiprolin			30 July 2015		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Oxytetracycline			10 October 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
P					
Paraquat	0.004	0.45	27 June 2003	1-year chronic feeding dog study; a NOAEL of 0.45 mg/kg bw/d was based on the likelihood that the observed pulmonary lesions would also occur after an acute exposure at the next higher dose.	
Penflufen	0.5	50	10 October 2012	Acute neurotoxicity rat study; a NOAEL of 50 mg/kg bw was based on decreased motor and locomotor activity at the next higher dose.	

39 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Phenmedipham			13 April 2011		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
2-Phenylphenol			31 July 2003		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose. (JMPR'99).
Penthiopyrad	1	125	10 February 17	Acute oral neurotoxicity rat study; a NOAEL of 125 mg/kg bw was based on clinical signs (decreased motor activity, decreased body temp, hunched position and unsteady gait) at the next higher dose.	
Pinoxaden	0.3	30	29 August 2005	Developmental toxicity rabbit study; a NOAEL of 30 mg/kg bw/d was based on early resorption, implantation loss, lower number of live births and reduced foetal weight at the next higher dose.	ARfD for pinoxaden only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Piperonyl butoxide			17 February 2020		ARfD considered unnecessary, due to its low oral toxicity and the absence of any neurological effects or developmental toxicity after a single dose.
Polyoxin D zinc salt			8 June 2021		ARfD considered unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Porcine gonadotrophins			25 June 2002		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Procymidone			11 October 2022		ARfD considered unnecessary, on the basis that anti-androgenic effects on development are unlikely to occur following a single exposure incident, and the observed effects in the acute neurotoxicity study do not require the establishment of an ARfD.
Prodiamine			13 October 2021		ARfD for prodiamine is not considered necessary due to its low acute oral toxicity and lack of neurological and development effects after a single dose.
Profoxydim			29 November 2006		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Prohexadione-calcium			18 January 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Propamocarb	2	200	26 November 2015	Acute neurotoxicity rat study; a NOAEL of 200 mg/kg bw was based on a reduced activity 1 h after dosing at the next higher dose.	
Propargite			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Propiconazole	0.3	30	30 August 2018	An ARfD of 0.3mg/kg bw was established based on a NOAEL of 30mg/kg bw/d in a developmental toxicity study in rats and a 100-fold safety factor. The NOAEL was identified on the basis of slight increases in rudimentary ribs and unossified sternebrae at 90mg/kg bw/d. This provides an adequate margin over the maternal toxicity and cleft palate seen at 300mg/kg bw/d. The NOAEL is also adequately protective against any acute local effects on the gastrointestinal tract based on the available data in dogs. Ataxia has also been noted in pregnant rats dosed at 360 mg/kg bw/d.	
Propineb	0.003	0.32	22 February 2017	Developmental rat study; a NOAEL of 0.32 mg/kg bw/d was based on skeletal variations at the next higher dose.	This group ARfD value which includes propineb and propylene thiourea (PTU) only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Propylene oxide	0.4	205	21 April 2006	Inhalation developmental toxicity rat study; a NOAEC of 300 ppm (equivalent to NOAEL of 205 mg/kg bw/d) was based on increased incidence of 7th cervical rib at the next higher dose.	ARfD for propylene oxide only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Propylene thiourea (PTU)	0.003	0.32	22 February 2017		See group ARfD for Propineb.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Propyzamide	0.13	40 [LOAEL]	11 December 2018	Based on a LOAEL of 40 mg/kg bw due to acute, reversible neurotoxicity (increased landing foot splay and decreased motor activity; without detectable neuropathology) in rats at this dose.	The total uncertainty factor applied is 3 for LOAEL to NOAEL extrapolation uncertainties, 10 for interspecies uncertainties and 10 for intraspecies uncertainties.
Proquinazid	1	100	10 February 2017	Acute neurotoxicity rat study; a NOAEL of 100 mg/kg bw was based on reduced motor activity at the next higher dose.	
Prosulfocarb	0.4	40	30 July 2007	Acute neurotoxicity rat study; a NOAEL of 40 mg/kg bw was based on reduced motor activity at the next higher dose.	
Prothioconazole	0.03	3	28 May 2008	Developmental rat study; a NOAEL of 3 mg/kg bw/d was based on increased incidence of 14th rib, increased resorptions and cleft palate at the next higher dose.	ARfD for prothioconazole only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary. Since the residue definition for risk assessment in all commodities is expressed as prothioconazole-desthio and this metabolite is of higher toxicity than the parent, a group ARfD was established to include prothioconazole-desthio.
Pydiflumetofen			21 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Pyraclostrobin	0.05	5	26 June 2008	Developmental rabbit study; a NOAEL of 5 mg/kg bw/d was based	ARfD for pyraclostrobin only applies to women of child-bearing age. An ARfD for

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				on early resorptions at the next higher dose.	the general population is considered to be unnecessary.
Pyraflufen-ethyl	0.2	20	17 December 2004	Developmental rabbit study; a NOAEL of 20 mg/kg bw/d was based on increased maternal mortality and morbidity at the next higher dose.	
Pyrasulfotole	0.2	200 [LOAEL]	20 August 2008	Acute neurotoxicity rat study; based on decreased motor and locomotor activity at a LOAEL of 200 mg/kg bw.	
Pyrethrins	0.2	20	31 July 2003	Acute neurotoxicity rat study; a NOAEL of 20 mg/kg bw was based on neurotoxicity observed at the next higher dose.	Adopted from JMPR '99.
Pyridalyl			29 April 2004		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Pyridate	2	177	12 June 2020	Based on an acute neurotoxicity study in rats. Death occurred within 1 day after dosing at the next higher dose of 500 mg/kg bw.	The ARfD applies to pyridate, pyridafol and pyridafol-N-glucoside expressed as pyridate. Adopted from JMPR (2019).
Pyrimethanil			10 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Pyriofenone			26 November 2014		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Pyroxasulfone			27 June 2013		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Pyroxsulam			14 April 2008		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Q					
Quinclorac	2	200	13 September 2004	Acute oral toxicity gavage mouse study; a NOAEL of 200 mg/kg bw was based on clinical signs at the next higher dose.	
Quinoxifen			15 January 2002		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
R					
Ractopamine hydrochloride	0.001	0.13	30 July 2002	Human study; a NOAEL of 0.13 mg/kg bw was based on increased heart rate at the next higher dose.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
S					
Saccharomyces cerevisiae			4 September 2002		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Saflufenacil	0.05	5	13 February 2017	Developmental rat study; a NOAEL of 5 mg/kg bw/d was based on an increased incidence of bent scapula and wavy ribs in the absence of maternal toxicity at the next higher dose.	ARfD for saflufenacil only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.
Sedaxane			24 April 2011		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Spinetoram			5 May 2008		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Spinosad			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Spirotetramat	1	100	26 May 2008	Acute neurotoxicity rat study; a NOAEL of 100 mg/kg bw was based on clinical signs and decreased motor activity at the next higher dose.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Spiroxamine	0.2	20	2 July 2001	Acute neurotoxicity rat study; a NOAEL of 20 mg/kg bw was based on decrease in landing footsplay at the next higher dose.	
Streptomyces lydicus			7 June 2016		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Sulfoxaflor	0.25	25	27 June 2013	Acute oral neurotoxicity rat study; a NOAEL of 25 mg/kg bw was based on decreased motor activity at the next higher dose.	
Sulfuryl Fluoride	0.3	31	24 August 2006	Acute inhalational neurotoxicity rat study; a NOAEL of 31 mg/kg bw(300 ppm) was based on the absence of any observed effects at the highest tested concentration of 300 ppm.	
T					
Tebuconazole	0.1	10	10 February 2023	Rabbit pre-natal developmental toxicity study; a NOAEL of 10 mg/kg bw/d due to the presence of disordered development (increased incidence of embryonic resorptions, abdominal fissures, and incidence of	ARfD for tebuconazole only applies to women of child-bearing age. An ARfD for the general population is not required. The NOAEL for maternotoxicity is 3 mg/kg bw/d due to slight hepatotoxicity at the next

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				litters with abnormal foetuses) at the next highest dose	highest dose. The degree of maternotoxicity is insufficient to explain the developmental effects.
Tepraloxydim			13 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Terbuthylazine			4 May 2001		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Tetraconazole	0.2	16	12 December 2002	4-week dietary rat study; a NOAEL of 16 mg/kg bw/d was based on clinical signs at the next higher dose.	
Tetraniliprole			17 July 2019		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Thiacloprid	0.03	3.1	20 July 2001	Acute oral neurotoxicity rat study; a NOAEL of 3.1 mg/kg bw was based on reduced motor and locomotor activity at the next higher dose.	
Thiram	0.1	10	2 July 2010	Acute neurotoxicity rat study; a NOAEL of 10 mg/kg bw was based on reduced locomotor activity at the next higher dose.	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Thymol			19 August 2020		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Tiafenacil	0.006	0.6	22 December 2020	One-generation rat reproductive study. A NOAEL of 0.6 mg/kg bw/d was based on increased total liver porphyrins at the next higher dose.	
Tilmicosin	0.4	36	29 August 2002	7-day oral dosing (capsule) dog study; a NOAEL of 10 mg/kg bw/d was based on the absence of clinical signs (ataxia, dyspnoea, bilateral mydriasis) during the first 4 days of dosing.	
Tolfenamic acid	0.005	[0.5]	16 January 2001	Lowest effective therapeutic dose (as a single dose) for treatment of pyresis in children.	
Toltrazuril	0.02	2	26 March 2020	Rabbit developmental studies; an overall NOAEL of 2 mg/kg bw/d with foetotoxicity at the next higher dose.	
Topramezone			16 June 2016		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Trifloxystrobin			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.

49 Acute reference doses for agricultural and veterinary chemicals

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
Trifloxysulfuron			13 February 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Trifludimoxazin			28 May 2020		An ARfD was considered unnecessary due to its low oral toxicity and the absence of any neurological effects or developmental toxicity after a single dose.
Trinexapac-ethyl			10 May 2017		ARfD considered to be unnecessary due to its low oral toxicity and the absence of any developmental toxicity after a single dose.
Tulathromycin	0.1	100	16 August 2006	Acute tolerance dog study; a LOAEL of 100 mg/kg bw was based on the occurrence of emesis and loose stools.	
U					
Ulocladium oudemansii			12 December 2003		ARfD unnecessary. Naturally occurring organism – residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism.
Z					
Zilpaterol	0.00004	0.00076 [LOAEL]	24 October 2016	Single dose human study; a LOAEL of 0.05 mg/person (equal to 0.00076 mg/kg bw) was based on the	

Chemical	ARfD (mg/kg bw)	NOAEL (mg/kg bw/d)	Date	Study	Comments
				observation of tremors at the lowest tested dose.	
