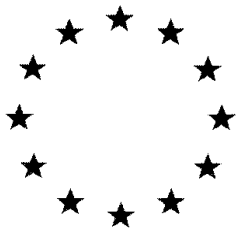
European Commission



VOLUME 1

- Flutolanil -

Rapporteur Member State: The Netherlands

August 2018

Draft Assessment Report and Proposed decision of the Netherlands prepared in the context of the possible approval of Flutolanil under Regulation (EC) 1107/2009

Version history page

Date	Version history
August 2018	Initial RAR

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Volume 1

Level 1

- *Active substance* –

Statement of subject matter and purpose for which this report has been prepared and background information on the application

1 Statement of subject matter and purpose for which this report has been prepared and background information on the application

1.1 Context in which the draft assessment was prepared.

1.1.1 Purpose for which the draft assessment report was prepared

This Renewal Assessment Report (RAR) is prepared for the renewal of the approval of the active substance flutolanil. Flutolanil is part of the AIR4 renewal programme for active substances (Commission Implementing Regulation (EU) No 844/2012).
A new MRL-proposal is included.

1.1.2 Arrangements between rapporteur Member State and co-rapporteur Member State

The Netherlands conducted the full evaluation (RMS) and prepared the RAR for the active substance flutolanil, and the RAR was peer reviewed by the Co-Rapporteur Member State United Kingdom.

1.1.3 EU Regulatory history for use in Plant Protection Products

Flutolanil is re-evaluated as an existing active substance by the Rapporteur Member State The Netherlands. The main data at that time was submitted by Nihon Nohyaku Co Ltd.
Flutolanil is approved since 1 March 2009 (Council Directive 2008/108/EEC of 26 November 2008).

The Review Report – Flutolanil SANCO/116/08 – rev. 1 is dated 16 May 2008.

The EFSA-conclusion is published on 28 July 2008 (EFSA Scientific Report (2008) 126, 1- 63 , Conclusion regarding the peer review of the pesticide risk assessment of the active substance flutolanil). The EFSA-conclusion provides endpoints as agreed during the first inclusion evaluation (Appendix 1 of the EFSA-conclusion).

A review of the existing Maximum residue levels (MRLs) for flutolanil according to Article 12 of Regulation (EC) No 396/2005 is available in EFSA Journal 2013;11(9):3360 [44 pp.] as published on 17 September 2013.

1.1.4 Evaluations carried out under other regulatory contexts

Not relevant.

1.2 Applicant(s) information

1.2.1 Name and address of applicant(s) for approval of the active substance

NIHON NOHYAKU CO., LTD

19-8, Kyobashi 1-Chome, Chuo-ku

Tokyo 104-8386 Japan

1.2.2 Producers of the active substance

Please refer to Vol. 4 for the sources of flutolanil

1.2.3 Information relating to the collective provisions of dossiers

Not applicable.

1.3 Identity of the active substance

1.3.1 Common name proposed or ISO-accepted and synonyms

ISO: Flutolanil

1.3.2 Chemical name (IUPAC and CA nomenclature)

IUPAC: α,α,α-trifluoro-3'-isopropoxy-*o*-toluanilide

CA: *N*-[3-(1-methylethoxy)phenyl]-2-(trifluoromethyl)benzamide

1.3.3 Producer's development code numbers

The development code numbers from the original DAR are NF-136 and AE-28247

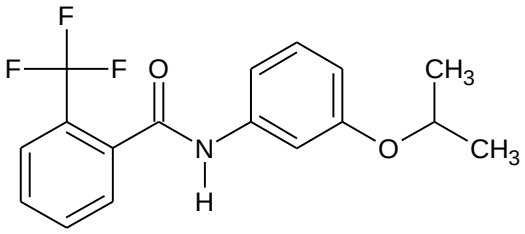
1.3.4 CAS, EC and CIPAC numbers

CAS-No:	66332-96-5
EINECS-No:	Not allocated
CIPAC-No:	524

1.3.5 Molecular and structural formulae, molecular mass

Molecular formula: $C_{17}H_{16}F_3NO_2$

Structural formula:



Molar mass: 323.3 g/mol

1.3.6 Method of manufacture (synthesis pathway) of the active substance

Confidential information – see Volume 4 for further details

1.3.7 Specification of purity of the active substance in g/kg

Minimum purity of active substance: 975 g/kg

1.3.8 Identity and content of additives (such as stabilisers) and impurities

1.3.8.1 Additives

Confidential information - see Volume 4 for further details

1.3.8.2 Significant impurities

Confidential information – see Volume 4 for further details

1.3.8.3 Relevant impurities

No relevant impurities have been identified for flutolanil

1.3.9 Analytical profile of batches

Confidential information – see Volume 4 for further details

1.4 Information on the plant protection product

1.4.1 Applicant

Head office and applicant's address:

Nihon Nohyaku Co Ltd.,
Kyobashi OM Bldg.,
19-8, Kyobashi 1-Chome,
Chuo-ku,
Tokyo,
104-8386,
JAPAN.

European address and applicant's contact:

Nichino Europe Co Ltd.,
5 Pioneer Court,
Vision Park,
Cambridge,
CB24 9PT
UNITED KINGDOM.

Contact:	Mr. Bill Pickering
E-mail:	BPickering@nichino-europe.com
Telephone number:	[redacted]
Fax number:	[redacted]

1.4.2 Producer of the plant protection product

Confidential information – see Volume 4 for further details

1.4.3 Trade name or proposed trade name and producer's development code number of the plant protection product

The representative product trade name is 'MONCUT 40 SC'. This is also known as 'Flutolanil 40SC', 'Monarch' and 'RhiNo'.

There are two versions of 'MONCUT 40 SC'; with or without a coloured dye depending upon the target market and field of use. The version without a dye is known by the development code names "40SC (EU)", "40SC (NPE-free)" or "EXP10066A". The version with a dye is known by the development code name "40SC (EU-D)".

1.4.4 Detailed quantitative and qualitative information on the composition of the plant protection product

1.4.4.1 Composition of the plant product

Pure active substance

content of pure active substance :	**460 g/l**	**40.7 (% w/w)**
limits :	437 – 483 g/l	38.7 – 42.7 (% w/w)

Technical active substance

content of technical active substance* :	**472 g/l**	**41.8 (% w/w)**
limits :	448 – 495 g/l	39.7 – 43.9 (% w/w)

* at a minimum purity of the technical active substance of 97.5%.

1.4.4.2 Information on the active substances

Type	**Name/Code Number**
ISO common name	Flutolanil (ISO accepted), no synonyms
CAS No	66332-96-5
EC No	Not yet allocated
CIPAC No	524
Salt, ester anion or cation present	None

1.4.4.3 Information on safeners, synergists and co-formulants

Confidential information – see Volume 4 for further details

1.4.5 Type and code of the plant protection product

Suspension concentrate [Code: SC]

1.4.6 Function

Fungicide

1.4.7 Field of use envisaged

The representative formulation of flutolanil, 'MONCUT 40SC' is to be used as a fungicide in agricultural situations. The representative uses are agricultural use as a potato tuber treatment and in horticultural situations as a soil treatment for the growing of tulip and iris bulbs.

1.4.8 Effects on harmful organisms

'MONCUT 40SC' contains 460 g/L flutolanil. Flutolanil is a systemic benzanilide fungicide with protective and curative actions.

1.5 **Detailed uses of the plant protection product** (to be included for each preparation for which documentation was submitted).

1.5.1 Details of representative uses

The intended use pattern is summarised in the GAP table in document D and this is copied below; with separate GAP tables for the dyed and un-dyed versions of the product. It is intended that flutolanil will be used to treat potato tubers pre-planting (BBCH 00 – 03) in stores using canopied hydraulic sprayer or spinning disc equipment on a roller table or at planting (BBCH 00 – 03) with on-planter or in-planter equipment. The other intended use is as a soil treatment with broadcast spray equipment and incorporated into the soil pre planting with iris and tulip bulbs (BBCH 00).

It should be mentioned that planting density of potatoes can vary by EU member state or whether the potato is being grown for consumption as ware potatoes or for the generation of seed potatoes, the representative use in potatoes supported for the renewal of flutolanil is at a planting rate of 4 tonnes potatoes/ha since this is considered representative of the majority of intended EU uses.

Especially for seed potatoes which are often planted at higher densities the proposed GAP is unlikely to be realistic for all member states, as several member states report higher planting densities of up to 5 or 7 tons per hectare, planting densities compatible with the proposed GAP also occur. The GAP is realistic for ware and starch potatoes, which is the majority of the potato acreage.

PPP (product name/code)	Moncut 40SC / 40SC(EU) [**without dye]**	Formulation Type	Suspension Concentrate (SC)
Active Substance	Flutolanil	Conc. of as	460 g/L
Safener	None	Conc. of safener	Not applicable
Synergist	None	Conc. of synergist	Not applicable
Applicant	Nihon-Nohyaku		
Zone	Northern, Central and Southern Zones	professional use	☒
		non-professional use	☐

Verified by MS: yes

Crop and/ or situation	**Member State**	**Product name**	**F G or I**	**Pests or Group of pests controlled**	**Formulation**		**Application**				**Application rate per treatment**			**PHI** (days)	**Remarks:**
					Type	**Conc. of as**	**Method Kind**	**Growth stage & season**	**number min max**	**interval between applications (days)**	**kg as/hL min max**	**water L/ha min max**	**kg as/ha min max**		
(a)			**(b)**	**(c)**	**(d-f)**	**(i)**	**(f-h)**	**(j)**	**(k)**					**(l)**	**(m)**
Potato Seed tuber treatment (ware, seed and starch potatoes)	NL & BE	Moncut 40 SC	F I	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---	4.6	--	0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha. Use appropriate water volumes – 2 L water/t tubers
Potato Seed tuber treatment (ware, seed and starch potatoes)	NL & BE	Moncut 40 SC	F	Rhizoctonia solani	SC	460 g/l	On planter treatment as tuber falls into furrow	BBCH 00 – 03 (at planting)	1	---	0.46 – 0.613	60 - 80	0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Potato Seed tuber treatment (ware, seed and starch potatoes)	NL & BE	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	In planter treatment before catching up by planting chains.	BBCH 00 – 03 (at planting)	1	---	4.6 – 9.2	4 - 8	0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha
Tulip, Iris	NL & BE	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	Broadcast application with boom sprayer, followed by soil incorporation.	BBCH 00 Oct - Dec	1	---	0.69 – 1.84	150 - 400	2.76	---	Incorporation into the soil, 10 – 15 cm

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha

(m) PHI - minimum pre-harvest interval

Intended uses supported in the EU for which data have been provided

PPP (product name/code)	Moncut 40 SC / 40SC(EU-D) **[with dye]**	Formulation Type	Suspension Concentrate (SC)
Active Substance	Flutolanil	Conc. of as	460 g/L
Safener	None	Conc. of safener	Not applicable
Synergist	None	Conc. of synergist	Not applicable
Applicant	Nihon-Nohyaku		
Zone	Northern, Central and Southern Zones	professional use	☒
		non-professional use	☐

Verified by MS: yes

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Potato Seed tuber treatment (ware seed and starch potatoes)	EU except NL & BE	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---	4.6	--	0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha. Use appropriate water volumes – 2 L water/t tubers
Potato Seed tuber treatment (ware seed and starch potatoes)	EU except NL & BE	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	On planter treatment as tuber falls into furrow	BBCH 00 – 03 (at planting)	1	---	0.46 – 0.613	60 - 80	0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Potato Seed tuber treatment (ware seed and starch potatoes)	EU except NL & BE	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	In planter treatment before catching up by planting chains.	BBCH 00 – 03 (at planting)	1	---	4.6 – 9.2	4 - 8	0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha
Tulip, Iris	EU except NL & BE	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	Broadcast application with boom sprayer followed by soil incorporation.	BBCH 00 Oct - Dec	1	---	0.69 – 1.84	150 - 400	2.76	---	Incorporation into the soil, 10 – 15 cm

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha

(m) PHI - minimum pre-harvest interval

1.5.2 Further information on representative uses

Details on method of application for specialised applications
For seed potatoes in stores, 'MONCUT 40SC' is applied using canopied hydraulic sprayer or spinning disc equipment on a roller table. For treatment of potatoes at planting, 'MONCUT 40SC' is applied as an in- or on-planter treatment. For the use on flower bulbs, 'MONCUT 40SC' is applied to bare soil with broadcast spray equipment and incorporated into the soil pre planting. More detailed information is provided in Volume 3, 3CP paragraph B.3.5.

Necessary waiting period or other precautions to avoid phytotoxic effects on succeeding crops;
No waiting periods or other precautions are proposed since 'MONCUT 40SC' is not phytotoxic to succeeding crops (i.e. cereals, tubers, beans, fruit vegetables, leafy crops, root vegetables, fruits, pasture and flowers).

Proposed instructions for use.
The gap in 1.5.1 has an overview of the proposed representative uses and dose rates.

1.5.3 Details of other uses applied for to support the setting of MRLs for uses beyond the representative uses

The method of application in the GAP table presented below (in furrow treatment) differs from the method of application of the representative uses in the GA)P table in paragraph 1.5.1.

PPP (product name/code)	Moncut 70DF	Formulation Type	Water dispersible granule (WG)
Active Substance	Flutolanil	Conc. of as	700 g/KG
Safener	None	Conc. of safener	Not applicable
Synergist	None	Conc. of synergist	Not applicable
Applicant	Nihon-Nohyaku		
Zone	Northern, Central and Southern Zones	professional use	☒
		non-professional use	☐

Verified by MS: yes

Crop and/ or situation	Member State	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of as	Method Kind	Growth stage & season	number min max	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)					(l)	(m)
Potatoes In furrow-treatment at planting	N/S-EU	Proposed Moncut 70DF	F	*Rhizoctonia solani*	WG	700 g	Tractor mounted planter -directed hydraulic sprayer	BBCH 00 – 03 at planting	1	Not relevant	0,84-2,8	75 - 250 l/ha	2.100	Not relevant	In furrow application directed at soil

1.5.4 Overview on authorisations in EU Member States

PPP (product name/code)	Moncut 40SC	Formulation Type	Suspension Concentrate (SC)
Active Substance	Flutolanil	Conc. of as	460 g/L
Safener	None	Conc. of safener	Not applicable
Synergist	None	Conc. of synergist	Not applicable
Applicant	Nihon-Nohyaku		
Zone	Northern, Central and Southern Zones	professional use	☒
		non-professional use	☐

Verified by MS:

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Potato Seed tuber treatment	AT	Moncut	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.368*		0.2 l/t in 2 -3 l water/t *Based on a planting rate of 4 t tubers/ha.
Potato Seed tuber treatment	BE	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.368*		0.2 l/t in 2 -3 l water/t *Based on a planting rate of 4 t tubers/ha.

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Potato Seed tuber treatment	CZ	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.276*		0.2 l/t in 2 -3 l water/t *Based on a planting rate of 3 t tubers/ha
Potato Seed tuber treatment	CZ	Moncut 40 SC	F	*Rhizoctonia solani*	SC	460 g/l	On planter treatment as tuber falls into furrow	BBCH 00 – 03 (before planting)	1	---	0.345 – 0.46	60 - 80	0.276*		0.2L product/t *Based on a planting rate of 3 t tubers/ha
Potato Seed tuber treatment	DE	Moncut 460SC	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.230*		0.2 l/t in 2 -3 l water/t *Based on a planting rate of 2.5 t tubers/ha
Potato Seed tuber treatment	DE	Moncut 460SC	F	*Rhizoctonia solani*	SC	460 g/l	On planter treatment as tuber falls into furrow	BBCH 00 – 03 (before planting)	1	---	0.288 – 0.38	60 - 80	0.230*		0.2L product/t *Based on a planting rate of 2.5 t tubers/ha
Potato Seed tuber treatment	FI	Moncut 40SC	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.230*		0.2 l/t in 2 -3 l water/t *Based on a planting rate of 2.5 t tubers/ha

Crop and/ or situation (a)	Member State	Product name	FG or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Potato Seed tuber treatment	FI	Moncut 40SC	F	*Rhizoctonia solani*	SC	460 g/l	Dipping	BBCH 00 – 03 (before planting)	1	---	0.069	15-25 l / ton of seed	0.230*		0.15% (0.15 l / 100 l of water),
Potato Seed tuber treatment	FR	Iota / Rialto	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.331*		0.18 l/t in 2 -3 l water/t *Based on a planting rate of 4 t tubers/ha.
Potato Seed tuber treatment	EL	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	On planter treatment as tuber falls into furrow	BBCH 00 – 03 (at planting)	1	---	---	10	0.0575 – 0.0863		
Potato Seed tuber treatment	EL	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	In planter treatment before catching up by planting chains.	BBCH 00 – 03 (at planting)	1	---	---	10	0.0575 – 0.0863	---	
Green beans	EL	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	Drip irrigation	BBCH 13 – 15	2	15	---	N/A	0.0345 - 0.0690	3	
Artichoke cuttings	EL	MONCUT 46 SC	FI	*Rhizoctonia solani*	SC	460 g/l	Dipping	BBCH 00-05(before transplanting	1	---	0.0575 - 0.0690	N/A	---	---	
Peppers	EL	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	Drip irrigation	BBCH 13 – 15	1	---	---	N/A	0.0345 - 0.0690	47	

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Carnations	EL	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	Handheld spray of plant neck area	BBCH 00 – 13 (after transplantation)	1	---	0.000575	50-60	---	---	
Potato Seed tuber treatment	IE	Rhino	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---	---		0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha. Use appropriate water volumes
Potato Seed tuber	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	*Seed treatment*	BBCH 00 March April	1	---	0.288 – 0.38	60 - 80	0.184 – 0.46*		0.2 l/t in 2 -3 l water//t *Based on a planting rate of 2 - 5 t tubers/ha
Potato ware tuber	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	Seed treatment	BBCH 00 March April	1	---	0.288 – 0.38	60 - 80	0.184 – 0.46*		0.2 l/t in 2 -3 l water//t *Based on a planting rate of 2 - 5 t tubers/ha
Potato starch tuber	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	Seed treatment	BBCH 00 March April	1	---	0.288 – 0.38	60 - 80	0.184 – 0.46*		0.2 l/t in 2 -3 l water//t *Based on a planting rate of 2 - 5 t tubers/ha
Tulip, Iris	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	Broadcast application with boom sprayer	BBCH 00 Oct - Dec	1	---	0.69 – 1.84	150 - 400	2.76	---	Incorporation into the soil, 10 – 15 cm

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Tulip, Iris	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	Band application to planted bulbs and soil	BBCH 00 Oct - Dec	1	---	0.345 – 0.92	150 - 400	1.38	---	
Tulip, Iris	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	In furrow application to planted bulbs and soil	BBCH 00 Oct - Dec	1	---	0.345 – 0.92	150 - 400	1.38	---	
Minor use Summer Flowers	NL	Monarch	F	*Rhizoctonia solani*	SC	460 g/l	Broadcast application shortly after planting	BBCH 00 - 10 Mar - May	1	---	0.276	1000	2.76	---	
Potato Seed tuber treatment	POL	Moncut 460 SC	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---			0.276*		0.2 l/t in 2 -3 l water/t *Based on a planting rate of 3 t tubers/ha
Potato Seed tuber treatment	ES	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	On planter treatment as tuber falls into furrow	BBCH 00 – 03 (at planting)	1	---	---	10	0.0575 – 0.0863		
Potato Seed tuber treatment	ES	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	In planter treatment before catching up by planting chains.	BBCH 00 – 03 (at planting)	1	---	---	10	0.0575 – 0.0863	---	

Crop and/ or situation (a)	Member State	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	Method Kind (f-h)	Growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Green beans	ES	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	Drip irrigation	BBCH 13 – 15	2	15	---	N/A	0.0345 - 0.0690	3	
Artichoke cuttings	ES	MONCUT 46 SC	FI	*Rhizoctonia solani*	SC	460 g/l	Dipping	BBCH 00-05(before transplanting	1	---	0.0575 - 0.0690	N/A	---	---	
Peppers	ES	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	Drip irrigation	BBCH 13 – 15	1	---	---	N/A	0.0345 - 0.0690	47	
Carnations	ES	MONCUT 46 SC	F	*Rhizoctonia solani*	SC	460 g/l	Handheld spray of plant neck area	BBCH 00 – 13 (after transplantation)	1	---	0.000575	50-60	---	---	
Potato Seed tuber treatment	UK	Rhino	F	*Rhizoctonia solani*	SC	460 g/l	In store treatment Canopied hydraulic or spinning disc equipment	BBCH 00 – 03 (before planting)	1	---	---		0.368*	---	0.2L product/t *Based on a planting rate of 4 t tubers/ha. Use appropriate water volumes

Volume 1

Level 2

- *Active Substance* –

Summary of active substance hazard and of product risk assessment

2 Summary of active substance hazard of product risk assessment

2.1 Identity

2.1.1 Summary of identity

See for data and the specification regarding flutolanil, impurities, plant scale details the confidential annex C/Volume 4.

The minimum purity of the active substance is 975 g/kg.

2.2 Physical and chemical properties

2.2.1 Summary of physical and chemical properties of the active substance

Flutolanil is a white powder at room temperature and is not flammable, oxidising or explosive. It has a vapour pressure of 4.1 x 10^{-7} Pa at 20 ^{o}C and 1.0 x 10^{-6} Pa at 25 ^{o}C. Flutolanil is slightly soluble in water (8.01 mg/L at 20 ^{o}C and neutral pH) but highly soluble in organic solvents, except *n*-hexane. The n-octanol/water partition coefficient log P_{OW} = 3.17. No dissociation constant has been calculated, as no dissociation is possible based on the structure of the molecule.

2.2.2 Summary of physical and chemical properties of the plant protection product

MONCUT 40 SC is an opaque, white, free-flowing medium viscosity homogeneous liquid without discernible odour. The formulation has no flashpoint prior to boiling, and has an auto-ignition temperature of 461 ^{o}C. It has no explosive or oxidising properties. The pH of the neat formulation is 8.7, of a 1% dilution 8.5. Viscosity at 20 ^{o}C is 111 – 416 mPa.s and 93 – 381 mPa.s at 40 ^{o}C. Surface tension at 20 ^{o}C is 31.9 mNm^{-1} for the neat formulation. The formulation has been demonstrated to be stable in studies for 2 weeks at 54 ^{o}C and for 2 years at room temperature.

MONCUT 40 SC DYE is an opaque, purple, free-flowing medium viscosity homogeneous liquid without discernible odour. The formulation has no flashpoint prior to boiling, and has an auto-ignition temperature of 461 ^{o}C. It has no explosive or oxidising properties. The pH of the neat formulation is 7.0, of a 1% dilution 7.3. Viscosity at 20 ^{o}C is 112 – 419 mPa.s and 111 – 455 mPa.s at 40 ^{o}C. Surface tension at 20 ^{o}C is 32.3 mNm^{-1} for the neat formulation. The formulation has been demonstrated to be stable in studies for 2 weeks at 54 ^{o}C and for 2 years at room temperature.

2.3 Data on application and efficacy

2.3.1 Summary of effectiveness

Flutolanil is a systemic benzanilide fungicide with protective and curative actions. Flutolanil acts through the inhibition of succinate dehydrogenase complex of the mitochondrial respiratory chain in susceptible fungi.

It should be mentioned that planting density of potatoes can vary by EU member state or whether the potato is being grown for consumption as ware potatoes or for the generation of seed potatoes, the representative use in potatoes supported for the renewal of flutolanil is at a planting rate of 4 tonnes potatoes/ha since this is considered representative of the majority of intended EU uses.

Especially for seed potatoes which are often planted at higher densities the proposed GAP is unlikely to be realistic for all member states, as several memberstates report higher planting densities of up to 5 or 7 tons per hectare, planting densities compatible with the proposed GAP also occur. The GAP is realistic for ware and starch potatoes, which is the majority of the potato acreage.

Considering that the substance is approved and that the extant authorisations of plant protection products containing flutolanil have already been evaluated according to the Uniform Principles, no other efficacy information is considered to be necessary at this time.

2.3.2 Summary of information on the development of resistance

Flutolanil (chemical group: phenylbenzamides) belongs to the group of succinate dehydrogenase inhibitors ("SDHI"), a fungicide group with a vast number of different active substances (table 3.7-The FRAC code is 7.

Basic properties of this group such as persistent activity and single-site mode of action indicate a medium – high risk of development of resistance. This is also the general conclusion of the FRAC working group on SDHI fungicides (Table 3.7-1). The proposed representative use is control of Rhizoctonia solani, this pathogen is not listed among the fungi that have developed resistance against FRAC group 7.

The proposed gap is found to be realistic for the representative use concerning resistance risk and management

2.3.3 Summary of adverse effect on treated crops

Flutolanil is not phytotoxic to treated crops, from experience gained over a number of years no adverse effects on treated crops are expected when the representative formulation, 'MONCUT 40SC' is used according to the label instructions.

2.3.4 Summary of observations on other undesirable or unintended side-effects

No other undesirable or unintended side effects have been observed.

2.4 Further information

2.4.1 Summary of methods and precautions concerning handling, storage, transport or fire

See the respective sections B.4 for further information

2.4.2 Summary of procedures for destruction or decontamination

See the respective sections B.4 for further information

2.4.3 Summary of emergency measures in case of an accident

See the respective sections B.4 for further information

2.5 Methods of analysis

2.5.1 Methods used for the generation of pre-authorisation data

Adequate analytical methods are provided for the generation of pre-authorisation data.

2.5.2 Methods for post control and monitoring purposes

Analytical methods for monitoring purposes are submitted.

2.6 Effects on human and animal health

2.6.1 Summary of absorption, distribution, metabolism and excretion in mammals

The studies are in broad agreement, that flutolanil is absorbed , but rapidly excreted in urine and faeces, mainly as metabolites, while there is minimal exposure of, and no bioaccumulation in, the organs and tissues. The absorption of flutolanil was found to be approximately 50 – 70% depending on the application of single or repeated doses of 20 mg/kg bw flutolanil administered by gavage. After repeated exposure at 20 mg/kg bw/day absorption was approximately 70% based on urinary excretion while after a single exposure absorption was approximately 50%. However, in one of the single exposure studies oral absorption was found to be 70% following exposure to 20 mg/kg bw/day, which is in line with the absorption values found in the repeated dose studies. Thus, based on the available data, the dermal absorption is determined to be 70%. This is in line with the conclusion drawn on the oral absorption during the first approval of flutolanil. Saturation was found to occur at higher dose levels of flutolanil (1000 mg/kg bw). In specific support of the in vivo mutagenicity studies, bone (the femur) or bone marrow were shown to be exposed to similar low levels to those seen in other tissues. While the [redacted] (2012) study showed a detectable amount only for female marrow, the values were generally at or around the limit of detection, there was no evidence of a general gender difference in distribution, and therefore it may safely be inferred that the male marrow was similarly exposed.

Metabolism is by breakdown of the isopropyl group, hydroxylation of the 4-position in the aniline ring, and sulphate- or glucuronide-conjugation of the 3,4-position in the aniline ring. Limited cleavage of the amido bridge of the molecule was observed in the most recent study ([redacted] 2012), which also indicated no significant sex differences, while the earlier study ([redacted] 1992) indicated that females conjugated flutolanil to a greater extent than males.

The in vitro comparative metabolism study demonstrated no significant qualitative differences in the metabolic pathway between the rat, mouse, rabbit, dog and human.

2.6.2 Summary of acute toxicity

Flutolanil technical was shown to be of low acute toxicity by oral, dermal or inhalation routes of exposure. It was not irritant to eyes or skin, and did not cause skin sensitization. The results of the acute toxicity, irritation and sensitisation studies are presented in table 2.6.2-1 and 2.6.2-2.

Table 2.6.2-1 Summary of the acute toxicity studies

Test substance	Route	Species	LD_{50}/LC_{50}	Classification	Reference
Flutolanil	oral	Rat	LD50 > 10000 mg/kg bw	None	[redacted] 1982a
Flutolanil	oral	Mouse	LD50 > 10000 mg/kg bw	None	[redacted] 1982b
Flutolanil	dermal	Rat	LD50 > 5000 mg/kg bw	None	[redacted] 1982a
Flutolanil	Inhalation	Rat	LC_{50} > 5.98 mg/L/4h[1] (body) LC_{50} > 2 mg/L/4h (snout)	None	[redacted] 1984 [redacted] 2012

Table 2.6.2-2 Summary of the irritation and sensitisation studies

Test substance	Route	Species	Effect	Classification	Reference
Flutolanil	Skin irritation	Rabbit	No irritation	None	[redacted] 1986a
Flutolanil	Eye irritation	Rabbit	No irritation	None	[redacted] 1986b
Flutolanil	Sensitization (Magnusson & Kligman)	Guinea pig	Not sensitizing	None	[redacted] 1986c

2.6.3 Summary of short-term toxicity

Repeated toxicity studies performed in rat, mouse and dog did not show any mortality.

The only consistent trend among the oral short-term studies was for the finding at high dosages of increased liver weight with hypertrophy and swelling of hepatocytes. Moreover, an effect on thyroid weight (>20%) was also observed in the 90-day dog study at the high dose. The NOAEL values determined are all based on effects observed in the liver. For rat, the NOAEL was determined at 180 mg/kg bw/day and 37 mg/kg bw/day based on a 28-day and 90-day study, respectively. For mouse a NOAEL of 680 was determined based on reduced weight gain with increased liver weight observed in a 90 days study. The dog was found to be the most sensitive species for liver effects as a NOAEL of 80 mg/kg bw/day was determined based on increased liver weight with hepatocyte swelling and pallor. In addition to the oral short-term toxicity studies, a dermal short-term toxicity study was performed for 21 days in which no effects were observed in rats exposed to 1000 mg/kg bw/day. A summary of the short-term toxicity studies are presented in Table 2.6.3.1.

Table 2.6.3-1 Summary of the short-term toxicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
Flutolanil	28 days, oral, dietary	Rat	180 mg/kg/day	916 mg/kg bw	increased liver weights and activated centrilobular hepatocytes at ≥ 916 mg/kg/day	[redacted] 1977
Flutolanil	90 days,	Rat	37	299 mg/kg	increased	[redacted]

	oral, dietary		mg/kg/day	/day	thyroid/parathyroid weight	1986a
Flutolanil*	90 days, oral, dietary	Mouse	680 mg/kg/day	7510 mg/kg/day	reduced weight gain with increased liver weight at 7510 mg/kg/day	[redacted] 1987
Flutolanil	90 days, oral, capsule	Dog	80 mg/kg/day	400 mg/kg/day	increased liver weight with hepatocyte swelling and pallor at 400 mg/kg/day	[redacted] 1986b
Flutolanil	21 days, dermal	Rat	>1000 mg/kg/day	-	limit dose, 5 days/week; no effects	[redacted] 1990
Flutolanil	28 days, oral, dietary	Rat	61.1 mg/kg bw/day	245 mg/kg bw/day	reduction in overall spleen cell count and viable cells/ spleen	[redacted] 2011
Flutolanil	Single dose by gavage	Rat	2000 mg/kg bw/day	-	Highest dose tested; no effects	[redacted] 2011

* The study is considered supportive.

2.6.4 Summary of genotoxicity

Flutolanil was shown to be non-mutagenic in a series of appropriate tests, *in vitro* and *in vivo*, and is therefore not classified for mutagenicity. The weak positive shown in one in vitro chromosome aberration test using hamster lung cells (Tokiwa, 1986) was negated by the later testing and regarded as spurious. In support of the *in vivo* studies, the ADME study of [redacted] 2012 has demonstrated exposure of the bone marrow, while the earlier [redacted] (1992) study also showed this by inference from the amounts demonstrated in bone (the femur). It should be noted that the in vivo tests were performed with mice. Although based on the available studies mice appear less sensitive to flutalonil compared to rats and dogs, the available in vivo studies are considered to provide sufficient information on genotoxicity considering that the results of the in vivo tests are in line with the in vitro tests and that relatively high doses were used in mice. Moreover, in the in vivo micronucleus test there was a mild decrease in immature versus total erythrocyte ratio which, although not statistically significant, suggest that the bone marrow was exposed.

Table 2.6.4-1 *In vitro* genotoxicity studies

Test substance	Type of study		Result		Reference
	Indicator cells	**Endpoint**	**without activation**	**with activation**	
Flutalonil	*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538, *E. coli* WP2 uvrA	point mutations	Negative	Negative	Moriya, 1981
Flutolanil	*Bacillus subtilis* (H17, M45)	DNA repair	Negative	Negative	Moriya, 1981
Flutolanil	Chinese hamster lung	chromosome aberration	Negative	Weak positive	Tokiwa,

	cells				1986
	Human lymphocytes	chromosome aberration	125 to 1000 µg/mL with and without S9	Negative	Jenkinson, 1990
Flutolanil	L5178Y TK+/- mouse lymphoma cells	gene mutations	6 to 100 µg/mL, with and without S9	Negative	Heidemann, 1989
Flutolanil	Rat hepatocytes	Unscheduled DNA synthesis	2.67 to 80.00 µg/mL	Negative	Fautz, 1989

Table 6.4.3.2 *In vivo* genotoxicity studies

Test substance	Type of study		Result	Reference
	Species	Endpoint		
flutalonil	Male and female BDF1 mice, bone marrow cells	micronucleus formation in erythrocytes	negative	[redacted] 1983
	Male S1c/ICR mice	micronucleus formation in erythrocytes	negative	[redacted] 2012

2.6.5 Summary of long-term toxicity and carcinogenicity

Three long-term toxicity studies are available in which rats, mice and dogs were exposed to flutalonil for 104, 79 and 104 weeks, respectively. In all three species, flutolanil could be administered at dosages in excess of the currently accepted limit value without clear evidence of any severe toxicity. Typically, body weight gain was slightly reduced, while liver weight was increased, and there was no evidence that flutolanil caused any neoplastic change.

Table 2.6.5-1 Summary of the long-term toxicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
flutalonil	Oral, 104 weeks	rat	8.7 mg/kg bw/day	87 mg/kg bw/day	slight anaemia in females and histopathological splenic changes observed in males	[redacted]. 1982
flutalonil	Oral, 79 weeks	mouse	32 mg/kg bw/day	162 mg/kg bw/day	Increased incidence of periacinar hepatocytic fatty vacuolation (M)	[redacted] 1990
flutalonil	Oral, 104 weeks	dog	50 mg/kg bw/day	250 mg/kg bw/day	clinical signs (emesis, salivation, excretion of soft faeces)	[redacted]1982

2.6.6 Summary of reproductive toxicity

A two-generation study was performed with flutolanil. In this study no reproductive effects were observed at the highest dose level. Parental animals showed increased liver weights when dosed at the highest level (20 000 ppm). The parental NOAEL was based on this increased liver weight (approximately 20%) and was set at 157 mg/kg bw/day. A NOAEL of 1614 mg/kw bw/day was determined for offspring and reproduction. Based on the two-generation study, flutolanil should not be classified as toxic for reproduction.

No signs of malformations were observed in oral developmental studies in rat and rabbit. Based on these studies a NOAEL of ≥1000 mg/kg bw/day was determined for maternal toxicity. Based on the occurrence of a positive trend of resorptions and deaths a LOAEL of 200 mg/kg bw/day was determined for embryofetal toxicity. The effects observed are not considered to be a secondary non-specific consequence of other toxic effects and based on the limited animal data available, classification for cat. 2 developmental toxicity is proposed. A summary of the reproduction and teratogenicity studies is presented in Table 2.6.6-1.

Table 2.6.6-1 Summary of the reproduction and teratogenicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
flutolanil (purity 97.67%, 98.3%)	Dietary 2-generation study of reproductive toxicity	rat	Reproduction: > 1614 mg/kg bw/day Offspring: > 1614 mg/kg bw/day Parental: 157 mg/kg bw/day	Reproduction: - Offspring: - Parental: 1614 mg/kg bw/day	Parental: increased liver weight	[redacted] 1991
Flutolanil (purity 97.5%)	Oral developmental toxicity study, day 6-15	rat	Maternal: ≥1000 mg/kg bw/day Embryofetal toxicity: ≥1000 mg/kg bw/day	Maternal: - Embryofetal toxicity: -	-	[redacted] 1987, as amended 1992
Flutolanil (purity 97.5%)	Oral developmental toxicity study, day 6-15 of gestation	rabbit	Maternal: ≥1000 mg/kg bw/day Embryofetal toxicity: 40 mg/kg bw/day	Maternal: - Embryofetal toxicity: 200 mg/kg bw/day	Embryofetal: positive trend of resorptions and deaths	[redacted] 1987
flutolanil 99.1%	Oral developmental toxicity study, Day 6-27	rabbit	Maternal: ≥ 1000 mg/kg bw/day Embryofetal toxicity: ≥1000 mg/kg	Maternal: - Embryofetal toxicity: -	-	[redacted] 2012

			bw/day			

2.6.7 Summary of neurotoxicity

Flutolanil does not have chemical structures that are similar or related to those capable of inducing delayed neurotoxicity, such as organophosphates, and there was no evidence of neurotoxicity in the studies that have been conducted with flutolanil, including specific subacute (4-week) neurotoxicity studies in rats.

Table 2.6.7-1 Summary of the neurotoxicity studies

Test substance	Duration, route	Species	NOAEL (mg/kg bw/day	LOAEL (mg/kg bw/day)	Critical effects	Reference
flutolanil	Acute	rat	≥2000 mg/kg	-	No effects observed	[redacted] (2011)
flutolanil	Semi-chronic, oral	rat	≥1000 mg/kg bw/day	-	No effects observed	[redacted] (2012)

2.6.8 Summary of further toxicological studies on the active substance

As a supplementary study a 4-week dietary T cell-dependent antibody assay with fllutolanil was performed. Based on this study an effect induced by flutolanil cannot be completely excluded. The dose-related reduction in overall spleen cell count and viable cells/ spleen might indicate a potential immune suppression. A NOAEL of 750 ppm was therefore concluded, equivalent to an overall mean dosage of 61.1 mg/kg/day for males, 74.6 mg/kg/day for females.

The potential of flutolanil and any major metabolites to interact with endocrine systems in mammals has been reviewed, to facilitate an assessment of whether flutolanil may be judged to be an endocrine disrupter (ED) within the framework of European legislation. The evidence shows that flutolanil does not interact with molecular endpoints known to cause endocrine activity. Flutolanil also had no endocrine activity in mammalian assays specific for endocrine disruption and in other regulatory studies with endpoints relevant for endocrine disruption. This weight of evidence indicates that it does not interact with mammalian endocrine systems in studies designed to detect effects relevant for human health. When performing in vivo endocrine studies in rat also the endocrine effects caused by these metabolites were determined since the metabolites M2 and M4 are considered as being the main rat metabolites (>10%). The major mammalian metabolites M-2 and M-4 have also been concluded to have no effect on endocrine systems. This conclusion is in line with the weight of evidence assessment made by the USEPA (2015).

The following tables have been taken from the report of the USEPA (2015) on the tier 1 screening assays for flutolanil. The summaries of the individual studies are included in Volume 3 CA B.6

Table B.2.6.8-1: Estrogenic/Anti-Estrogenic Pathway for Flutolanil (USEPA, 2015)

Lines of Evidence Indicating Potential Interaction with the Estrogenic/Anti-Estrogenic Pathway for Flutolanil[1]															
Study Type/ Literature Citation	ER Binding	ER Activation	Steroidogenesis	Sex Steroid Hormones	Uterine Weight	Ovarian Weight/ GSI	Ovarian/Gonad Staging and Histopathology	Pituitary Weight	Estrous Cyclicity	Age & Weight at VO	2° Sex Characteristics	Fertility (Frt)/ Fecundity (Fcd)	Vitellogenin	Systemic Toxicity[2]	Overt Toxicity Observed[3]
EDSP Tier 1 Assay															
ER Binding (MRID 48616805)	N														
ERTA	Requirement satisfied by OSRI (Kojima *et al.*, 2004; MRID 48033008; see below)														
Aromatase (MRID 48616803)			N												
Steroidogenesis (MRID 48616808)			N												
Uterotrophic (MRID 48616809)					N				NE					N	N
Female Pubertal Rat (MRID 48671101)					N	N	N	N	N	N				N	N
FSTRA (MRID 48616806)				NE		↑15, 30, 64% (L, M, H)	P (L, M, H)[4]				N	Frt: N[5]; Fcd: ↓100% (H)	↓72 % (H)		N (H)[6]
OSRI															
ERTA (Kojima *et al.*, 2004) MRID 48033008		N													
Two-generation reproduction (Rat; MRID 41850805)					NE	NE	N	NE	NE			N			N

Lines of Evidence Indicating Potential Interaction with the Estrogenic/Anti-Estrogenic Pathway for Flutolanil[1]															
Study Type/ Literature Citation	ER Binding	ER Activation	Steroidogenesis	Sex Steroid Hormones	Uterine Weight	Ovarian Weight/ GSI	Ovarian/Gonad Staging and Histopathology	Pituitary Weight	Estrous Cyclicity	Age & Weight at VO	2° Sex Characteristics	Fertility (Frt)/ Fecundity (Fcd)	Vitellogenin	Systemic Toxicity[2]	Overt Toxicity Observed[3]
Developmental toxicity (Rat; MRID 41850804)					NE							N		N	N
Developmental toxicity (Rabbit; MRID 40342924)					NR							N		N	N
Chronic toxicity/ carcinogenicity (Rat; MRID 40342921)					NE	N	N	N						X (H)	N
Carcinogenicity (Mouse; MRID 41850803)					NE	NE	N	NE						N	N
Chronic toxicity (Dog; MRID 40342922)					NE	N	N	N						X (M,H)	N
Subchronic Toxicity (Rat; MRID 4342919)					NE	N	N	NE						X (M, H)	N
Subchronic Toxicity (Dog; MRID 40342920)					NE	N	N	NE						X (H)	N
Avian reproduction (Quail; MRID 42932301)												P (H)[7]		N	N
Avian reproduction (Duck; MRID 42932302)												P (H)[8]		N	N

1. Key to responses: L=Low treatment, ML=Medium-low treatment, M=Medium treatment, MH=Medium-high treatment, H=High treatment. Arrows (↓ or
↑) indicate the direction of the response. A shaded cell indicates that is parameter is not routinely evaluated or is not applicable in this assay. Changes in weight are absolute unless otherwise indicated.
2. The systemic toxicity in the Tier 1 assays are presented in this column (*e.g.* KW= kidney weight). The systemic toxicity for the OSRI is indicated by an X
in this column. For details see Section IV. A 3. The overt toxicity in the Tier 1 assays are presented in this column (*e.g.* ↓BW). The overt toxicity for the OSRI is indicated by an X in this column. For

details see Section IV. A
4. Ovaries displayed a mild to severe increase in atresia (15 of 16) at the high concentration (1.2 mg/L). Increases in gonad size were observed in all treatment
groups (8 to 14 of 16) concomitant with an increased presence of vitellogenic oocytes. 5. Fertility could not be assessed at the high concentration as no eggs were produced. Fertility was not affected at the two lower concentrations. 6. Five fish were reported as lethargic on Day 1 which progressively decreased to one fish by Day 4 which suggests the fish may have been stressed at test initiation but did not persist throughout the duration of the study. Additionally, there were no effects on survival or growth parameters. 7. Reduction in eggs laid at the highest treatment level by 17% compared to the negative control and was considered biologically significant.
8. Egg shell thickness was decreased 5% (effect not treatment-responsive) at the high dietary concentration. P Positive finding N Negative finding (*in vitro*)/No effect (*in vivo*)
NE Not examined NR Not reported

Table B.2.6.8-2: Androgenic/Anti-Androgenic Pathway for Flutolanil (USEPA, 2015)

Lines of Evidence Indicating Potential Interaction with the Androgenic/Anti-Androgenic Pathway for Flutolanil[1]														
Study Type/ Literature Citation	AR Binding/ AR activation	Steroidogenesis	Sex Steroid Hormones	Testes Weight/GSI	Gonad Staging and Histopathology	Epididymides Weight	Epididymides Histopathology	Pituitary Weight	Accessory Sex Organ Weights/ 2° Sex Characteristics	Fertility (Frty/ Fecundity (Fcd)	Age and Weight at PPS	Vitellogenin	Systemic Toxicity[2]	Overt Toxicity Observed[3]
EDSP Tier 1 Assay														
AR Binding (MRID 48616802)	E[4]													
Steroidogenesis (MRID 48616908)		N												
Hershberger (MRID 48616807)			NE						N				N	N
Male Pubertal Rat (MRID 48671101)			N	N	N	N	N	N	N		N		N	N
FSTRA (MRID 48616806)			NE	N	P (H)[5]				Tubercle score: (21 v 27) (H) fat pad ↓36% (H)	N[6]		N		N[7]
OSRI														
ARTA (Kojima *et al.*, 2004)	N													
Two-Generation Reproduction (Rat; MRID 41850805)				NE	N	NE	N	NE	NE				N	N
Chronic Toxicity / Carcinogenicity (Rat; MRID 40342921)				N	N	NE	N	N	NE				X (H)	N
Carcinogenicity (Mouse; MRID 41850803)				N	N	NE	N	NE	NE				N	N

Lines of Evidence Indicating Potential Interaction with the Androgenic/Anti-Androgenic Pathway for Flutolanil[1]														
Study Type/ Literature Citation	AR Binding/ AR activation	Steroidogenesis	Sex Steroid Hormones	Testes Weight/GSI	Gonad Staging and Histopathology	Epididymides Weight	Epididymides Histopathology	Pituitary Weight	Accessory Sex Organ Weights/ 2° Sex Characteristics	Fertility (Frty/ Fecundity (Fcd)	Age and Weight at PPS	Vitellogenin	Systemic Toxicity[2]	Overt Toxicity Observed[3]
Chronic toxicity (Dog; MRID 40342922)				NE	N	NE	N	N	NE				X (M, H)	N
Subchronic Toxicity (Rat; MRID 40342919)				N	N	NE	N	NE	NE				X (M, H)	N
Subchronic Toxicity (Dog; MRID 40342920)				N	N	N	N	NE	NE				X (H)	N
Avian reproduction (Quail; MRID 42932301)										N			N	N
Avian reproduction (Duck; MRID 42932302)										N			N	N

1. Key to responses: L=Low treatment, ML=Medium-low treatment, M=Medium treatment, MH=Medium-high treatment, H=High treatment. Arrows (↓ or ↑) indicate the direction of the response. A shaded cell indicates that is parameter is not routinely evaluated or is not applicable in this assay. Changes in weight are absolute unless otherwise indicated. Abbreviations for androgen sensitive tissues: Seminal vesicles (SV), Ventral prostate (VP), Dorsal prostate (DP), Prostate (PR), Levator ani-bulbocavernosus (LABC), Epididymides (E), Cowper's gland (CG), glans penis (GP). 2. The systemic toxicity in the Tier 1 assays are presented in this column (*e.g*. KW= kidney weight). The systemic toxicity for the OSRI is indicated by an X in this column. For details see Section IV. A 3. The overt toxicity in the Tier 1 assays are presented in this column (*e.g*. ↓BW). The overt toxicity for the OSRI is indicated by an X in this column.
4. Mean specific-binding decreases in the presence of flutolanil were variable, and not dose specific, in Run 1 (>50% but <75% at several concentrations). Flutolanil did not reduce binding <75% in Runs 2 and 3. 5. Multiple, often related, abnormalities in the testes including increases in the number of spermatogonia (mild to moderate), increases in primary spermatocytes
(moderate), decreases in secondary spermatocytes (mild to moderate), and/or decreases in spermatids (mild to moderate) in the three of eight males in the high treatment group (1.2 mg/L). These microscopic alterations interfered with staging of the testes in two of these males.
6. Fertility could not be assessed at the high concentration as no eggs were produced. Fertility was not affected at the two lower concentrations
7. Five fish were reported as lethargic on Day 1 which progressively decreased to one fish by Day 4 which suggests the fish may have been stressed at test initiation but did not persist throughout the duration of the study. Additionally, there were no effects on survival or growth parameters
E Equivocal assay response
P Positive finding N Negative finding (*in vitro*)/No effect (*in vivo*)
NE Not examined

Table B.2.6.832: Thyroid Pathway for Flutolanil (USEPA, 2015)

Lines of Evidence Indicating Potential Interaction with the Thyroid Pathway for Flutolanil[1]									
Study Type/ Literature Citation	Thyroid Weight	Thyroid: Gross and Histopathology	Serum T_4 Levels	Serum TSH levels	Pituitary Weight	Developmental stage (± or asynchronous, HLL)	Growth (BW, SVL)	Systemic Toxicity[2]	Overt Toxicity Observed[3]
EDSP Tier 1 Assays									
Male Pubertal Rat (MRID 48671101)	N	N	N	N	N			N	N
Female Pubertal Rat (MRID 48671101)	N	N	N	N	N			N	N
AMA (MRID 48616801)	N	N[4]				Day 21 NF stage: ↑2 stages[5] Day 21 HLL: ↑28,26,23% (L, M, H)[6]	Day 7 BW: ↑40, 54% Day 21 BW: ↑20, 35% Day 7 SVL: ↑15, 18% Day 21 SVL: ↑5, 9% (L, M)[7]		N
OSRI									
Chronic Toxicity/ Carcinogenicity (Rat; MRID 40342921)	N	N			N			X (H)	N
Carcinogenicity (Mouse; MRID 41850803)	NE	N			NE			N	N
Chronic toxicity (Dog; MRID 40342922)	N	N			N			N	X (M, H)
Subchronic Toxicity (Rat; MRID 40342919)	N	N			NE			X (M, H)	N
Subchronic Toxicity (Dog; MRID 40342920)	N	N			NE			X (H)	N

1. Key to responses: L=Low treatment, ML=Medium-low treatment, M=Medium treatment, MH=Medium-high treatment, H=High treatment. . Arrows (↓ or ↑) indicate the direction of the response. A shaded cell indicates that is parameter is not routinely evaluated or is not applicable in this assay.
2. The systemic toxicity in the Tier 1 assays are presented in this column (*e.g*. KW= kidney weight). The systemic toxicity for the OSRI is indicated by an X in this column. For details see Section IV. A 3. The overt toxicity in the Tier 1 assays are presented in this column (*e.g*. ↓BW). The overt toxicity for the OSRI is indicated by an X in this column. For details see Section IV. A 4. Although not statistically-significant, increases in the severity and incidence of thyroid hypertrophy and increased colloid area were apparent in all treatment groups. However, the severity of thyroid hypertrophy and increased colloid area was significantly increased in the solvent control relative to the negative control, suggesting that the observed changes were related to the presence of the solvent.
5. Increased median developmental stage (59 vs. 57 in the negative control). Median NF stage of the solvent control was also 59, suggesting that the observed changes were related to the presence of the solvent.
6 Day 21 HLL of the solvent control was significantly increased by 47% compare to the negative control, suggesting that the observed changes were related to the presence of the solvent. 7 Day 7 and 21 SVL of the solvent control was increased marginally ($p = 0.053$) by 11 and 5%, respectively, relative to the negative control. Day 7 and 21 BW of the solvent control were increased by 28% (NS) and 22% ($p<0.05$), respectively, relative to the negative control. Increased body weight on Day 7 (↑40 and 54%) and Day 21 (↑20 and 35%) in the low- and medium-dose groups, respectively. This suggests that the observed changes in growth were related to the presence of the solvent.
P Positive finding
N Negative finding NE Not examined

2.6.9 Summary of toxicological data on impurities and metabolites

For information on impurities, refer to Document J.

The safety of two newly-identified metabolites of flutolanil requires investigation. These are 2 (trifluoromethyl)-benzamide (coded M-101) and 2-(trifluoromethyl)-benzoic acid (coded M-102), and arise from cleavage of the amide bridge in the flutolanil molecule. These compounds have been detected as minor metabolites in rats, appearing in urine at 0.05 to 0.08% of administered radioactivity at an oral dose of 20 mg/kg ([redacted] 2012, B.6.1.1.3). The metabolism was indicated in earlier studies not to be dependent on dose.

In support of re-approval of flutolanil, a Letter of Access has been obtained permitting access to relevant data from the dossier supporting approval of the product fluopyram. Although the fluopyram dossier does not contain studies specifically on M-101 or M-102 alone, the ADME studies indicate that fluopyram is metabolized such that the animals are exposed to considerably higher levels of M-101 and M-102 than is the case with flutolanil.

An ADME study by [redacted] (2008) with fluopyram (DAR B.6.1.1) used compound labelled in the appropriate phenyl ring, and showed that at single dosages of 5 or 250 mg/kg the urine contained 16 to 25% of M-101 (termed 'fluopyram-benzamide') and 4 to 7% of M-102 ('fluopyram-benzoic acid') in terms of percentage of administered radioactivity. Meanwhile, in the ADME study with flutolanil ([redacted] 2012, B.6.1.1.3), again using appropriately labelled material, a 20 mg/kg dose of flutolanil resulted in a urine content of 0.06% of M-101 and 0.05 to 0.08% of M-102 in terms of percentage of administered radioactivity. This indicates that in the fluopyram studies, rats would have been exposed to levels of these two metabolites greatly exceeding the levels obtained with flutolanil (by a factor of at least 250 for M 101 and at least 50 for M-102, assuming that the excreted amounts adequately reflect internal dosage).

The preceding indicates that the rat studies with fluopyram provide adequate toxicological cover for the metabolites M-101 and M-102, in support of the flutolanil re-approval. An overall NOAEL of 12.5 mg/kg/day was determined for the short-term toxicity of fluopyram, from a 90-day rat study, while the

overall NOAEL for long-term toxicity/carcinogenicity was 1.2 mg/kg/day, again from a rat study. For flutolanil, the overall NOAEL (short-term toxicity) is 37 mg/kg/day, from a 90-day rat study, while the long-term NOAEL is 8.7 mg/kg/day, again from a rat study.

M-101

Acute oral toxicity

The acute oral LD50 of 2-(trifluoromethyl)-benzamide (M-101) in female rats was estimated to be greater than 300 mg/kg, but less than 2,000 mg/kg.

Table 2.6.9.1-1: Summary of acute oral toxicity of M-101

Test Species/Sex	Result (LD50)	Remarks	Reference
Female Sprague-Dawley	300 – 2000 mg/kg bw	Based on the outcome of the study, 2-(trifluoromethyl)-benzamide should be classified as harmful if swallowed (H302).	[redacted] (2011)

Dose-repeated toxicity studies

In rats exposed to M-101 for 28 or 29 days a slight depression of body weight gain was observed in both sexes at 800 ppm and food consumption was depressed in the first week of treatment at 800 ppm. There were no treatment related ophthalmological findings. At the 800 ppm group small but significant hematological findings were observed which were considered treatment related. In males and females of the 800 ppm group, enlargement, accentuated lobular pattern and dark colouration of the liver were observed. The incidence of discolouration in the kidneys was increased significantly in males, and 2 males showed enlargement of the kidneys, while 1 male showed enlargement of the thyroid glands, but there were no similar changes in females. In the 200 ppm group, there were no statistically significant changes, but some changes were thought to be related to administration of the test item: accentuated lobular pattern in 1 male and 1 female, and discolouration of the kidneys in 2 males. In the 50 ppm group, there were no abnormalities in males or females. In the 200ppm and 800ppm significant increases in the absolute and relative weight of the liver, kidneys and thyroid glands were observed. In the 800ppm group also increased testis weights were observed. Histopathology and immunohistochemistry revealed effects on the kidney (excessive accumulation of hyaline droplets, tubular epithelial cell; necrosis / degeneration, renal tubules; basophilic, renal tubules) in male rats dosed 200ppm and 800ppm M-101. Excessive accumulation of hyaline droplets, tubular epithelial cell was also seen in male rats dosed 50ppm M-101. These effects were not observed in female rats. In both males and females effects on the liver were observed (hypertrophy, hepatocyte, centrilobular) following treatment with 200ppm and 800ppm. The NOAEL for M-101 in the diet of rats was 50 ppm, equivalent to an average of 4.2 mg/kg/day for males, 4.4 mg/kg/day for females. This excludes the α_{2u}-globulin deposition in male kidneys, which is not relevant for human risk assessment.

Table 2.6.9.1-2: Summary of dose-repeated oral toxicity of M-101

Test Species/Sex	Exposure	NOAEL/ LOAEL	Remarks	Reference

	route, doses and duration	(mg/kg bw/day)		
Male and female Sprague-Dawley	Exposure via diet at concentrations of 0 (control), 50, 200 or 800 ppm for 28 or 29 days	NOAEL: 4.2 mg/kg bw	Study is considered acceptable.	[redacted] (2012)

Genotoxicity

The metabolite 2-(trifluoromethyl)-benzamide (M-101, 100% purity) was tested in a reverse mutation test using the pre-incubation procedure, with and without metabolic activation, in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, plus *Escherichia coli* WP2 uvrA. There was no significant increase in revertants in any of the bacterial strains, either with or without the S9 metabolic activation system, at any dosage of the test item, while the positive controls each showed the expected mutagenic activity. It was concluded that 2-(trifluoromethyl)-benzamide (M-101) was non-mutagenic in the bacterial test systems at up to 5000 µg/plate.

M-101 was assayed for the ability to induce mutation at the *tk* locus (5-trifluorothymidine [TFT] resistance) in mouse lymphoma cells using a fluctuation protocol. It was concluded that M-101 (2-(trifluoromethyl)-benzamide) did not induce mutation at the *tk* locus of L5178Y mouse lymphoma cells when tested at up to 10 mM for 3 h in the absence and presence of a rat liver metabolite activation system (S-9), and at up to toxic concentrations for 24 h in the absence of S-9.

Based on an in vitro chromosome aberration assay using duplicate human lymphocyte cultures prepared from the pooled blood of three male donors in a single experiment it was concluded that M-101 did not induce structural chromosome aberrations when tested up to a concentration equivalent to 10 mM (limit dose) in the absence or presence of a metabolic activation system (S-9).

Table 2.6.9.1-3: Results of *in vitro* and *in vivo* mutagenicity studies.

Test	Test system	Result	Remarks	Reference
	In vitro studies			
Ames	*Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 and *Escherichia coli* WP2 uvrA	negative	Study is considered acceptable	Inagaki, K (2011)
Mammalian gene mutation	mouse lymphoma L5178Y cells	negative	Study is considered acceptable	Lloyd, M (2016a)
Chromosome aberration	Human lymphocytes	negative	Study is considered acceptable	Lloyd, M (2016b)

M-102

Acute oral toxicity

The acute oral toxicity of M-102 was investigated in groups of 3 female Sprague-Dawley rats, using a dosage of 2000 mg/kg body weight (limit dose) in two successive dosing steps, based on the acute toxic class method. No mortality occurred and there were no abnormal clinical signs in any animal. Regular body weight gain was observed in all but one animal, which showed depressed gain on day 1 after dosing, but then gained weight thereafter. There were no gross pathological findings at necropsy after the 14-day post-dosing observation period. It was concluded that the acute oral LD_{50} for M-102 in rats was >2000 mg/kg body weight.

Table 2.6.9.1-4: Summary of acute oral toxicity of M-102

Test Species/Sex	Result (LD50)	Remarks	Reference
Female Sprague-Dawley rats	>2000 mg/kg	The study is considered acceptable. Based on the study no classification is required for acute oral toxicity.	[redacted] (2016)

Dose-repeated toxicity studies

M-102 (2-(trifluoromethyl)-benzoic acid, 100% purity) was mixed into powdered basal diet at concentrations of 0 (control), 600, 3000 or 15000 ppm and administered to test groups consisting of 10 male and 10 female Sprague Dawley rats, for 28 or 29 days. Achieved mean test item intake was 51.6-53.7, 252-269 and 1316-1359 mg/kg/day for males and females at the respective diet concentrations. During the treatment period, mortality and clinical signs were observed daily, and detailed clinical observations, body weights and food consumption were recorded weekly. Functional observations were conducted before treatment and in the 4th week of treatment for all animals. Ophthalmological examination was conducted before treatment for all animals and in the 4th week of treatment for all animals in the control and 15000 ppm dose groups. Urinalysis, haematology, blood chemistry, necropsy and organ weight measurements were conducted at the 4th week of treatment for all animals. Histopathological examination was performed for all animals in the control and 15000 ppm dose groups, while only organs with gross pathological findings were examined for the 600 and 3000 ppm groups.

Males receiving 15000 ppm showed increased liver weight. These males also showed an apparent increase of motor activity, but this was considered in context unlikely to be an effect of treatment. In blood chemistry, changes consistent with effects on the liver were noted in these animals, such as increase of ALT, Alb and A/G ratio and decrease of TG. Meanwhile, females at this dose level showed decreases of RBC, Hb and Ht in haematology, suggestive of mild anaemia. There was no evidence of treatment effect in either sex at the 600 or 3000 ppm dosages.

A NOAEL for M-102 administered in the diet to rats for 28-29 days was 3000 ppm, equivalent to 252 or 269 mg/kg/day for males and females respectively.

Table 2.6.9.1-5: Summary of dose-repeated oral toxicity of M-102

Test Species/Sex	Exposure	NOAEL/ LOAEL	Remarks	Reference

	route, doses and duration	(mg/kg bw/day)		
Male and female Sprague Dawley rats	Via diet at concentrations of 0 (control), 600, 3000 or 15000 ppm for 28 or 29 days	NOAEL: 252 mg/kg bw/day	Study is considered acceptable	[redacted] (2010)

Genotoxicity

The metabolite M-102 (2-(trifluoromethyl)-benzoic acid), 99.3% purity, was tested in a reverse mutation test, with and without metabolic activation, in *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535, TA1537 and TA1538. It was concluded that M-102 (2-(trifluoromethyl)-benzoic acid) was non-mutagenic in the bacterial test systems at up to 5000 µg/plate, under the conditions of the study.

M-102 was assayed for the ability to induce mutation at the *tk* locus (5-trifluorothymidine [TFT] resistance) in mouse lymphoma cells using a fluctuation protocol. It was concluded that M-102 induced mutation at the *tk* locus of L5178Y mouse lymphoma cells when tested up to toxic concentrations for 24 h in the absence of a rat liver metabolic activation system (S-9). Further, a preponderance of small colonies in the increases suggested a clastogenic effect, rather than gene mutation. In the same test system, M-102 did not induce mutation when tested up to a maximum concentration equivalent to 10 mM for 3 h in the absence or presence of S-9. Based ont his result, a complementary study was performed demonstrating that when tested at up to toxic concentrations for 24 h in the absence of S-9, there were no increases in mutant frequencies exceeding the global evaluation factor of 126 (compared to concurrent controls) in any treated cultures. There was a statistically significant linear trend ($p \leq 0.01$) with a maximum increase in mutant frequencies observed in any treated culture of approximately 95 (at 1500 µg/mL, the highest concentration analyzed, giving 10% relative total growth), but as this fell below the global evaluation factor of 126 the trend was considered not biologically relevant.

Based on a chromosome aberration test it was concluded that M-102 did not induce structural chromosome aberrations in human peripheral blood lymphocytes when tested up to a concentration equivalent to 10 mM (limit dose) in the absence or presence of a metabolic activation system (S-9). Although clastogenic effects were observed in the first local lymph note assay, this observation was not confirmed in the second local lymph note assay. Moreover, the in vitro chromosome aberration test no clastogenic effects were observed. Thus, based on a weight of evidence approach it was concluded that M-102 is not genotoxic.

Table 2.6.9.1-6: Results of *in vitro* and *in vivo* mutagenicity studies.

Test	Test system	Result	Remarks	Reference
	In vitro studies			
Ames	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and TA102	negative	Study is considered acceptable	Lloyd, M (2016c)

Mammalian gene mutation	Mouse lymphoma L5178Y cells	positive in the absence of S9	Study is considered acceptable	Lloyd, M (2016d)
Mammalian gene mutation	Mouse lymphoma L5178Y cells	negative	Study is considered acceptable	Lloyd, M (2016e)
Chromosome aberration test	Human lymphocytes	negative	Study is considered acceptable	Lloyd, M (2016f)

Reference values for M-101 and M-102

Both M-101 and M-102 occur at <10% in urine following flutolanil administration. Therefore, the reference values determined for flutolanil are not considered applicable to these metabolites.
A full data package is not available for metabolites M-101 and M-102. However, for both metabolites a 28 day study is available that can be used to set a reference value. Based on the NOAEL 0f 4.2 mg/kg bw/day the metabolite M-101 appears to be more toxic than the parent.

The ADI was set by taking into account the NOAEL values from the 28-day studies for M-101 and M-102, a safety factor of 100 to account for inter- and intra-individual differences and an additional safety factor of 6 was applied to take into into account the extrapolation from the short term study from which the NOAEL was derived to chronic exposure, and an additional factor of 3 to account for the limited data package, resulting in a total safety factor of 1800.

ADI M-101: 4.2 mg/kg bw/day / 1800 = **0.002 mg/kg bw/day**
ADI M-102: 252 mg/kg bw/day / 1800 = **0.14 mg/kg bw/day**

Based on the limited data package for both metabolites, an ARfD cannot be set for metabolites M-101 and M-102.

M2 and M4
The metabolites M2 and M4 are considered as being the main rat metabolites. Formation of metabolite M2 and M4 in the metabolism of flutolanil was found to be >10% and therefore it can be concluded that the toxicological studies with flutolanil provide adequate information to cover for M2 and M4.

2.6.10 Summary of medical data and information

Based on medical surveillance from manufacturing plants, there have been no incidences or indications (including sensitization) related to flutolanil.

2.6.11 Toxicological end point for assessment of risk following long-term dietary exposure – ADI

For establishing an ADI for flutolanil, chronic studies are considered to be the most relevant. Considering all studies available, the chronic study providing the lowest NOAEL is the 104 week

during study with rats (NOAEL 8.7 mg/kg bw/day, based on slight anaemia in females and histopathological splenic changes observed in males). Using a safety factor of 100, results in an ADI of 0.09 mg/kg bw/day. The ADI has not changed from the previous Annex 1 evaluation.

2.6.12 Toxicological end point for assessment of risk following acute dietary exposure – ARfD (acute reference dose)

There is no need to set an ARfD for flutolanil in view of its low acute toxicity, the absence of clinical signs and effects pertinent to administration of single doses. However, the effects observed observed in the developmental studies (reorptions and embryonal death) in the absence of maternal toxicity are considered relevant for setting an ARfD.

Based on the NOAEL of 40 mg/kg bw/d from the developmental rabbit study in which resportions and deaths occurring in 5 different litters, and a safety factor of 100 the ARfD is determined to be 0.4 mg/kg bw/day.

2.6.13 Toxicological end point for assessment of occupational, bystander and residents risks – AOEL

For establishing an AOEL for flutolanil, semi-chronic studies are considered to be the most relevant. Considering all studies available, the semi-chronic study providing the lowest NOAEL is the 90 days study with rats (NOAEL 37 mg/kg bw/day, based on increased thyroid/parathyroid weight at 299 mg/kg/day). Using a safety factor of 100, and correcting for oral absorption (approximately 70%), results in an AOEL of 0.26 mg/kg bw/day. The AOEL is thus somewhat lower than the value derived in the previous Annex 1 evaluation.

Based on the effects observed observed in the developmental studies (reorptions and embryonal death) in the absence of maternal toxicity are considered relevant for setting an Acute AOEL (AAOEL). Based on the NOAEL of 40 mg/kg bw/d from the developmental rabbit study in which resportions and deaths occurring in 5 different litters, a safety factor of 100, and correcting for the oral absorption of 70%, the AAOEL is determined to be 0.28 mg/kg bw/day.

2.6.14 Summary of product and risk assessment

Exposures and risk assessments are specified in Table 2.6.14-1, 2.6.14-2 and 2.6.14-3.

Operator

Estimations of potential operator exposure for the formulation MONCUT 40SC applied by means of broadcast application are made using the EFSA AOEM model.

Table 2.3.6-1 Operator exposure and risk assessment

Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)[1]	% of AOEL[2]
tractor mounted boom sprayer application outdoors to low crops – tulip, iris			

6 kg MONCUT 40SC/ha corresponding to 2.76 kg flutolanil per ha			
AOEM, longer term - 50 ha/day - 60 kg operator	No PPE (work wear)	1.185	**456**
	PPE (work wear and gloves during mixing, loading and application)	0.059	23

[1] Systemic exposure based on dermal absorption of 25% for mixing and loading and 70% for application of MONUCUT 40SC for application in tulip and iris.

There is no satisfactory model to estimate the application of flutolanil to potato tubers using conventional canopied hydraulic or spinning disc equipment. A study has been conducted to measure the exposure to operators using this equipment. Taking into account the results from the operator exposure study, the operator exposure to flutolanil can be calculated as follows:

Normal workwear worn, gloves not worn:

((Actual dermal exposure excluding hands + potential hand exposure) x dermal absorption) + inhalation exposure/bodyweight)

((10.0926 + 150.8753) x 0.70) + 0.868 / 60 = 1.89 mg/kg

This is equivalent to 727% of the AOEL. Therefore the risks to operators not wearing gloves is considered to be unacceptable.

Normal workwear and gloves are worn:

((Actual dermal exposure excluding hands + actual hand exposure) x dermal absorption) + inhalation exposure/bodyweight)

((10.0926 + 4.2398) x 0.70) + 0.868 / 60 = 0.18 mg/kg

This is equivalent to 69% of the AOEL.

Bystander and resident

Table 2.3.6-2 Bystander and resident exposure and risk assessment

Exposure group	Exposure route	Total absorbed dose (mg/kg bw/day)[1]	% of AOEL
tractor mounted boom sprayer application outdoors to low crops – tulip and iris			
6 kg MONCUT 40SC/ha corresponding to 2.76 kg flutolanil per ha			
Resident, child	Spray drift	0.3458	**132.99**
	Vapour	0.0011	0.41
	Surface deposits	0.0297	11.42
	Entry into treated crops	0.3260	**125.39**
	All pathways (mean)	0.4732	**181.99**
Resident, adult	Spray drift	0.0828	31.83
	Vapour	0.0002	0.09
	Surface deposits	0.0132	5.06

	Entry into treated crops	0.1811	69.66
	All pathways (mean)	0.1936	74.46

A bystander risk assessment is required for PPPs that have significant acute toxicity or the potential to exert toxic effects after a single exposure. Since for flutolanil an AAOEL was determined (0.28 mg/kg bw/day) a risk assessment was made for the bystander using this value.

Table 2.3.6-3 Bystander exposure prediction and risk assessment

Exposure group	Exposure route	Total absorbed dose (mg/kg bw/day)[1]	% of AOEL
tractor mounted boom sprayer application outdoors to low crops – tulip and iris			
6 kg MONCUT 40SC/ha corresponding to 2.76 kg flutolanil per ha			
Resident, child	Spray drift	0.7836	**279.86**
	Vapour	0.0011	0.38
	Surface deposits	0.0895	31.96
	Entry into treated crops	0.3260	**116.44**
Resident, adult	Spray drift	0.0002	76.12
	Vapour	0.0397	0.08
	Surface deposits	0.1811	14.17
	Entry into treated crops	0.7836	64.69

The resident and bystander exposure estimates show that the exposure exceeds the AOEL or AAOEL for children. However, for the use on flower bulbs, MONCUT 40SC is applied to bare soil with broadcast spray equipment and incorporated into the soil pre planting (BBCH00). Therefore, the scenario 'entry into treated crops' is not considered relevant for the intended application of MONCUT 40SC and the EFSA AOEM thus represents an overestimation.

For adults it is concluded that there is no undue risk to any bystander or residents after accidental exposure to MONCUT 50 SC.

For children a refined risk assessment is made considering the use of vehicle mounted drift reduction.

Table 2.3.6-4 Resident exposure prediction and risk assessment – drift reduction

Exposure group	Exposure route	Total absorbed dose (mg/kg bw/day)[1]	% of AOEL
tractor mounted boom sprayer application outdoors to low crops – tulip and iris			
6 kg MONCUT 40SC/ha corresponding to 2.76 kg flutolanil per ha			
Resident, child	Spray drift	0.1729	66.49
	Vapour	0.0011	0.41
	Surface deposits	0.0148	5.71

	Entry into treated crops	0.3260	**125.39**
	All pathways (mean)	0.3671	**141.19**

Table B.6.4.2-4 Bystander exposure prediction and risk assessment – drift reduction

Exposure group	Exposure route	Total absorbed dose (mg/kg bw/day)[1]	% of AOEL
tractor mounted boom sprayer application outdoors to low crops – tulip and iris			
6 kg MONCUT 40SC/ha corresponding to 2.76 kg flutolanil per ha			
Resident, child	Spray drift	0.3918	**139.93**
	Vapour	0.0011	0.38
	Surface deposits	0.0447	15.98
	Entry into treated crops	0.3260	**116.44**

The resident exposure estimates for children using drift reduction show that the exposure still exceeds the (A)AOEL (141% and 116% of the AOEL). However, as indicated above for the use on flower bulbs, MONCUT 40SC is applied to bare soil with broadcast spray equipment and incorporated into the soil pre planting (BBCH00). Children are thus not expected to be exposed to deposits present on treated crops and the scenario 'entry into treated crops' can thus be considered not relevant. For residential children it can thus be concluded that there is no undue risk after accidental exposure to MONCUT 40SC following exposure via spray drift, vapour and surface deposits provided that drift reduction is applied. However, for bystanders the exposure to children resulting from drift still exceeds the AAOEL when using drift reduction (140% of the AAOEL).

Worker

The application of Moncut 40SC to flower bulbs is as an overall spray to bare soil followed by incorporation to a depth of at least 10 cm. There is no requirement for workers to re-enter the treated area after application, therefore an assessment of the risks to workers is not considered necessary.

Moncut 40SC that is applied to potato tubers during the planting process are covered by soil immediately they fall to the ground. The soil is formed into ridges 15–20 cm high, therefore workers re-entering the treated field are not at risk of exposure to Moncut 40SC.

Application to potatoes by conventional canopied hydraulic or spinning disc equipment involves tubers being treated under a canopy and then moved by conveyor belt into containers. There is no acceptable model available to estimate the exposure of workers to this type of activity. Based on the outcomes of a study the following exposure estimates were made:

Worker wering normal workwear worn, gloves not worn:

((3.376 + 150.875) x 0.70) + 0.868 / 60 = 1.81 mg/kg

This is equivalent to 696% of the AOEL. Therefore the risks to workers not wearing gloves is considered to be unacceptable.

Worker wearing normal workwear and gloves:
((3.376 + 1.171) x 0.70) + 0.868 / 60 = 0.07 mg/kg

This is equivalent to 27% of the AOEL.

Conclusions on risk assessments for operators, bystanders and workers

Operator
The EFSA AOEM estimates show that for the intended use of the formulation MONCUT 40SC is considered acceptable provided that PPE is worn.

Bystander and residents
The bystander and resident exposure estimates made for adults show that the exposure is below the AOEL. Therefore, It is concluded that there is no undue risk to any adult bystander or adult residents after accidental exposure to MONCUT 40SC. However, for children no safe use can be indicated and therefore the applicant is requested to provide a refined risk assessment or drift reduction needs to be applied.

Worker
It is concluded that there is no unacceptable risk anticipated for the protected worker wearing gloves when re-entering crops treated with MONCUT 40SC on the day of application.

2.7 Residues

2.7.1 Summary of storage stability of residues

For the initial approval of flutolanil, storage stability was demonstrated in plant matrices for a period up to 18 months at -18ºC in high starch content matrices (wheat grain) and 67 months (potato) and high oil content matrix (oilseed rape). Storage stability was also demonstrated in wheat straw up to 18 months at -18ºC.
For the renewal of flutolanil, the notifier submitted additional storage stability studies for flutolanil and metabolites M-2, M-4, M-101, M-102 and their conjugates in high starch content matrix (potato) and high water content matrix (spinach).
No storage stability in animal matrices has been evaluated during the initial peer review.
For the renewal of flutolanil, the notifier submitted storage stability studies with flutolanil and its metabolites M-2, M-4, M-7, M-101 and M-102 in potato, spinach, whole milk and animal products. Storage stability of conjugates has not been investigated separately. Extrapolation of stability of the metabolites to their conjugates is acceptable, since conjugates are expected to be not less stable.

The storage stability data for flutolanil are summarised in table 2.7.1-1 and for flutolanil metabolites in table 2.7.1-2.

Table 2.7.1-1: Summarised storage stability results for flutolanil in plant and animal matrices

Matrix	Length of storage stability (months)	Source
Potato	67	Original DAR, RAR: B.7.1.1
Potato	18	Addendum 1A to the DAR, RAR: B.7.1.2
Potato	12	RAR: B.7.1.3
Wheat grain	18	Addendum 1A to the DAR, RAR: B.7.1.2
Wheat straw	18	Addendum 1A to the DAR, RAR: B.7.1.2
Rape	18	Addendum 1A to the DAR, RAR: B.7.1.2
Spinach	12	RAR: B.7.1.3
Whole milk	3.7	RAR: B.7.1.4
Muscle (beef)	4	RAR: B.7.1.5
Fat (beef)	not stable	RAR: B.7.1.5
Liver (chicken)	4	RAR: B.7.1.5
Egg	4	RAR: B.7.1.5
Muscle (bovine)	2.5	RAR: B.7.1.7
Liver (bovine)	3	RAR: B.7.1.7
Kidney (bovine)	2.5	RAR: B.7.1.7
Fat (bovine)	2.5	RAR: B.7.1.7
Milk	3	RAR: B.7.1.7

Table 2.7.1-2: Summarised storage stability results for flutolanil metabolites: M-2, M-4, M-7, M-101 in plant and animal matrices

Matrix	Length of storage stability (months)	Source
Metabolite M-2		
Potato	9	RAR: B.7.1.3
Spinach	9	RAR: B.7.1.3
Whole milk	3.7	RAR: B.7.1.4
Muscle (beef)	4	RAR: B.7.1.5
Fat (beef)	Not stable	RAR: B.7.1.5
Liver (chicken)	4	RAR: B.7.1.5
Egg	4	RAR: B.7.1.5

Muscle (chicken)	14	RAR: B.7.1.6
Liver (chicken)	14	RAR: B.7.1.6
Muscle (bovine)	Not stable	RAR: B.7.1.7
Liver (bovine)	3	RAR: B.7.1.7
Kidney (bovine)	2.5	RAR: B.7.1.7
Fat (bovine)	2.5	RAR: B.7.1.7
Milk	3	RAR: B.7.1.7
Metabolite M-4		
Potato	12	RAR: B.7.1.3
Spinach	12	RAR: B.7.1.3
Whole milk	3.7	RAR: B.7.1.4
Muscle (beef)	4	RAR: B.7.1.5
Fat (beef)	Not stable	RAR: B.7.1.5
Liver (chicken)	4	RAR: B.7.1.5
Egg	4	RAR: B.7.1.5
Muscle (chicken)	14	RAR: B.7.1.6
Liver (chicken)	14	RAR: B.7.1.6
Muscle (bovine)	2.5	RAR: B.7.1.7
Liver (bovine)	3	RAR: B.7.1.7
Kidney (bovine)	2.5	RAR: B.7.1.7
Fat (bovine)	2.5	RAR: B.7.1.7
Milk	3	RAR: B.7.1.7
Metabolite M-7		
Whole milk	3.7	RAR: B.7.1.4
Muscle (beef)	4	RAR: B.7.1.5
Fat (beef)	Not stable	RAR: B.7.1.5
Liver (chicken)	4	RAR: B.7.1.5
Egg	4	RAR: B.7.1.5
Muscle (bovine)	Not stable	RAR: B.7.1.7
Liver (bovine)	3	RAR: B.7.1.7
Kidney (bovine)	2.5	RAR: B.7.1.7
Fat (bovine)	2.5	RAR: B.7.1.7
Milk	3	RAR: B.7.1.7
Metabolite M-101		
Potato	12	RAR: B.7.1.3
Spinach	12	RAR: B.7.1.3
Eggs	14	RAR: B.7.1.6
Muscle (bovine)	2.5	RAR: B.7.1.7
Liver (bovine)	3	RAR: B.7.1.7
Kidney (bovine)	2.5	RAR: B.7.1.7

Fat (bovine)	2.5	RAR: B.7.1.7
Milk	3	RAR: B.7.1.7
Metabolite M-102		
Potato	12	RAR: B.7.1.3
Spinach	12	RAR: B.7.1.3

To conclude, storage stability of flutolanil has been demonstrated in potato (high starch matrix) up to 67 months, wheat grain (high starch matrix) and oil seed rape (high oil matrix) up to 18 months and spinach (high water matrix) up to 12 months.
Storage stability of metabolites M-4 and M-101 has been demonstrated in potato (high starch matrix) and spinach (high water matrix) for 12 months.
In animal commodities flutolanil was demonstrated to be stable up to 4 months in beef muscle, chicken liver and eggs, 2,5 months in bovine kidney. In fat flutolanil was stable 2.5 months and in milk 3 months. Metabolite M-4 was stable in milk 3 months, in beef muscle 4 months and in chicken muscle 14 months and in liver (chicken) 14 months.
Metabolite M-101 was stable in eggs 14 months, in muscle (bovine), liver (bovine), kidney (bovine) up to 2.5 months and in milk 3 months. Acceptance of the results from the studies evaluated in Volume 3, B.7.1.4 and B.7.1.5 should await submission of the analytical method validation.

2.7.2 Summary of metabolism, distribution and expression of residues in plants, poultry, lactating ruminants, pigs and fish

During the initial EU review of the active substance flutolanil, the metabolism in plant has been studied in root crops (potatoes), pulses and oilseed (peanut) and (cereal) rice. In animal matrices, metabolism has been studied in goats and laying hens.
For the purpose of the renewal new metabolism studies have been submitted: in plants in leafy crops (cabbage), miscellaneous crops (paddy rice) and root crops (potatoes). New metabolism studies have also been submitted in animal matrices: in laying hens and two in lactating ruminants.

Plant commodities

Potato (root and tuber vegetable group)

In the potato study evaluated during the initial peer review, three different treatment regimes were investigated: row treatment, with an application rate of 4.5 kg active substance/ha (12N) on the day of planting and two seed treatments 120 and 360 g/ton (topical application, corresponding to 1.3N and 3.9N), with harvest of mature potato tubers (PHI 131 days) and harvest of immature potato tubers (PHI 52 days), respectively. After the seed treatment and subsequent harvest of immature tubers, parent compound flutolanil was the most present (57% TRR, 16 µg/kg parent eq). In mature tubers after seed treatment parent compound flutolanil, Metabolite A and Metabolite B have been identified (16%, 23% and 14% TRR, respectively). In mature tuber after the row treatment flutolanil was the most present residue (35% TRR, 42 µg/kg parent eq), together with Metabolite A and B, 21% TRR (24 µg/kg parent eq) and 6% TRR (4 µg/kg parent eq), respectively. It was further concluded in the study that

metabolite A and metabolite B represent conjugates of M-4 (desisopropyl flutolanil) and M-2 (hydroxyl-flutolanil), respectively.
In the newly submitted metabolism study on potatoes, flutolanil was applied on seed potatoes with an application rate of 553 g as/ha (1.4N) and into soil (in furrow treatment) with an nominal application rate of 2100 g as/ha (5.7N for renewal cGAP and 1N for cGAP proposed during MRL application; actual rate was 2530 g as/ha, which corresponds to 1.2N). Residues were determined in immature foliage, immature tuber and mature tuber of the potato plants.
At harvest seed treated immature potato tubers and mature tuber contained TRRs of 0.065 mg eq./kg and 0.067 mg eq./kg, respectively. Extractable radioactive residues were 84.7% and 74.7% in immature and mature tubers, respectively.
The major components detected in potatoes grown from seed treated tubers were: for immature tubers flutolanil (47.8% TRR, 0.031 mg/kg) and metabolite M-102 (20% TRR, 0.013 mg eq./kg). For mature tubers the major identified compounds were parent flutolanil (19.4% TRR, 0.013 mg eq./kg), metabolite M-102 (16.4 TRR, 0.011 mg eq./kg), metabolite M-101 (11.9% TRR, 0.008 mg eq./kg) and metabolite M-4 free and conjugated (<10.5 % TRR, 0.007 mg eq./kg). In seed treated tubers unextracted residues bound in post extracted-solids (PES, non-extractable residues) were <0.05 mg eq./kg and were therefore not characterised further.
At harvest, in furrow treated immature tubers and mature tubers contained TRRs of 0.680 mg eq./kg and 0.486 mg eq./kg, respectively. Extractable residues were 73.6% and 73.2% of the TRR in immature and mature tuber, respectively. The major components detected in potatoes grown from in furrow treatment were in immature potatoes: flutolanil (21.5% TRR, 0.146 mg eq./kg), metabolite M-102 (24.5% TRR, 0.167 mg eq./kg) and metabolite M-101 (10.9% TRR, 0.074 mg eq./kg). In mature tubers flutolanil was not the most abundant residue (9.9% TRR, 0.048 mg/kg), while metabolite M-102 was the major compound (38.3% TRR, 0.186 mg eq./kg). In furrow treated tubers PES were up to 26.7% TRR in mature tubers. PES were further characterised by incubating with cellulase, followed by refluxing with 6N HCl and 10N NaOH. Metabolites M-101 and M-102 were identified from organic layer: 1% TRR and 7% TRR, respectively.

Peanut (oilseed)
Metabolism in peanuts after foliar spray has been investigated during the initial peer review. In each plant tissue (vines, hulls, nuts), 57-91% TRR was recovered as extractable residue. In vines and hulls, flutolanil (conjugated and unconjugated), metabolite M (conjugated and unconjugated) were the most abundant residues. In nuts, parent compound flutolanil was present in very minor concentration (1% TRR, 0.004 mg/kg). The major part of radioactivity in nuts was localised in unidentified conjugates or unconjugated metabolites (49%). Attempts to identify the metabolites were done, however were not very successful due to difficult oil matrix. Characterisation of those conjugated and unconjugated metabolites was performed. Among the conjugated compounds identified, metabolite M-4 was present (10.2% TRR, 0.04 mg eq./kg). Indications were that these fractions may have resulted from a strong association of the flutolanil residue with peanut lipids. Nevertheless, this conjugated material (49.4% TRR) was characterised as hexane soluble (28.7%), sediment from trituration (2.2%), highly polar column fraction 1 (9.0%), residual hydrolysed aqueous (2.6%), and minor components of post-

hydrolysis organic soluble (from HPLC, 6.9%). Residue levels were also compared with those obtained by a multi-residue method in which flutolanil related metabolites are converted to trifluorobenzoic acid and analysed by GC-MS. The total extractable residue in each tissue (including aqueous soluble or unidentified radioactivity by HPLC/TLC plus Metabolite A & B) showed excellent accountability (89-106%) with the multi-residue method of analysis.

Rice (miscellaneous crop)

In the rice metabolism study evaluated during the initial peer review, rice plants received two spray applications with an overall dose of 1.06 kg/ha. In mature rice grain, foliage and husk from 76 to 96.8 % of the TRR has been released by solvent extraction. Unextracted residues in PES accounted for 15.4% TRR in foliage collected below the water line. 3.2% TRR in foliage above the water line, 11.8 % in husks and 24.1% in grain.

Flutolanil was the major residue found in foliage (up to 93.2% TRR, 19.16 mg/kg), husks (78.3%TRR, 5.63 mg/kg) and grain (64 % TRR, 0.20 mg/kg). Metabolite M-4 was a minor metabolite up to 5.3% TRR (0.38 mg/kg) in husks and 2.3% TRR (0.01 mg/kg) in rice grain.

In newly submitted study, metabolism in rice was investigated as paddy application (phenyl and aniline labelled flutolanil) with an application rate of 8.4 kg as/ha and as foliar application (phenyl labelled flutolanil) with an application rate of 1.5 kg as/ha (in total). TRR in brown rice grain ranged from 3.06 mg eq./kg in plants paddy-treated with [phenyl-U-^{14}C]-flutolanil to 2.12 mg eq./kg in plants paddy-treated with [aniline-U-^{14}C]-flutolanil. Non-extractable residues in rice grain were only maximally 0.3% TRR (0.01 mg eq/kg) after paddy application. Extractable residues were 56.3%, 80.73% and 96.7% TRR in hulls, straw and grain, respectively (phenyl label) and 56.3%, 88%, 100% in hulls, straw and grain (aniline label), respectively for paddy-treated rice. Unextracted bound residues in PES were detected in straw (11.10-19.27 % TRR) and hull samples (up to 43.75% TRR) for paddy-application of phenyl-labelled flutolanil. The majority of radioactivity was not solubilized with either cellulase or hydrolytic treatment with acid and alkaline. The radioactivity released by strong alkaline hydrolysis was identified as metabolite M-4.

In rice grain treated by paddy application flutolanil, metabolite M-4 and M-4 glycoside conjugate represented 47.36 (1.45 mg/kg) to 82.95% (1.76 mg/kg) TRR, 9.78 (0.3 mg/kg) to 10.02% (0.21 mg/kg) TRR and 1.82 (0.04 mg/kg) – 2.94% (0.09 mg/kg) TRR, respectively. Metabolite M-6 was also observed in concentration: 4.33% TRR (0.13 mg eq/kg) in phenyl label and 4.16% TRR (0.09 mg/kg) aniline label.

In rice grain from plants treated with labelled phenyl, the phenyl ring metabolites M-101 and M-102 also formed significant part of residues: 23.23% (0.71 mg/kg) and 10.80% (0.33 mg/kg) TRR, respectively. No specific aniline ring metabolites were detected.

Paddy treated straw contained TRRs up to 188.70 mg eq./kg. The major components of the rice straw were flutolanil (up to 43.61%, 82.30 mg/kg), metabolite M-4 free up to 7.41% TRR (11.2 mg eq./kg) and M-4 glycoside conjugate up to 29.30% TRR (44.32 mg eq/kg). Additional amounts of M-4 were released from bound plant residues in straw after refluxing in strong base. Metabolite M-101 was detected at significant level of 1.47 mg eq./kg (0.78% TRR) and metabolite M-102 at level 0.73 mg eq./kg (0.39% TRR).

Additionally, in rice straw a number of other metabolites were detected in significant amounts (above the 0.05 mg/kg): M-6 (up to 1.40 mg eq./kg, 0.74%TRR), M-7 (up to 0.91 mg eq./kg, 0.6% TRR), M-11 (up to 0.49 mg eq./kg, 0.32%TRR). Since rice straw can be used as part of animal diet in Europe, this residue might be of significance when rice is treated with flutolanil.
In rice grain treated as foliar application flutolanil was the major residue: 95.81% (0.09 mg/kg) TRR. All other metabolites in rice grain were below 10% (<0.01 mg/kg). Flutolanil was also the most prominent residue in straw (95.11% TRR, 17.18 mg/kg) and in hulls (99.49% TRR, 61.49 mg/kg) after the foliar application.
In addition, a number of minor metabolites (maximum 4.33% TRR) were observed in rice plants (paddy and foliar application); M-2, M-3 (both as free metabolite and conjugate), M-6, M-7 and M-11.

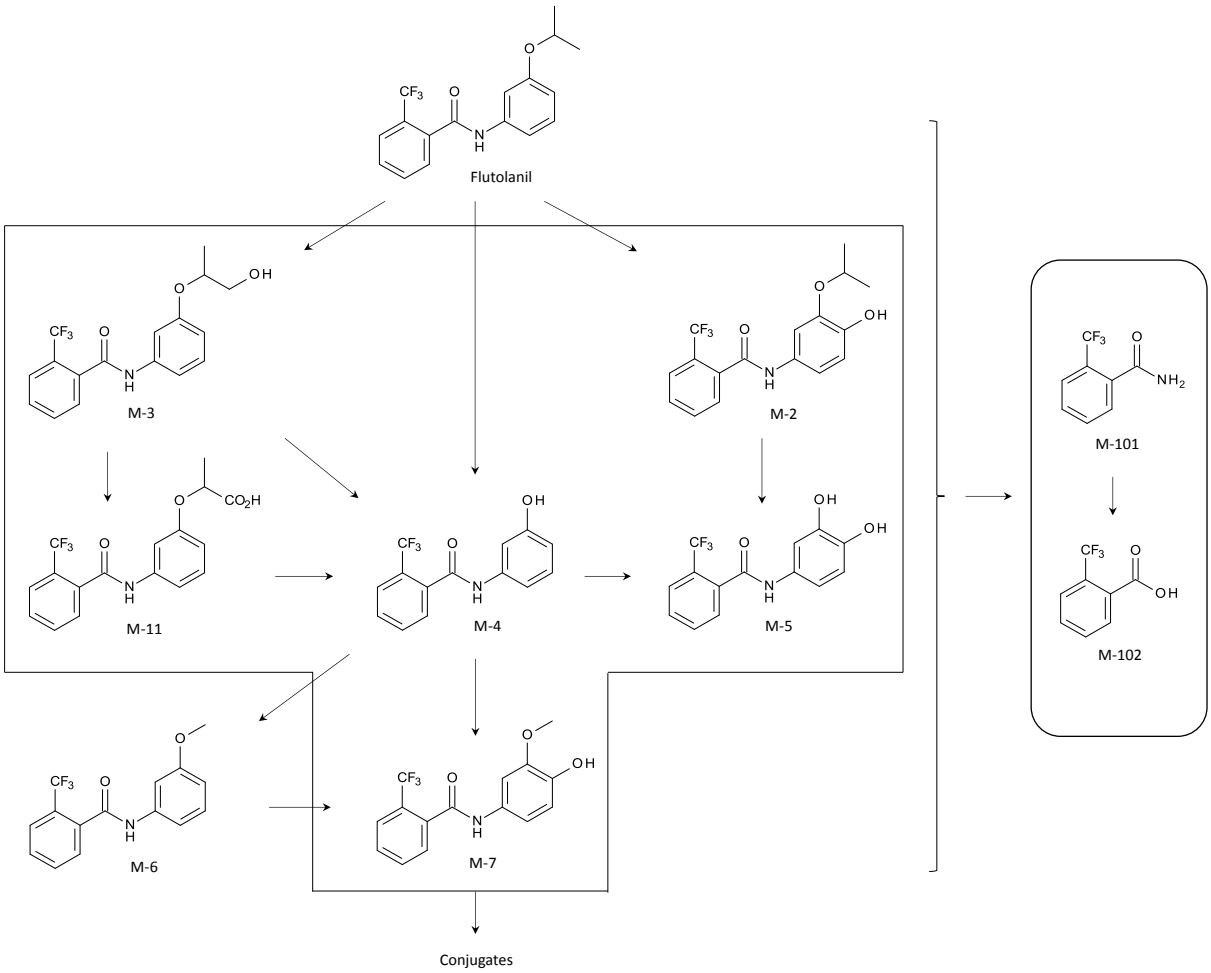
Cabbage
Flutolanil (phenyl and aniline label) has been applied to soil prior to transplanting cabbage with an application rate of 8 kg as/ha or treated cabbage plants received two foliar applications of flutolanil (phenyl label) at 1.8 kg as/ha in total.
Following soil application radioactive residues in immature cabbage heads ranged from 1.34 mg eq/kg (phenyl label) to 1.40 mg eq/kg (aniline label) and in mature cabbage heads from 0.21 to 0.26 mg eq/kg. Cabbage heads and outer leaves were extracted and analysed with between 79.2 to 97% of extractable residues. Unextracted bound residues in PES accounted for 9.93 – 20.81% TRR in cabbage heads and 2.97 – 6.12 % in outer leaves. PES residues were further characterised by cellulose and strong acidic/basic extractions.
Following foliar application of [phenyl-U-^{14}C]-flutolanil radioactive residues in the head and outer leaves of cabbage were 0.09 mg eq./kg and 90.89 mg eq./kg, respectively. In cabbage heads and outer leaves more than 99% of the TRR consisted of extractable residues, whereas minimal radioactivity was remaining in PES (maximum 1.1% TRR).
In cabbage treated by soil application the most prominent residues in both the head and outer leaves were: flutolanil, metabolite M-4 (free) and metabolite M-4 conjugated, representing 49.31 to 69.17% TRR (0.10 to 2.31 mg/kg), 5.19 to 8.51% TRR (0.01 to 0.26 mg eq/kg) and 13.84 to 25.14% TRR (0.04 to 0.79 mg eq/kg), respectively.
The major residue in cabbage treated by foliar application was flutolanil which formed 90.41 to 98.54 % TRR at harvest. Metabolite M-4 free and its glucoside conjugate was found to be a minor metabolite (7.57% TRR, sum of TRR's, <0.02 mg eq. /kg). In phenyl labelled treated cabbage, the phenyl ring metabolites M-101 and M-102 were found in trace amount (<1% TRR, < 0.01 mg eq./kg). In addition, M-2, M-3, M-5, M-6, M-7, M-11 were observed as minor metabolites (maximum 1.19% TRR).
The majority of post extraction solids (PES) in cabbage was identified as metabolite M-4, assumed to be released from residues strongly bound to biomolecules.

Overall conclusion on plants metabolism:
From the all available metabolism studies it can be concluded that flutolanil is mainly hydroxylated to metabolite M-4, followed by formation of its corresponding glycoside conjugates. Other (minor) metabolites (M-2, M-3, M-6, M-7 and M-11) were degraded form the parent compound by

hydroxylation (M-2, M-3) and carboxylation (M-11). Flutolanil is also further degraded to the metabolite M-101 by cleavage at the carboxamide, followed by its hydrolysis to M-102. Other minor metabolites (M-3, M-6, M-7 and M-11) were degraded form the parent compound. Proposed metabolic pathway is presented in a Figure 2.7.2-1.

Potatoes are the defended use during the flutolanil renewal. The metabolism of flutolanil (phenyl and aniline ring) has been investigated in potatoes as seed treatment and in-furrow applications to the soil at planting, covering the group of root and tuber vegetables. Based on the available metabolism studies, flutolanil was one of the major metabolites in potato tubers after seed treatment. Metabolites A and B, M-101 and M-102 were also found in comparable to flutolanil concentrations.
Flutolanil and metabolite M-102 were the most relevant residues in potato tubers after in-furrow treatment. Metabolite M-4 free and conjugated was detected at lower concentrations. Metabolite M-2 free and conjugated and M-101 were also detected in potatoes after in-furrow treatment however as minor metabolites.
The metabolic profile of flutolanil in all other crop groups: oilseed and pulses (peanut), leafy vegetables (cabbage) and miscellaneous crops (rice) was found to be qualitatively similar. Residues comprised mainly of flutolanil and metabolite M-4 free and conjugated. Additionally, in paddy treated rice the two phenyl ring metabolites M-101 and M-102 formed a significant part of the residues in brown rice , the metabolite M-6 was also observed. .

Figure 2.7.2-1: Proposed metabolic pathway of flutolanil in primary crops.



Animal commodities

Lactating ruminants

In the original DAR there was one goat metabolism study available. Due to limitations the study has not been considered acceptable.

In the first study submitted for the renewal, metabolism of aniline-labelled flutolanil has been studied in lactating goat after five consecutive daily oral doses at a rate of 13.26 mg/kg in the diet (equivalent to 0.27 mg/kg bw/day). Approximately 74% of the dose was recovered. Excretion of the active substance proceeded mainly via urine (55% dose). In faeces, excreted radioactivity accounted for 16% of the dose. A low amount of radioactivity was excreted in milk (<0.02% dose in milk fat and 0.3 % in the aqueous milk fraction) and 0.4% of the dose was detected in tissues. Radioactivity was detected in all tissues with the greater concentrations detected in kidney (0.377 mg eq/kg) and liver (0.23 mg eq/kg). Radioactivity detected in muscle (loin and flank) was very low (<0.01 mg/kg) and those samples were not further extracted.

In edible tissues, the majority of the radioactivity was successfully extracted: in milk aqueous fraction 100% TRR, liver 70% TRR, kidney 73% TRR and fat 100% TRR.

Residues bound in PES were the highest in the liver and kidney and were further extracted following treatment with protease enzyme, strong acid and strong base (only kidney).

In milk fat fraction flutolanil, free M-4, its sulfate ester and glucuronide conjugate represented 13.8% (0.012 mg eq./kg), 2.6% (0.002 mg eq./kg), 12.3% (0.011 mg eq./kg) and 15.9% TRR (0.014 mg eq./kg), respectively and overall accounted for 44.5% TRR. In the aqueous fraction of milk, the only major residues were M-4 sulfate and M-4 glucuronide conjugates, which represented 21.1% and 26.9% of the TRR (0.021 and 0.026 mg eq./kg) respectively.
In liver, flutolanil was detected at 4.9% TRR (0.011 mg/kg), metabolite M-4 with its sulfate and glucuronide conjugates accounted for 17.7% (0.041 mg eq./kg), 4.2% (0.01 mg eq./kg) and 13.1% (0.03 mg eq./kg) TRR, respectively. Metabolites M-2, M-3, M-6 and M-11 were detected as minor metabolites in liver (maximum 2,9% TRR, 0.007 mg eq./kg), together with a number of unidentified metabolites (maximum 3.6% TRR, 0.0083 mg/kg).
Flutolanil was a minor metabolite in kidney (0.3% TRR, 0.0013 mg/kg). The major residues in kidney were M-4 sulfate ester (22.4% TRR, 0.085 mg eq./kg) and M-4 glucuronide conjugate (23.4% TRR. 0.088 mg eq./kg), small amount of free M-4 were detected in kidney; 5.7%TRR, 0.022 mg eq./kg. Also traces of metabolites M-2 and M-11 were detected in kidney: maximum 6.1 % TRR (0.02 mg eq./kg).
The low residues in fat was composed of mainly flutolanil (44.7% TRR, 0.006 mg/kg), which was accompanied by small amounts of M-3 (5.3% TRR, <0.001 mg/ eq./kg) and M-4 (9.1% TRR, 0.001 mg eq./kg), none of which exceeded 0.01 mg/kg.
From the study it can be concluded that flutolanil and its metabolites were rapidly excreted by lactating goats with 74% of the administrated dose recovered in excreta (99% of the recovered dose), tissues (kidney, liver, fat and muscle) retained only low levels of radioactivity. There is no evidence of bioaccumulation of flutolanil residues in the goat.
In the second study submitted for the purpose of renewal, metabolism of phenyl-labelled flutolanil has been investigated in lactating goat after five consecutive daily oral doses at a rate of 34.7 mg/kg in the diet (equivalent to 0.95 mg/kg bw/d),
Approximately 78% of the dose was recovered. Excretion of flutolanil proceeded mainly via urine (50% dose). In faeces, excreted radioactivity accounted for 19% of the dose. A further 8% was recovered in the gastro-intestinal tract. A low amount was excreted in milk (<0.1% dose) and 0.3% of the dose was detected in tissues. Levels of radioactivity detected in muscle (rump, foreleg and loin) were <0.01 mg/kg, hence those matrices were not further extracted. Edible tissues containing significant residues were extracted and majority of the radioactivity was successfully extracted: 70% liver, 99% kidney, 88% fat, 94% milk. Radioactivity released from post extraction solids (PES) following sequential treatment with protease enzyme, acid and base, accounted for 19% TRR in liver and 3% in fat.
Residues in milk reached a plateau within 2-3 days of dosing. In milk the only significant residue was metabolite M-4 glucuronide conjugate (45.6% TRR, 0.013 mg eq./kg). Other metabolites in milk were detected in small amounts: flutolanil (6% TRR, 0.002 mg/kg), M-4 (2.2% TRR, 0.001 mg eq./kg) and M-4 sulfate ester (8.2% TRR, 0.002 mg eq./kg).
In liver flutolanil was not detected. The major residue identified in liver was M-2 and its glucuronide conjugate, which accounted for 11.9 % TRR (0.047 mg eq./kg) and 37.7% TRR (0.147 mg eq./kg), respectively. Minor metabolites (M-4, M-7, M-11, both as free and sulfate or glucuronide conjugates) were detected in liver in neutral and weak acid extracts, representing maximum of <10% TRR (sum of each TRR value). Additionally, small amounts of phenyl ring metabolites M-101 and M-102 were found

(maximum 6.5% TRR, 0.025 mg eq./kg). From the further PES extraction, trace amounts of flutolanil (0.4% TRR, 0.002 mg/kg), were released, together with metabolites M-2, M-4, M-11, M-102 and M-101. Total levels of metabolites M-4 and M-101, including those released by PES extraction, represented 10% and 17.2% of the TRR in liver.

In kidney flutolanil was not detected. The major residues identified were M-2 and M-4 glucuronide conjugates (59.0% and 15.2% TRR, 0.151 and 0.039 mg eq./kg, respectively) accompanied by smaller amounts of free M-2 and M-4 (4.8% and 1.5% TRR, 0.012 and 0.004 mg eq./kg, respectively), plus the M-4 sulfate conjugate (6.6% TRR, 0.017 mg eq./kg). Overall M-2 and M-4, both free and conjugated, accounted for a total of 63.8% and 23.3% TRR in kidney. M-7 and its glucuronide conjugate, M-11, M-101 and M-102 were detected as minor metabolites in kidney (maximum 2.4% TRR, 0.006 mg eq./kg).

The low residues in fat was composed of mainly flutolanil (47.6% TRR) and M-2 (25.3% TRR), neither of which exceeded 0.01 mg/kg (maximum 0.006 mg/kg).

The metabolic profile in urine was very similar to the kidney. No flutolanil was detected and the largest components identified in the urine were the M-2 glucuronide conjugate (representing 25.4% of the cumulative applied dose), M-4 glucuronide conjugate (11.1%) and M-4 sulfate ester (5.6%). Overall M-2 and M-4 with their conjugates accounted for 26.4 and 16.9% of the dose in urine. M-7 and M-11, along with their sulfate and glucuronide conjugates were found as minor metabolites (maximum 2.4%) and no phenyl ring metabolites were detected in urine.

In faeces flutolanil and M-2 were the major components identified (6.6 and 11.2% of the dose). Trace amounts of M-4, M-7 and M-101 was observed (<1%).

In conclusion, if goats were exposed to flutolanil residues through the diet, the residues are rapidly metabolised and excreted. There is no evidence of bioaccumulation of flutolanil residues in goats.

Poultry, Laying hen

In the initial peer review metabolism of [aniline ring-U-^{14}C] flutolanil has been investigated in laying hens at doses of 0.035 and 1 mg/kg bw/day. At 24 hours after the last dose more than 85% of the cumulative radioactivity was excreted via urine and faeces. Radioactivity in eggs, muscle, skin and fat was below the detection limit. The highest radioactivity was detected in liver and kidney. In excreta (urine and faeces) major metabolite was unchanged flutolanil and α, α, α -trifluoro-3'-hydroxy-o-toluanilide (M-4/DIP) and the glucuronide conjugate of M-4. In kidney and liver, radioactivity was almost completely associated with glucuronide/sulphate conjugates of M-4.

In the new study submitted for the renewal process, metabolism in laying hens was investigated after 14 consecutive daily oral doses at a rate of 13.7 mg/kg in the diet (0.78 mg/kg bw/day) with [phenyl-U-^{14}C]-flutolanil.

Approximately 94% of the dose was recovered in excreta and cage washes, accounting for 90.4% and 3% of the dose. A low amount of radioactivity was detected in eggs (<0.1% dose) and 0.1% of dose was detected in tissues.

In liver flutolanil was detected at 2.6% TRR (0.014 mg/kg). The major component was the phenyl ring metabolite M-101 (16.6% TRR, 0.086 mg eq./kg). Metabolites M-2 and M-4 both as free and glucuronide conjugates were detected as minor metabolites 7% (0.036 mg eq./kg) and 9% TRR (0.047

mg eq./kg), respectively. Other identified metabolites did not exceed 3.5% TRR (0.006 mg eq./kg). No flutolanil was identified by further extraction of PES samples. The major metabolite identified in PES extracts was M-101 (28.6% TRR, 0.148 mg eq./kg).
Flutolanil was identified as the major component in fat (42.8% TRR, 0.054 mg/kg). In addition, metabolites M-2, M-4, M-5, M-101 and M-102 were detected in fat as minor metabolites, with maximum 6.1% TRR, 0.008 mg eq./kg).
In muscle flutolanil was detected as 6.3% TRR (0.002 mg/kg). The major metabolite was M-101 (45.8% TRR, 0.016 mg eq./kg). Minor metabolites M-2, M-4, M-5 and M-102 were detected in trace amounts, with maximum of 1.6 % TRR (0.001 mg eq./kg).
In eggs, a similar pattern as in muscle was seen. The major component was metabolite M-101 (36.5% TRR, 0.019 mg eq./kg). Flutolanil was detected at 5,4%TRR (0.003 mg/kg) with trace amount of metabolite M-4 (2.2% TRR, 0.001 mg eq./kg). By further extraction of the PES fraction no flutolanil was detected. The major metabolite in the Pes extracts was M-101 (15.3% TRR, 0.007 mg eq./kg) along with M-4 (0.7% TRR, <0.001 mg eq./kg).
In excreta flutolanil, M-2 and M-4 were the main components identified (10.3, 7.8 and 14.6% of the dose). No other components exceeded 5% of the dose. Metabolites M-3, M-5, M-11, M-101 and M-102 were observed in smaller amounts (maximum 3.3% dose).
It can be concluded that flutolanil is rapidly excreted (93.4% of the administrated dose). Tissues (liver, fat, muscle) retained only low levels of radioactivity (0.1%). The TRR for eggs ranges up to 0.063 mg eq./kg which represented <0.1% of the administrated dose.

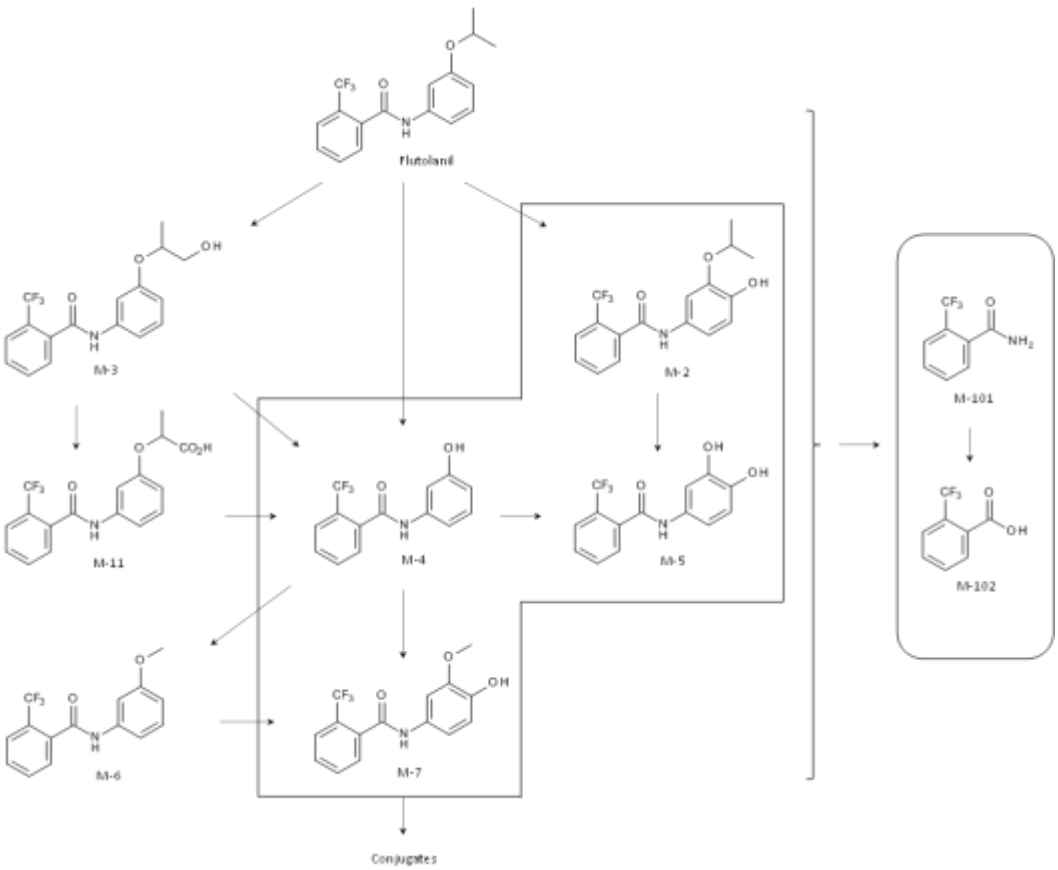
Overall conclusions on livestock metabolism

Metabolism of flutolanil in animals has been investigated in laying hens and lactating goats (both aniline and phenyl labelled ring).
From all available metabolism studies in livestock it can be concluded that flutolanil is mainly hydroxylated to metabolites M-4 and M-2, followed by formation of their corresponding glycoside or sulfate conjugates. In hens and as a minor pathway in goats, flutolanil is also further degraded to the metabolite M-101 by cleavage at the carboxamide, followed by its hydrolysis to M-102.
Other minor metabolites (M-3, M-5, M-6, M-7 and M-11) were degraded from the parent compound.
The proposed metabolic pathway is presented in a Figure 2.7.2-2
In hens, flutolanil and its metabolites were rapidly excreted (>99% of the recovered dose). In muscles, liver and eggs, the main metabolite was metabolite M-101. M-2 and M-4 and their conjugates were formed in liver, fat, muscle and eggs (M-4 only). Flutolanil was the major residue in fat. In muscle, liver and eggs, flutolanil has been detected as a minor component. Other metabolites: M-3, M-5 and M-7 were also detected in poultry tissue as minor metabolites.

In lactating goats, 90% of the recovered dose has been excreted. Flutolanil was the major residue in goat fat. Metabolite M-4, free and conjugated, was the main metabolite in milk, liver and kidney. Metabolite M-2, free and conjugated, was the major metabolite in liver and kidney (second study only). Other metabolites: M-3, M-6, M-7, M-11, M-101 and M-102 have been detected in goat tissues as minor metabolites.

The metabolic profile of flutolanil in hens and goats was similar to the rat. It should be noted that flutolanil and its main metabolites has been indentified as major metabolites in rat. Hence, toxicological profile of M-2 and M-4 (free and conjugated) is covered by toxicological references of parent compound flutolanil. Metabolites M-101 and M-102 have been defined as not relevant in rat and toxicity has been evaluated.
When the livestock is exposed to flutolanil, the metabolism profile is known and can be followed (see Figure 2.7.2-2). However, there is no data on metabolism in livestock of main plants metabolites to which animals can be exposed: M-4 (free and conjugated) and metabolite M-101. Since toxicological profile of metabolite M-4 is covered by the toxicological endpoints of the parent compound, additional metabolism studies in animals for metabolite M-4 are covered by flutolanil and not required. However, a need of separate metabolism study for metabolite M-101 should be possibly discussed. On the other hand, by the livestock feeding studies, it was clearly concluded than no metabolite M-101 has been detected in animal tissues also in the higher dose rates than calculated dietary burden.

Figure 2.7.2.-2: Proposed metabolic pathway of flutolanil in animals



Since metabolism in rats and ruminants was demonstrated to be similar, the findings in ruminants can also be extrapolated to pigs.

No metabolism study in fish has been submitted for the renewal process. Potato protein can be used as a part of fish diet. Flutolanil has been recovered in fat tissue in poultry (0.127 mg eq./kg) and in

goat (0.012-0.043 mg equi./kg), which suggest that flutolanil is fat soluble and can be recovered in animal tissues.
Investigation of metabolism of flutolanil in fish might be required.

2.7.3 Definition of the residue

Plant matrices

The metabolic pathway of flutolanil in the investigated plant groups (root and tuber vegetables, oilseed and pulses, leafy vegetables and miscellaneous group) is qualitatively similar.
Parent compound flutolanil has been detected in significant amounts in almost all investigated crops, except peanuts and it is proposed as a residue definition for monitoring in plants commodities, except oilseed and pulses.
In peanut nuts flutolanil was almost not found (1% TRR, 0.004 mg/kg), only in vines (18.5% TRR, 2.20 mg/kg) and hulls (11.2% TRR, 0.34 mg/kg). . The main metabolite in nuts was metabolite M-4 (10.2% TRR, 0.04 mg/kg). The major part of radioactivity in nuts was localised in unidentified conjugates or unconjugated metabolites (49%). Attempts to identify the metabolites were done, however were not very successful due to difficult oil matrix. Since, in other three plant gropus, flutolanil was the main residue detected and it is present in peanut vines and hulls, it could be possibly discussed to propose provisional residue definition in pulses in oilseed as parent compound: flutolanil.

For the risk assessment, results from all the available metabolism studies and residue studies (primary and succeeding cops) are taken into consideration and the following metabolites have been identified as the most significant in plant matrices:

Flutolanil: parent compound flutolanil has been identified in all the investigated plant matrices (in peanuts in very low concentration) and should be part of the residue definition of the risk assessment.

Metabolite M-2 free and conjugated has been observed in a significant percentage of the TRR in edible crop only in the studies from the original DAR in mature potatoes (max. 14% TRR, 0.002 mg eq./kg). It is also one of the major rat metabolites and its toxicity has been considered at the same level as the parent compound. In other investigated plant matrices (root and tuber vegetables, leafy vegetables, pulses and oilseeds, miscellaneous vegetables), this metabolite has not been identified in significant amounts in crop parts used as food. In the available supervised residue trials on potatoes (seed treatment and in furrow treatment), metabolite M-2 (free and conjugated) has been measured and in all the trials it was not detected above the LOQ of 0.01 mg/kg. Metabolite M-2 and its conjugates have been included in the current residue definition for risk assessment. However, based on the newly submitted metabolism studies, it is considered not significant in plant matrices and since it is not identified in the residue trials in potatoes (defended use), and its toxicity is similar as the parent, it is proposed not to include metabolite M-2 (free and conjugated) into the residue definition for risk assessment.

Metabolite M-4 free and conjugated has been observed as a major metabolite in most investigated plant matrices. It has been also identified as one of the major metabolites in rat. Therefore, it is proposed to include this metabolite in the residue definition for risk assessment in plant matrices. The toxicological profile of metabolite M-4 is covered by the toxicological endpoints of the parent compound flutolanil.

Metabolite M-101 and M-102 have been detected in the newly submitted metabolism studies in several plant matrices. In potatoes metabolite M-101 constituted of 11,9% TRR (0,008 mg eq./kg) and 8,5% TRR (0,041 mg eq./kg) in seed and in-furrow treatment respectively. In rice, metabolite M-101 was one of the main metabolites and was detected in amounts of 23%TRR (0,71 mg eq./kg) in brown rice after paddy application. In mature cabbage, metabolite M-101 was a minor metabolite and did not exceed 1% TRR.
Metabolite M-102 was a main metabolite in potato tubers after in-furrow treatment (31,3%TRR; 0,152 mg eq./kg) and in paddy treated rice (18,8% TRR; 0,33 mg eq./kg). In mature cabbage, metabolite M-102 was a minor metabolite and did not exceed 1% TRR.
Metabolites M-101 and M-102 are also part of the main metabolites in rotational crops.
Metabolites M-101 and M-102 are only minor metabolites in rats. Therefore, it has been concluded that the reference values determined for flutolanil are not considered applicable to these metabolites. For metabolite M-101 an ADI was set of 0.002 mg/kg bw/day and for metabolite M-102, an ADI was set of 0.14 mg/kg bw/day.
From the available toxicological data, it can be concluded that metabolite M-101 is more toxic than the parent compound flutolanil (ADI of 0.09 mg/kg bw/day). This metabolite was not detected in supervised residue trials on potatoes, except in two trials in furrow treatment (0.012 and 0.018 mg/kg). Supervised residue trials with rice in which M-101 has been determined are not available, since rice is not part of the representative uses.
Metabolite M-101 has been investigated in field trials with rotational crops. In leafy crops (spinach), metabolite M-101 has been found up to 0.03 mg/kg at 120 days PBI. It was also detected in cereals whole plant and straw. Based on that information and since the toxicity of metabolite M-101 is considered higher that flutolanil, it is proposed to include the metabolite M-101 in the residue definition for risk assessment for rotational crops. For primary crops pending data from supervised residue trials with flutolanil in rice or possiblt other cereals, this metabolite should also be taken into consideration.
Metabolite M-102 was identified in metabolism studies with potato tubers (in furrow treatment) and rice. No information is available on the magnitude of this metabolite in rice. In the available supervised residue trials, this metabolite was detected up to 0.041 mg/kg in potato tubers after in-furrow treatment.
Metabolite M-102 is one of the major metabolites in rotational crops. It has been found in leafy rotational crops (up to 0.03 mg/kg in spinach leaves at 120d PBI) and cereals (including grain, with residues up to 0.03 mg/kg at 30 days PBI).
On the other hand, based on the toxicological reference value of metabolite M-102 (ADI: 0,14 mg/kg bw/day) it can be concluded that it is less toxic than the parent compound flutolanil (ADI: 0.09 mg/kg

bw/day) and metabolite M-101 (ADI: 0.002 mg/kg bw/day). Taking all the arguments above, it is proposed not to include metabolite M-102 in the residue definition for risk assessment.
No ARfD has been set for metabolites M-101 and M-102.

Rice straw can be used in animal diet and significant residues in rice straw should be possibly taken into account when use on rice is requested.

Trifluoroacetic acid (TFA): Metabolite TFA was found in rotational crops in all crops at all investigated time points. However, it is known that TFA can be derived from a number of pesticides and non-pesticide sources from molecules containing a CF_3 moiety. Therefore, it is not proposed to be included in the plant residue definition for risk assessment or monitoring. A general approach is required for metabolite TFA.

Residue definitions proposed by RMS in the renewal process:
Residue definition for monitoring in plant matrices: parent compound flutolanil
Residue definition for risk assessment:

1. Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil
2. Metabolite M-101

It should be noted that for the plant matrices the applicant proposed as residue definition for risk assessment: sum of flutolanil, metabolites M-2 and M-4 and their conjugates, M-101 and M-102 and its conjuagtes, expressed as flutolanil. However, RMS is of the opinion that metabolite M-2 and M-102 and its conjugates, are not required in the RD-RA. The argumentation for this is included above in the paragraph 2.7.3.

Animal matrices
The residue definition for enforcement and risk assessment in animal commodities has been based on the available metabolism studies in goats and hens. The metabolism of flutolanil is qualitatively similar in goat and poultry.
In hens, flutolanil has been detected in all matrices. In fat, flutolanil was one of the major metabolites up to 42,8% TRR (0.054 mg/kg), in other matrices parent compound was detected up to 6,3% TRR (0,002 mg/kg) in muscle and 2,6% TRR (0,014 mg/kg) in liver. Metabolite M-101 was the major metabolite in eggs (36,5%; 0,019 mg eq./kg), liver (16,6%; 0,086 mg eq./kg) and muscle (45,8% TRR; 0,016 mg eq./kg).
On the other hand, based on the poultry feeding studies, metabolite M-101 was not detected in significant level in the dose group 2 (0.076 mg/kg bw/d).
In lactating goats, flutolanil was in general a minor metabolite, except in fat (up to 47.6% TRR, 0,006 mg/kg). In the first metabolism study in goats (90N), metabolite M-4 and its conjugates have been the major residues in all the investigated matrices, except for fat tissue. In the second metabolism study in goats, metabolite M-2 and its conjugate were the major metabolites in liver and kidney. However, it is noted, that this study is much more overdosed (300N) and metabolite M-2 is no longer detected in

high levels, when the dose concentration is less overdosed (90N). Therefore, it is proposed not to include metabolite M-2 and its conjugates in the residue definition for monitoring and risk assessment. Metabolite M-102 was not detected in goat tissues (300N). Metabolite M-101 was only detected in milk fat and aquatic fraction (maximum 9.2% TRR, 0,004 mg eq./kg).

The applicant proposed flutolanil only as RD for risk assessment and monitoring in animal commodities. However, based on the available data two separate residue definitions for poultry and ruminants are proposed by RMS:
For poultry:
Residue definition for monitoring is proposed as parent compound flutolanil
Residue definition for risk assessment:

1. Flutolanil
2. Metabolite M-101

For ruminants:
Residue definition for monitoring is proposed as metabolite M-4 (free and conjugated)
Residue definition for risk assessment is proposed as sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil.

RMS is aware that the proposition to include conjugated form of metabolite M-4 can be considered undesirable. However, metabolite M-4 free and conjugated seems an important marker of residues in ruminants. Proposed residue definitions are therefore open for discussion.

2.7.4 Summary of residue trials in plants and identification of critical GAP

The cGAP proposed for the flutolanil renewal:
Potatoes (EU):
Potato seed treatment (ware, seed, starch potatoes):
In store treatment (indoor/outdoor): 1x 0.368 kg as/ha (based on a planting rate of 4 ton tubers/ha), BBCH 00-03 (before planting).
On planter treatment as tuber falls into furrow (outdoor): 1x 0.368 kg as/ha (based on a planting rate of 4 ton tubers/ha), BBCH 00-03 (at planting)
In planter treatment before catching up by planting chains (outdoor): 1x 0.368 kg as/ha (based on a planting rate of 4 ton tubers/ha), BBCH 00-03 (at planting)

Ornamental crops (non-edible):
Tulip, iris: 1x 2.76 kg as/ha, incorporation into the soil (10-15 cm). Since ornamental crops are non edible crops, assessment of magnitude of the residues is not required.

The cGAP proposed in the framework of the MRL application:
Potato in furrow treatment at planting (EU):
1x 2.10 kg as/ha, BBCH 00-03 (at planting), in furrow application, directed at soil.

For seed potatoes treatment the following residue levels have been selected, according to the proposed cGAP:
Flutolanil (RD-Mo):
NEU: 5x< 0.01; 0.01; 2x 0.014; 2x0.02; <0.022; 0.022; 2x0.03; 0.035; 0.05; 0.09 mg/kg
SEU: 7x <0.01; 2x 0.01; 2x0.03; 0.04 mg/kg
Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil (RD-RA):
NEU: 5x<0.02; 0.02; 2x 0.03; 0.04; 0.06; 0.1 mg/kg
SEU: 7x <0.02; 2x 0.02; 2x 0.04; 0.05 mg/kg
Metabolite M-101 (RD-RA):
NEU: 11x <0.01 mg/kg
SEU: 12x <0.01 mg/kg

For in-furrow potatoes treatment the following residue levels have been selected, according to the proposed cGAP:
Flutolanil (RD-Mo):
NEU: 6x <0,01; 0,03; 0,04; 0,08; 0,09; 0,1; 0,11 mg/kg
SEU: 3x<0,01; 0,01; 4x 0,02; 0,03; 0,04; 0,09; 0.13 mg/kg

Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil (RD-RA):
NEU: 6x <0.02; 0,04; 0,05; 0,1; 0,11; 2x 0,13 mg/kg
SEU: 3x <0,02; 0,02; 4x 0,03; 0,04; 0,06; 0,12; 0,18 mg/kg

Metabolite M-101 (RD-RA):
NEU: 12x <0,01 mg/kg
SEU: 10x <0,01; 0,012; 0.018 mg/kg

2.7.5 Summary of feeding studies in poultry, ruminants, pigs and fish

Potatoes and its by-products form part of livestock diet. Moreover, residues of flutolanil and its metabolites have been found in rotational cereal forage and straw, which are also part of the animal diet. Therefore, the median and maximum dietary burden were calculated for the different groups of livestock. In Table 2.7.5-1, inputs values for the dietary burden calculation are reported for representative use on potato seed treatment. Since, in the rotational crop study performed according with cGAP for the seed treatment no residues have been detected, residues of rotational crops are not taken into account in the first calculation.

Table 2.7.5-1 Inputs values for dietary burden calculation to support representative uses (potato seed treatment)

Feed commodity	Median dietary burden		maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition (plant): 1. Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil				
Potato	0.02	STMR	0.1	HR
Potato (process waste)	0.4	STMR*default PF (0.02*20)	n/a	Only STMR apply
Potato (dried pulp)	0.76	STMR*default PF (0.02*38)	n/a	Only STMR apply
Risk assessment residue definition: 2. M-101				
Potato	0.006	STMR	0.006	HR
Potato (process waste)	0.006	STMR	-	Only STMR apply
Potato (dried pulp)	0.006	STMR	-	Only STMR apply

Table 2.7.5-2 Inputs values for combined dietary burden calculation to support representative uses (potato seed treatment) and MRL application uses (in-furrow treatment)

Feed commodity	Median dietary burden		maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: 1. Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil				
Potato	0.03	STMR	0.18	HR
Potato (process waste)	0.6	STMR*default PF (0.03*20)	-	STMR apply
Potato (dried pulp)	1.14	STMR*default PF (0.03*38)	-	STMR apply
Cereal forage (barley)	-	-	0.09	HR in rotational cereal forage (whole plant) at 120 days PBI
Cereal straw	-	-	0.13	HR in rotational cereal straw at 30 days PBI
Risk assessment residue definition: 2. M-101				
Potato	0.01	STMR	0.018	HR
Potato (process waste)	0.01	STMR	-	STMR apply
Potato (dried pulp)	0.01	STMR	-	STMR apply
Cereal forage (barley)	-	-	0.01	HR in rotational cereal whole plant (all PBI)
Cereal straw	-	-	0.03	HR in rotational cereal straw at 270 days PBI

Table 2.7.5-3: Calculation of livestock exposure for combined residues of flutolanil and metabolite M-4, expressed as flutolanil (defended use: potato seed treatment)

		Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Intake >0.004 mg/kg bw/d
Ruminant	Beef cattle	0.036	0.033	Potato, process waste	1.48	Yes
	Dairy cattle	0.044	0.040	Potato, process waste	1.15	Yes
	Ram/Ewe	0.049	0.045	Potato, process waste	1.5	Yes
	Lamb	0.033	0.029	Potato, process waste	0.77	Yes
Pig/Swine	Breeding	0.021	0.017	Potato, process waste	0.92	Yes
	Finishing	0.013	0.007	Potato, dried pulp	0.42	Yes
Poultry	Broiler	0.016	0.013	Potato, dried pulp	0.22	Yes
	Layer	0.012	0.01	Potato, dried pulp	0.18	Yes
	Turkey	0.007	0.001	Potato, culls	0.1	Yes

Table 2.7.5-4: Calculation of livestock exposure for combined residues of metabolite M-101 (defended use: potato seed treatment)

		Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Intake >0.004 mg/kg bw/d
Ruminant	Beef cattle	0.001	0.0007	Potato, process waste	0.03	No
	Dairy cattle	0.001	0.0009	Potato, process waste	0.02	No
	Ram/Ewe	0.001	0.001	Potato, process waste	0.0	No
	Lamb	0.001	0.0007	Potato, process waste	0.02	No
Pig/Swine	Breeding	0.001	0.001	Potato, process waste	0.03	No
	Finishing	0.000	0.000	Potato, dried pulp	0.02	No
Poultry	Broiler	0.000	0.000	Potato, dried pulp	0.00	No
	Layer	0.000	0.000	Potato, dried pulp	0.00	No
	Turkey	0.000	0.000	Potato, culls	0.01	No

Table 2.7.5-5: Calculation of livestock exposure for combined residues of flutolanil and metabolite M-4, expressed as flutolanil (combined: defended use and MRL application: potato seed and in-furrow treatment)

		Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Intake >0.004 mg/kg bw/d
Ruminant	Beef cattle	0.057	0.0512	Potato, process waste	2.36	Yes
	Dairy cattle	0.072	0.0629	Potato, process waste	1.86	Yes
	Ram/Ewe	0.079	0.0722	Potato, process waste	2.4	Yes
	Lamb	0.057	0.0502	Potato, process waste	1.33	Yes
Pig/Swine	Breeding	0.033	0.025	Potato, process waste	1.45	Yes
	Finishing	0.021	0.01	Potato, dried pulp	0.71	Yes
Poultry	Broiler	0.025	0.019	Potato, dried pulp	0.35	Yes
	Layer	0.02	0.015	Potato, dried pulp	0.30	Yes
	Turkey	0.013	0.002	Potato, culls	0.18	Yes

Table 2.7.5-6: Calculation of livestock exposure for combined residues of metabolite M-101 combined: defended use and MRL application: potato seed and in-furrow treatment)

		Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Intake >0.004 mg/kg bw/d
Ruminant	Beef cattle	0.002	0.0014	Potato, culls	0.07	No
	Dairy cattle	0.002	0.0019	Potato, culls	0.06	No
	Ram/Ewe	0.002	0.0020	Potato, culls	0.1	No
	Lamb	0.002	0.0020	Potato, culls	0.05	No
Pig/Swine	Breeding	0.001	0.001	Potato, culls	0.06	No
	Finishing	0.001	0.001	Potato, culls	0.05	No
Poultry	Broiler	0.001	0.001	Potato, culls	0.01	No
	Layer	0.001	0.001	Potato, culls	0.01	No
	Turkey	0.001	0.001	Potato, culls	0.02	No

The results of the dietary burden calculations (see Tables above) show that the trigger value of 0.004 mg/kg bw/d is exceeded for all groups of livestock for flutolanil.

During the initial peer review no feeding studies have been evaluated. For the renewal feeding studies with poultry and ruminant have been submitted. Representative use potato seed treatment is taken into account.

In the poultry feeding study five groups of laying hens were dosed: Group 1: 0 mg/kg flutolanil in diet; Group 2: 1 mg/kg in diet (equivalent to 0.076 mg/kg bw/d); Group 3: 10 mg/kg (equivalent to 0.692 mg/kg bw/d); Group 4: 30 mg/kg (equivalent to 2.35 mg/kg bw/d) and Group 5: 100 mg/kg (equivalent to 7.63 mg/kg bw/d). For flutolanil, the maximum dietary burden for poultry is 0.016 mg/kg bw/d for broiler, hence the lowest feeding level of 0.076 mg/kg bw/d (Group 2) is at 4.8N. No residues of flutolanil and its metabolites were found in eggs during the study time up to 28 days. Furthermore, in the feeding group 2, no residues of flutolanil and its metabolites: M-2 (free and conjugated), M-4 (free and conjugated), M-7, M-101 and M-102 have been detected above the LOQ in the investigated poultry tissues: liver, muscle, abdominal fat, skin and subcutaneous fat. It can be concluded, based on the study, that no residues according to the residue definition for monitoring and risk assessment are expected in edible poultry tissues and eggs.

In feeding studies with dairy cows, four groups of animals (and one control) received flutolanil in the diet at dose level: Group 1: 0 mg/kg (control group); Group 2: 3 mg/kg (0.120 mg/kg bw/d); Group 3: 30 mg/kg (1.186 mg/kg bw/d); Group 4: 90 mg/kg (3.37 mg/kg bw/d) and Group 5: 300mg/kg (11.95 mg/kg bw/d).

The maximum dietary burden for ruminants is 0.049 mg/kg bw/d for ram/ewe and 0.044 mg/kg bw/d for dairy cattle. Hence the lowest feeding level of 0.120 mg/kg bw/d (Group 2) corresponds to 2.4 for ram and 2.7N for dairy cattle.

No residues of flutolanil and its metabolites M-2 (free and conjugated), M-4 (free and conjugated), M-7 and M-101 have been detected above the LOQ (0.01 mg/kg) in milk, skimmed milk and milk fat during the study time of 28 days.

Parent compound flutolanil has not been detected above the LOQ in ruminant's tissues: kidney, liver, muscle, subcutaneous fat, ornamental fat and perirenal fat. Metabolite M-2 (conjugated) has been identified in kidney at a level of 0.04 mg/kg (mean of three values) and in one sample in liver at the LOQ: 0.01 mg/kg.

Metabolite M-4 (conjugated) has been identified in kidney at a level of 0.015 mg/kg (mean of three values). Further, no metabolites of flutolanil have been detected in ruminant tissues.

The calculated dietary burden for the metabolite M-101 did not exceeded the trigger intake of 0.004 mg/kg bw/d for all animal groups. Also, no residues of metabolite M-101 have been detected in feeding studies at feeding levels: 0.076 mg/kg bw/d for hens and 0.120 mg/kg bw/d. Those feeding levels are considers overestimation of the actual level of the metabolite M-101 in animal diet.

For MRL application data, the available feeding studies also cover the calculated dietary burden for animals: 1,5N for ram/ewe, 1.7N for dairy cattle and 3.1N for broiler. No residues of flutolanil and metabolite M-4 (free and conjugated) and metabolite M-101 are expected in animal commodities including eggs and milk.

2.7.6 Summary of effects on processing

The potential of flutolanil to undergo hydrolysis, under conditions simulating pasteurisation, baking, brewing and boiling and sterilisation, was studied. Flutolanil was stable under all processing conditions. It is noted by RMS that no data on potential effect on processing is available for metabolite M-4 (free and conjugated) and metabolite M-101, which belong to residue definition for risk assessment.

Studies investigated distribution of residues in peel and pulp are not relevant for the defended use on potato. However, during the initial peer review one study has been evaluated investigating distribution of residues in potato tubers, peeled potato and potato peel. Based on the study peel is the main part of translocation of flutolanil in potato. No detectable residues were found in potato tuber and peeled potato.

Further, no processing studies have been submitted for the application. The theoretical maximum daily intake TMDI is less than 10% of the ADI, for both compounds included in the residue definition for risk assessment: sum of flutolanil and metabolite M-4 (free and conjugated) and metabolite M-101, hence processing studies are not required. However, it should be noted, that when other uses are taken into account processing studies could be possibly desirable.

2.7.7 Summary of residues in rotational crops

Metabolism of flutolanil in rotational crops.

In the initial peer review a confined rotational study was conducted using [aniline ring ^{14}C] flutolanil to address the potential uptake and metabolism of flutolanil residues into succeeding crops. Two additional confined crop rotation studies have been submitted for the renewal of flutolanil.

In the confined study from the initial peer review soil was treated at a rate of 2.69 kg /ha and lettuce, oat/sorghum and radish have been planted. Investigated plant-back intervals (PBI) were 30; 120; 148 and 366 days. After 253-293 days radioactive residues in soil were measured at concentrations of 0.45-0.63 mg eq./kg, indicating slow elimination of residues in soil. In mature lettuce, the highest residues (flutolanil equivalents) were at 30 PBI: 0.18 mg/kg and decreased to 0.03 mg/kg at 148 PBI and 0.01 mg/kg at 366 PBI. In cereals, the highest concentration of flutolanil equivalents has been found in oat straw at the PBI of 30 days (0.80 mg/kg), in mature grain residues were 0.15; <0.01 and 0.01 mg/kg in 30, 148 and 366 PBI, respectively. In mature radish (roots and tops) the highest residues were measured at 30 days PBI (0.17 and 0.36 mg/kg respectively). Residues of flutolanl equivalents were 0.17 mg/kg in radish root at 120 PBI and decreased to 0.02 mg/kg at 366 PBI. In radish tops residues were 0.14 and 0.03 mg/kg at 120 and 366 PBI respectively. The metabolic profile was similar in all the crops. Residues were mainly comprised of (free and conjugated) flutolanil and metabolite M-4. Metabolic profile of cereal grain and hulls was not studied, which can be considered as a limitation of the study.

In the first additional study submitted for the renewal, bare soil was treated at a rate of 480 g as/ha with [phenyl-U-^{14}C] flutolanil (1.3 corresponding to the cGAP for seed treatment). Rotational crops (lettuce, radish and wheat) were sown 30, 120 and 270 days after treatment and immature and mature plant parts have been analysed. The levels of total radioactive residues were rather variable and in

some cases an increase in concentration for radish and wheat between 30 days PBI and 120 PBI has been observed. In all crops total radioactive residues decreased at 270 days PBI.
In mature lettuce flutolanil was detected as a minor component of the residue at 30 days PBI (1.5%; 0.004 mg/kg) and at 120 days PBI (1.1% TRR; 0.002 mg/kg). No parent compound was detected at the 270 days PBI in mature lettuce. At the 30 days PBI in mature lettuce the major identified metabolites were: trifluoroacetic acid (TFA) which comprised for 21.8% TRR (0.057 mg eq./kg) and M-101, 20.6% TRR (0.054 mg eq./kg), M-102 (13.4% TRR, 0.035 mg eq./kg) and metabolite M-4 (free and conjugated) 12.2% TRR (0.032 mg eq./kg). At 120 days PBI the main metabolite in mature lettuce was metabolite M-101 (39.6% TRR, 0.074 mg eq./kg) and metabolite TFA (18.2% TRR; 0.034 mg eq./kg). At the 270 plant back interval the major metabolite in mature lettuce was TFA with 87.5% TRR (0.028 mg eq./kg). Metabolite M-101 was identified as a minor metabolite (3.1% TRR, 0.001 mg eq./kg).
At all time points a number of “others” metabolites were also identified, however no single metabolite was measured at >10% or > 0.05 mg/kg (max. 3.1% TRR; 0.006 mg/kg).
In radish roots and radish tops parent compound flutolanil has not been identified at any of the plant back intervals. In radish root TFA was the main metabolite identified at 30, 120 and 270 days PBI at levels: 29.2 % TRR (0.033 mg eq./kg); 13.6 % TRR (0.019 mg eq./kg) and 20.7% TRR (0.006 mg eq./kg), respectively. In radish tops at 30 days PBI, TFA and M-101 were the most abundant residues: 37.9 % TRR (0.174 mg eq./kg) and 23.7% TRR (0.109 mg eq./kg), respectively. Metabolite M-102 (free and conjugated) has also been identified in significant amount (13.6% TRR; 0.062 mg eq./kg). At the 120 days PBI in radish tops metabolite TFA was 33.7% TRR (0.205 mg eq./kg), metabolite M-101 was 32.1% TRR (0.195 mg eq./kg) and metabolite M-102 (free and conjugated) was 19.7% TRR (0.12 mg eq./kg). In the 270 days PBI the only relevant metabolite in radish tops was TFA: 57.4 % TRR (0.058 mg eq./kg).
At all time points a number of “others” metabolites were also identified, however no single metabolite was measured at >10% or > 0.05 mg/kg (max. 4.3% TRR; 0.006 mg eq/kg).
In wheat forage and hay flutolanil has not been detected, with the exception of wheat forage at 30 days PBI (0.7% TRR, 0.007 mg/kg). The main metabolites in wheat forage were TFA at 30 and 120 days PBI: 18.4% TRR (0.194 mg eq./kg) and 23.3% TRR (0.253 mg eq./kg), respectively and metabolite M-101 at 30 and 120 days PBI; 14.7% TRR (0.155 mg eq./kg) and 31.8% TRR (0.346 mg eq./kg). At the 270 days PBI, there were no metabolites detected above 10%TRR, the highest concentration had an unknown metabolite (9.7% TRR, 0.022 mg eq./kg), metabolite TFA and M-101 also decreased in concentration: 6.2% TRR (0.014 mg eq./kg) and 1.3% TRR (0.003 mg eq./kg), respectively.
In wheat hay metabolite TFA has been present at all the plant-back intervals: 30, 120 and 270 at a concentration of 16.4% TRR (0.232 mg eq./kg), 22.6% TRR (0.425 mg eq./kg) and 26.9 mg eq./kg (0.029 mg eq./kg) respectively. Metabolite M-101 was detected as a major metabolite only at the 120 day PBI: 14% TRR (0.264 mg eq./kg). Metabolite M-102 has been identified as one of the major metabolites in wheat hay as rotational crop at all PBIs 30, 120 and 270 days: 13.6% TRR (0.192 mg eq./kg); 16.3 %TRR (0.307 mg eq./kg) and 44.4% TRR (0.048 mg eq./kg), respectively. At all time

points a number of “others” metabolites were also identified, however, no single metabolite was measured at >10% (max. 4.4% TRR; 0.048 mg eq./kg).
No parent compound flutolanil has been identified in wheat straw and grain as rotational crop at all investigated plant-back intervals.
In wheat straw, at the 30 days PBI, a number of minor metabolites have been identified with metabolite M-3 (free and conjugated,13.4% TRR , 0.23 mg eq./kg) and TFA as major metabolites: 13.4% TRR (0.23 mg/kg). At the 120 days PBI in wheat straw the main metabolites identified were: TFA: 13.6% TRR (0.322 mg/kg), metabolite M-3 free and conjugated (9%TRR, 0.214 mg/kg), metabolite M-101 (4.4% TRR, 0.104 mg/kg) and metabolite M-2 (2.9% TRR, 0.068 mg/kg). At 270 days PBI in wheat straw metabolite TFA has been the major metabolites: 37.5% TRR (0.039 mg/kg).
In wheat grain, as rotational crop, metabolite TFA has been the major metabolite at all plant-back intervals: 30, 120 and 270 days: 14.4% TRR (0.067 mg/kg); 7.4% TRR (0.045 mg/kg), 45% TRR (0.015 mg/kg). Additionally, at the120 PBI, metabolite M-102 has been identified at 21.6% TRR (0.132 mg/kg). Other metabolites were detected as minor metabolites.
In the second study submitted for the purpose of the renewal, bare soil was treated with flutolanil (phenyl-label) at a rate of 2100 g as/ha (5.7N for the seed treatment, 1N, in-furrow treatment in MRL application). Rotational crops (lettuce, radish and wheat) have been sown 30 days, 120 days and 270 days after treatment and immature and mature plant parts have been analysed. The levels of total radioactive residues were rather variable and in some cases an increase in concentration for radish and wheat between 30 days PBI and 120 PBI has been observed. In all crops total radioactive residues decreased at 270 day PBI.
In immature and mature lettuce the parent compound flutolanil has not been detected, except as minor component of the residue at 30 days PBI for immature lettuce (1%; 0.042 mg/kg) and in mature lettuce at 120 days PBI (1.2% TRR, 0.024 mg/kg). For both immature and mature lettuce the metabolite M-101 was the major residue at 30 and 120d PBI. In immature lettuce M-101 has been identified at all PBI: 30; 120 and 270 days at concentrations: 52.9% TRR (2.253 mg eq./kg); 62.1% TRR (1.615 mg eq./kg) and 13.6% TRR (0.029 mg eq./kg). In mature lettuce M-101 was detected at 30 days PBI: 29% TRR (0.639 mg eq./kg); 120 days PBI 44.7% TRR (0.9 mg eq./kg) and at 270 days PBI as a minor metabolite 3.9% TRR (0.008 mg eq./kg). Further, in mature lettuce metabolite M-102 has been also detected in high concentrations at all the PBIs: 30, 120; 270 days: 20.3% TRR (0.445 mg eq./kg); 19.5% TRR (0.397 mg eq./kg) and 30.4% TRR (0.062 mg eq./kg), respectively. Metabolite TFA has been detected as a major metabolite in immature and mature lettuce at the 270 days PBI: 29.9% TRR (0.064 mg eq./kg) and 39.2% TRR (0.08 mg eq./kg).
In radish, flutolanil has been identified only in radish roots, with the highest concentration at 30 days PBI 2.1% TRR (0.015 mg/kg). Further, in radish roots metabolites M-101, M-102 (free and conjugated) and TFA have been identified as major metabolites at all the PBIs. M-101 has been detected at a concentration of 12.4% TRR (0.089 mg eq./kg) at 30d PBI, 19.85 TRR (0.131 mg eq./kg) at 120d PBI and 5.65 TRR (0.006 mg eq./kg) at 270d PBI. Metabolite M-102 (free and conjugated) has been detected at a concentration of 16% TRR (0.115 mg eq./kg) at 30d PBI, 36.1% TRR (0.239 mg eq./kg) at 120d PBI and 31.8% TRR (0.034 mg eq./kg) at 270 PBI. TFA has also been detected in radish roots, with the highest concentration at 120d PBI: 11% TRR (0.073 mg eq./kg).

In radish tops no parent compound was identified. At the plant back interval of 30 and 120 days, metabolite M-101 has been identified as a major metabolite 54% TRR (3.076 mg eq./kg) and 63.4% TRR (2.595 mg eq./kg), respectively. At the 270d PBI concentration of metabolite M-101 has decreased to 8.1% TRR (0.039 mg eq./kg). M-102 (free and conjugated) has also been identified in radish tops atall plant back-intervals: 11.9% TRR (0.678 mg eq./kg) at 30d PBI, 12.7% TRR (0.52 mg eq./kg) at 120 PBI and 25.6% TRR (0.123 mg eq./kg). TFA was also identified in radish roots at all plant-back intervals, with the highest concentration at the 120 days PBI 10.9% TRR (0.444 mg eq./kg). In radish tops a number of "other" metabolites has been detected, however not further identified. The highest concentration of those metabolites was 4.7% TRR (0.265 mg eq./kg) at 30d PBI and 3.1% TRR (0.127 mg eq./kg) at 120d PBI in radish tops.
In wheat parent compound flutolanil has been found only in wheat forage at 120 PBI 0.5% TRR (0.052 mg/kg). Further in wheat forage and hay metabolite M-101, M-102 and TFA have been identified as the major metabolites at all PBI. In wheat forage at 30d PBI, M-101 was detected at concentration 53.9% TRR (3.531 mg eq./kg), at 120d PBI 63.8% TRR (7 mg eq./kg) and at 270 PBI 5.4%TRR (0.081 mg eq./kg). Metabolite M-102 increased to 30.7% TRR (0.465 mg eq./kg) at the 270 d PBI. Metabolite TFA at 30d PBI in wheat forage was at 12.6% TRR (0.828 mg eq./kg) and decreased to 10.4% TRR (0.157 mg/kg) at 270d PBI. In wheat hay, metabolite M-101 has been the major residue up to 46.7% TRR (11.34 mg eq./kg) at 120d PBI. Metabolite M-102 and TFA were also identified up to 38.4% TRR (0.267 mg eq./kg) and 17.4% TRR (0.121 mg eq./kg) at 270 PBI, respectively. In wheat straw a similar metabolic profile to wheat forage and hay has been observed with metabolites M-102 and TFA as the major metabolites and M-101 at up to 9.0% TRR.
In wheat grain metabolites M-102 and TFA were the major metabolites. Metabolite M-102, at the 30day PBI has been detected at 15.1% TRR (0.535 mg eq./kg), at 120d PBI: 12.2% TRR (0.362 mg eq/kg) and at 270days PB I 33% TRR (0.120 mg eq/kg). Metabolite TFA in wheat grain has been identified in the highest concentration at 30d PBI: 0.379 mg eq./kg (10.7% TRR) and decreased to 0.041 mg eq./kg (11.3%TRR)

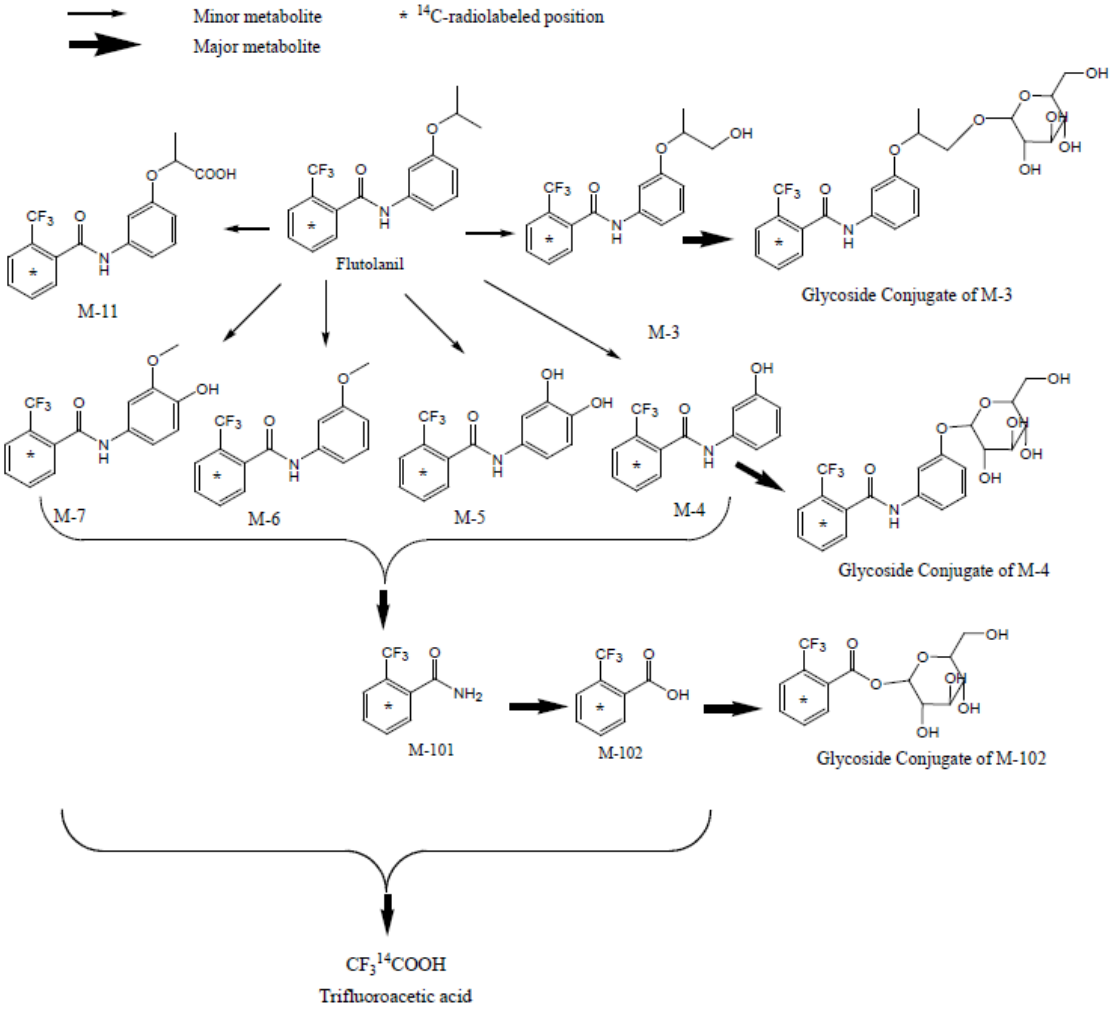
General conclusion metabolism in rotational crops:
In general, the metabolic pathway seems qualitatively comparable with the metabolism of the primary crops apart from additional identification of TFA (newly submitted studies).
In the older studies, from the initial DAR, where [aniline ring ^{14}C] flutolanil has been used: parent compound flutolanil and metabolite M-4 have been identified as the main metabolites. The two newly submitted studies ([phenyl-U-^{14}C]-flutolanil) show almost total degradation of the parent compound and a number of significant metabolites have been identified in rotational crops at different plant-back intervals. The main metabolites with a high concentration in all the rotational crops were metabolite M-101, metabolite M-102 (free and conjugated) and TFA (trifluoroacetic acid).
Metabolites M-3, M-4 (free and conjugated); M-5, M-7, M-11 have also all been found in the rotational crops, however generally as minor metabolites. It should be noted that metabolite M-101 is a very significant metabolite especially in leafy crops and forage at the two earliest plant-back intervals of 30 and 120 days.

The only difference between the metabolism of flutolanil in primary and rotational crops is formation of the metabolite TFA, which is not formed in primary crops. Formation of TFA is likely to arise following the complete degradation of the phenyl ring following the formation of the metabolites M-101 and M-102 (see Figure 2.7.7-1)

It should be noted that in the studies, metabolite TFA has been expressed as parent compound flutolanil, which leads to underestimation of the metabolite TFA due to respective molecular weights of flutolanil (323.31 g/mol) and TFA (114.02 g/mol). Additionally, since TFA contains only a single carbon atom derived from the [phenyl-U-^{14}C] ring, further 6-fold correction should be applied. As a consequence, a correction factor (CF) of 2.11 has been used to report the estimated concentrations of TFA. The detailed calculation of the CF and corrected values are reported in the Volume 3, B.7.6.1.2 and B.7.6.1.3.

As TFA can be derived from a number of pesticide and non-pesticide sources from molecules containing a CF_3 moiety, it is not proposed to be included in the plant residue definition for risk assessment or monitoring.

Figure 2.7.7-1 Proposed metabolic pathway of [phenyl-U-^{14}C]-flutolanil in rotational crops



Magnitude of the residues in rotational crops

There are three studies available, which investigate the magnitude of the residues in rotational crops. The first study has been evaluated during the initial peer review of flutolanil. However, due to the study limitations it is considered as supportive information only and not used for further evaluation.

The second and third study were submitted for the renewal. Field trials have been conducted in follow up crops (spinach, radish and barley). Residues of flutolanil and its metabolites M-2, M-4, M-102 and their conjugates and M-101 have been determined. Bare soil received an application of flutolanil at 480 g as/ha (1.3N for the potato seed treatment) and 2100 g as/ha (5.7N for potato seed treatment and 1N for the potato in-furrow treatment in MRL appliation). Follow up crops were drilled at 30, 120 and 270 days after application of the test item. In all crops, planted after the treatment of 480 g as/ha, no residues of flutolanil and its metabolites have been detected above the LOQ (0.01 mg/kg) at all plant-back intervals, except in two straw samples at 30 and 120 days PBI, where metabolite M-4 was detected at the LOQ (0.01 mg/kg). In the trials where the following crops were planted after the application of 2100 g flutolanil/ha residues of parent compound and its metabolites have been found above the LOQ in edible crop parts, except for metabolite M-2, which was not detected in any sample. Parent compound flutolanil has been detected in spinach at 120 days PBI (0.02 mg/kg), in radish leaves at 30d PBI (0.01 mg/kg), at 120d PBI (0.03 mg/kg) and at 270d PBI (0.02 mg/kg). In cereals flutolanil was detected only in straw at 30d PBI (0.03 mg/kg), 120d PBI (0.02 mg/kg) and 270d PBI (0.01 mg/kg). Metabolite M-4 was detected in spinach at 30d PBI (0.02mg/kg); 120d PBI (0.02 mg/kg) and 270d PBI (0.01 mg/kg). M-4 was not detected in radish roots, and in radish leaves at level of 0.02 mg/kg at 120d PBI and 0.01 mg/kg at 270d PBI. M-4 was not detected in barley grain from any of the samples and it was measured in straw up to 0.1 mg/kg at 30d PBI, 0.03 mg/kg at 120d PBI and up to 0.02 mg/kg at 270d PBI.

Metabolite M-101 has been identified particularly in leafy vegetables and leafy part of the crop. In spinach, M-101 was detected at 30d PBI at 0.01 mg/kg, at 120d PBI at 0.03 mg/kg and at 270d PBI at 0.02 mg/kg. In radish leaves M-101 was detected at 120 and 270d PBI at level of 0.02 mg/kg. In grain no M-101 was found and in straw at 30, 120 and 270 days PBI at levels 0.03, 0.01 and 0.01 mg/kg, respectively.

Metabolite M-102 was detected in spinach and cereals. In spinach M-102 was up to 0.02 mg/kg at 30d and 270d PBI and up to 0.03 mg/kg at 120d PBI. In cereals M-102 has been identified in grain at 30d PBI (0.03 mg/kg) and 120 and 270d PBI at the level of 0.02 mg/kg. In straw M-102 was only found at 30d PBI at the concentration of 0.02 mg/kg.

Based on these findings it can be concluded that no relevant residues in rotational crops are expected after potato seed treatment following the proposed cGAP.

After in-furrow potato treatment, residues of flutolanil and its metabolites cannot be excluded in rotational crops and should be included in the consumer risk assessment. Furthermore, residues in cereals (whole plant, grain and straw) are of importance for the dietary burden calculation. Based on the available data RMS does not proposed separate residue definitions for succeeding crops, since all relevant metabolites have been included in the general RD for risk assessment.

2.7.8 Summary of other studies

No studies investigating residues in honey and bee products are available. It is noted that currently no test method or guidance document is available for conducting a feeding study on bees. However, since potatoes are probably not relevant crops for producing honey from available nectar and/or honeydew and the proposed application time is not in any way related to the flowering stage of potatoes, such studies are considered not required.

2.7.9 Estimation of the potential and actual exposure through diet and other sources

Based on the available residue levels of the metabolites included in the residue definition for risk assessment, Conversion Factor (CF) from monitoring to risk assessment has been calculated. Proposed CF for potato is 2.

Table 2.7.9-1 Input values for calculation of dietary exposures for consumers

Food commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: 1. Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil				
Potato	0.4	MRL* proposed $CF_{RD\text{-}Mo\ to\ RD\text{-}RA}$ (0.2*2)	0.4	MRL* proposed $CF_{RD\text{-}Mo\ to\ RD\text{-}RA}$ (0.2*2)
Spinach	0.04	HR in rotational leafy crop (spinach) at 120 days PBI	0.04	HR in rotational leafy crop (spinach) at 120 days PBI
Whole group Leaf vegetables (0250000)	0.04	HR in rotational leafy crop (spinach) at 120 days PBI extrapolated to group leafy vegetables	0.04	HR in rotational leafy crop (spinach) at 120 days PBI extrapolated to group leafy vegetables
Egg	0.01*	MRL	0.01*	MRL
Poultry (1016000)	0.01*	MRL	0.01*	MRL
Milk	0.03*	MRL	0.03*	MRL
Ruminants: Meat	0.03*	MRL	0.03*	MRL
Ruminant: Fat	0.03*	MRL	0.03*	MRL
Ruminant: Liver	0.03*	MRL	0.03*	MRL
Ruminant: Kidney	0.05	MRL	0.05	MRL
Risk assessment residue definition: 2. M-101				
Potato	0.01	STMR in SRT	No ARfD was set, no acute risk assessment was performed.	
Spinach	0.03	HR in rotational leafy crop (spinach) at 120 days PBI		
Whole group Leaf vegetables (0250000)	0.03	HR in rotational leafy crop (spinach) at 120 days PBI		

		extrapolated to the whole group leaf vegetable	
Egg	0.01	STMR feeding studies	
Poultry (1016000)	0.01	STMR feeding studies	

Flutolanil

The dietary exposure for consumers was estimated using the toxicological endpoints for flutolanil from assessment point 2.6.11 in this document, the proposed MRLs for the representative uses, relevant residues in rotational crops and EFSA PRIMO rev.2.

The TMDI is maximally 3.8% of the ADI for Dutch children. It is concluded that no chronic risk has to be expected for any of the European consumer groups (see Table 2.7.9-2).

A calculation of the Estimated Short Term Intake (ESTI) was carried out for the use potato using EFSA PRIMO model rev.2 and proposed MRL. The calculated ESTI for potatoes is 15,4% of the ARfD for UK infant. Hence, it is concluded that no acute risk is expected (see Table 2.7.9-3).

Metabolite M-101

The dietary exposure for consumers was estimated using the toxicological endpoints for metabolite M-101 from point 2.6.9 in this document, the residue values resulting from the available residue data in primary, rotational crops, and animal tissues, and EFSA PRIMO rev.2.

The TMDI is maximally 4.9% of the ADI for Dutch children. It is concluded that no chronic risk has to be expected for any of the European consumer groups (see Table 2.7.9-4).

No ARfD has been set for metabolite M-101, hence no acute consumer risk assessment is required.

Table 2.7.9-2 Report of chronic dietary consumer intake assessment to flutolanil for the uses supported for renewal

Flutolanil			
Status of the active substance:	**Renewal**	Code no.	
LOQ (mg/kg bw):	0,01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0,09**	ARfD (mg/kg bw):	**Not required**
Source of ADI:	**RAR TOX**	Source of ARfD:	**RAR TOX**
Year of evaluation:	**2017**	Year of evaluation:	**2017**

Prepare workbook for refined calculations

Undo refined calculations

+

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment

	TMDI (range) in % of ADI minimum - maximum
	0 4
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
3,8	NL child	2,6	Potatoes	1,0	Milk and cream,	0,1	Swine: Meat	0,0
3,7	FR toddler	2,3	Potatoes	1,3	Milk and cream,	0,0	Bovine: Meat	0,0
2,8	UK Infant	1,4	Potatoes	1,3	Milk and cream,	0,0	Birds' eggs	0,0
2,8	FR infant	1,8	Potatoes	0,9	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
2,4	PT General population	2,4	Potatoes	0,0	Leaf vegetables & fresh herbs		FRUIT (FRESH OR FROZEN)	
2,3	SE general population 90th percentile	1,9	Potatoes	0,4	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
2,3	UK Toddler	1,6	Potatoes	0,7	Milk and cream,	0,0	Birds' eggs	0,0
2,1	WHO regional European diet	1,8	Potatoes	0,2	Milk and cream,	0,0	Swine: Meat	0,0
2,0	WHO cluster diet D	1,8	Potatoes	0,2	Milk and cream,	0,0	Bovine: Meat	0,0
1,9	WHO cluster diet E	1,7	Potatoes	0,1	Milk and cream,	0,0	Bovine: Meat	0,0
1,8	WHO Cluster diet F	1,5	Potatoes	0,1	Milk and cream,	0,0	Swine: Meat	0,0
1,7	DE child	1,1	Potatoes	0,5	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
1,6	LT adult	1,4	Potatoes	0,1	Milk and cream,	0,0	Swine: Meat	0,0
1,5	PL general population	1,5	Potatoes	0,0	Leaf vegetables & fresh herbs		FRUIT (FRESH OR FROZEN)	
1,5	NL general	1,2	Potatoes	0,2	Milk and cream,	0,0	Swine: Meat	0,0
1,5	DK child	1,1	Potatoes	0,4	Milk and cream,	0,0	Birds' eggs	0,0
1,4	WHO Cluster diet B	1,2	Potatoes	0,1	Milk and cream,	0,0	Bovine: Meat	0,0
1,4	ES child	0,8	Potatoes	0,4	Milk and cream,	0,0	Bovine: Meat	0,0
1,2	IE adult	1,0	Potatoes	0,1	Milk and cream,	0,0	Other swine products	0,0
0,9	DK adult	0,6	Potatoes	0,2	Milk and cream,	0,0	Bovine: Meat	0,0
0,7	FI adult	0,5	Potatoes	0,2	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
0,7	UK Adult	0,6	Potatoes	0,1	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
0,7	UK vegetarian	0,6	Potatoes	0,1	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
0,7	ES adult	0,4	Potatoes	0,2	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
0,6	FR all population	0,5	Potatoes	0,1	Milk and cream,	0,0	Leaf vegetables & fresh herbs	0,0
0,4	IT kids/toddler	0,4	Potatoes	0,0	Leaf vegetables & fresh herbs		FRUIT (FRESH OR FROZEN)	
0,3	IT adult	0,3	Potatoes	0,0	Leaf vegetables & fresh herbs		FRUIT (FRESH OR FROZEN)	

Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Flutolanil is unlikely to present a public health concern.

approval

Table 2.7.9-3 Report of acute consumer intake assessment to flutolanil for the uses supported for renewal

	Acute risk assessment /children						Acute risk assessment / adults / general population					
	The acute risk assessment is based on the ARfD.											
	For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.											
	In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.											
	Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		—	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		—	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		—	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		—
	IESTI 1	*)	**)	IESTI 2	*)	**)	IESTI 1	*)	**)	IESTI 2	*)	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	15,4	Potatoes	0,4 / -	11,0	Potatoes	0,4 / -	3,0	Potatoes	0,4 / -	2,3	Potatoes	0,4 / -
	0,9	Milk and milk	0,03 / -	0,9	Milk and milk	0,03 / -	0,2	Witloof	0,04 / -	0,1	Witloof	0,04 / -
	0,9	Scarole (broad-leaf	0,04 / -	0,5	Scarole (broad-leaf	0,04 / -	0,1	Milk and milk	0,03 / -	0,1	Milk and milk products: Cattle	0,03 / -
	0,5	Witloof	0,04 / -	0,4	Witloof	0,04 / -	0,1	Lettuce	0,04 / -	0,1	Purslane	0,04 / -
	0,3	Lettuce	0,04 / -	0,2	Spinach	0,04 / -	0,1	Purslane	0,04 / -	0,1	Spinach	0,04 / -

Table 2.7.9-4 Report of chronic dietary consumer intake assessment to metabolite M-101 for the uses supported for renewal of flutolanil

Metabolite M-101			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0,01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0,002**	ARfD (mg/kg bw):	**Not set**
Source of ADI:	**RAR Tox**	Source of ARfD:	
Year of evaluation:	**2017**	Year of evaluation:	

Prepare workbook for refined calculations

Undo refined calculations

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment

TMDI (range) in % of ADI minimum - maximum	
1	5
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
4,9	NL child	2,9	Potatoes	1,3	Leaf vegetables & fresh herbs	0,4	Poultry -chicken, geese, duck,	3,6
4,6	FR toddler	2,5	Potatoes	1,1	Leaf vegetables & fresh herbs	0,5	Birds' eggs	3,5
3,5	WHO regional European diet	2,0	Potatoes	0,7	Leaf vegetables & fresh herbs	0,5	Poultry -chicken, geese, duck,	2,8
3,4	FR infant	2,1	Potatoes	0,8	Leaf vegetables & fresh herbs	0,3	Poultry -chicken, geese, duck,	2,6
3,3	SE general population 90th percentile	2,1	Potatoes	0,8	Leaf vegetables & fresh herbs	0,4	Birds' eggs	2,5
3,2	WHO cluster diet E	1,9	Potatoes	0,5	Poultry -chicken, geese, duck,	0,5	Leaf vegetables & fresh herbs	2,7
2,9	WHO Cluster diet B	1,3	Potatoes	0,9	Leaf vegetables & fresh herbs	0,5	Poultry -chicken, geese, duck,	2,1
2,8	PT General population	2,7	Potatoes	0,2	Leaf vegetables & fresh herbs		FRUIT (FRESH OR FROZEN)	2,7
2,8	ES child	0,9	Potatoes	0,9	Leaf vegetables & fresh herbs	0,6	Poultry -chicken, geese, duck,	1,9
2,7	WHO cluster diet D	2,0	Potatoes	0,2	Leaf vegetables & fresh herbs	0,2	Birds' eggs	2,4
2,6	DE child	1,3	Potatoes	0,6	Birds' eggs	0,5	Leaf vegetables & fresh herbs	2,1
2,6	WHO Cluster diet F	1,7	Potatoes	0,5	Leaf vegetables & fresh herbs	0,2	Poultry -chicken, geese, duck,	2,2
2,5	UK Infant	1,6	Potatoes	0,7	Birds' eggs	0,2	Poultry -chicken, geese, duck,	2,5
2,5	UK Toddler	1,7	Potatoes	0,4	Birds' eggs	0,2	Poultry -chicken, geese, duck,	2,4
2,5	NL general	1,4	Potatoes	0,8	Leaf vegetables & fresh herbs	0,2	Poultry -chicken, geese, duck,	1,7
2,1	DK child	1,2	Potatoes	0,4	Birds' eggs	0,3	Poultry -chicken, geese, duck,	1,9
2,1	ES adult	1,0	Leaf vegetables & fresh herbs	0,5	Potatoes	0,3	Poultry -chicken, geese, duck,	1,0
2,0	LT adult	1,6	Potatoes	0,2	Birds' eggs	0,2	Poultry -chicken, geese, duck,	1,9
1,9	IE adult	1,1	Potatoes	0,4	Leaf vegetables & fresh herbs	0,2	Poultry -chicken, geese, duck,	1,5
1,8	PL general population	1,7	Potatoes	0,0	Leaf vegetables & fresh herbs		FRUIT (FRESH OR FROZEN)	1,7
1,7	FR all population	0,7	Leaf vegetables & fresh herbs	0,6	Potatoes	0,3	Poultry -chicken, geese, duck,	1,0
1,5	IT adult	1,2	Leaf vegetables & fresh herbs	0,3	Potatoes		FRUIT (FRESH OR FROZEN)	0,3
1,4	IT kids/toddler	0,9	Leaf vegetables & fresh herbs	0,4	Potatoes		FRUIT (FRESH OR FROZEN)	0,4
1,3	UK Adult	0,7	Potatoes	0,2	Poultry -chicken, geese, duck,	0,2	Leaf vegetables & fresh herbs	1,1
1,2	DK adult	0,7	Potatoes	0,2	Leaf vegetables & fresh herbs	0,2	Birds' eggs	1,0
1,1	UK vegetarian	0,7	Potatoes	0,3	Leaf vegetables & fresh herbs	0,2	Birds' eggs	0,9
1,0	FI adult	0,6	Potatoes	0,1	Poultry -chicken, geese, duck,	0,1	Leaf vegetables & fresh herbs	0,9

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Metabolite M-101 is unlikely to present a public health concern.

2.7.10 Proposed MRLs and compliance with existing MRLs

Table 2.7.10-1: Overview of the proposed MRLs and compliance with existing MRLs for flutolanil

Commodity	Results from supervised residue trials (mg/kg)	STMR	HR	Pro-posed MRL	Existing MRL[1]	Remarks
Potato (seed treatment)	*NEU* 5x <0.01; <0.022; 0.01; 2x 0.014; 2x 0.02; 0.022; 2x 0.03; 0.035; 0.05; 0.09	0.02	0.09	0.15	0.1	Sufficient trial data are available. The proposed MRL is higher than the existing MRL. The MRL should be increased.
	SEU 7x <0.01; 2x 0.01; 2x 0.03; 0.04	0.01	0.04	0.06		
Potato (in furrow application)	*NEU* 6x<0.01; 0.03; 0.04; 0.08; 0.09; 0.1; 0.11	0.02	0.11	0.20	0.1	Sufficient trial data are available. The proposed MRL is higher than the existing MRL. The MRL should be increased.
	SEU 3x <0.01; 0.01; 4x 0.02; 0.03; 0.04; 0.09; 0.13	0.02	0.13	0.20		

2.7.11 Proposed import tolerance and compliance with existing import tolerances

Import tolerances are not proposed in the framework of the renewal of flutolanil.

2.8 Fate and behaviour in the environment

2.8.1 Summary of fate and behaviour in soil

In aerobic soil flutolanil degrades by the following reactions:

- Hydrolysis of ether bond to phenol at 3'-position (M-4 production from flutolanil, M-5 from M-2).
- Hydroxylation to form phenol at 4'-position (M-2 from flutolanil, M-5 from M-4, M-7 from M-6).
- Methylation of phenol at 3'-position (M-6 from M-4, M-7 from M-5).

- Oxidation of terminal methyl moiety of isopropyl part (M-3 and M-11 from flutolanil). The proposed metabolic pathway is shown below:

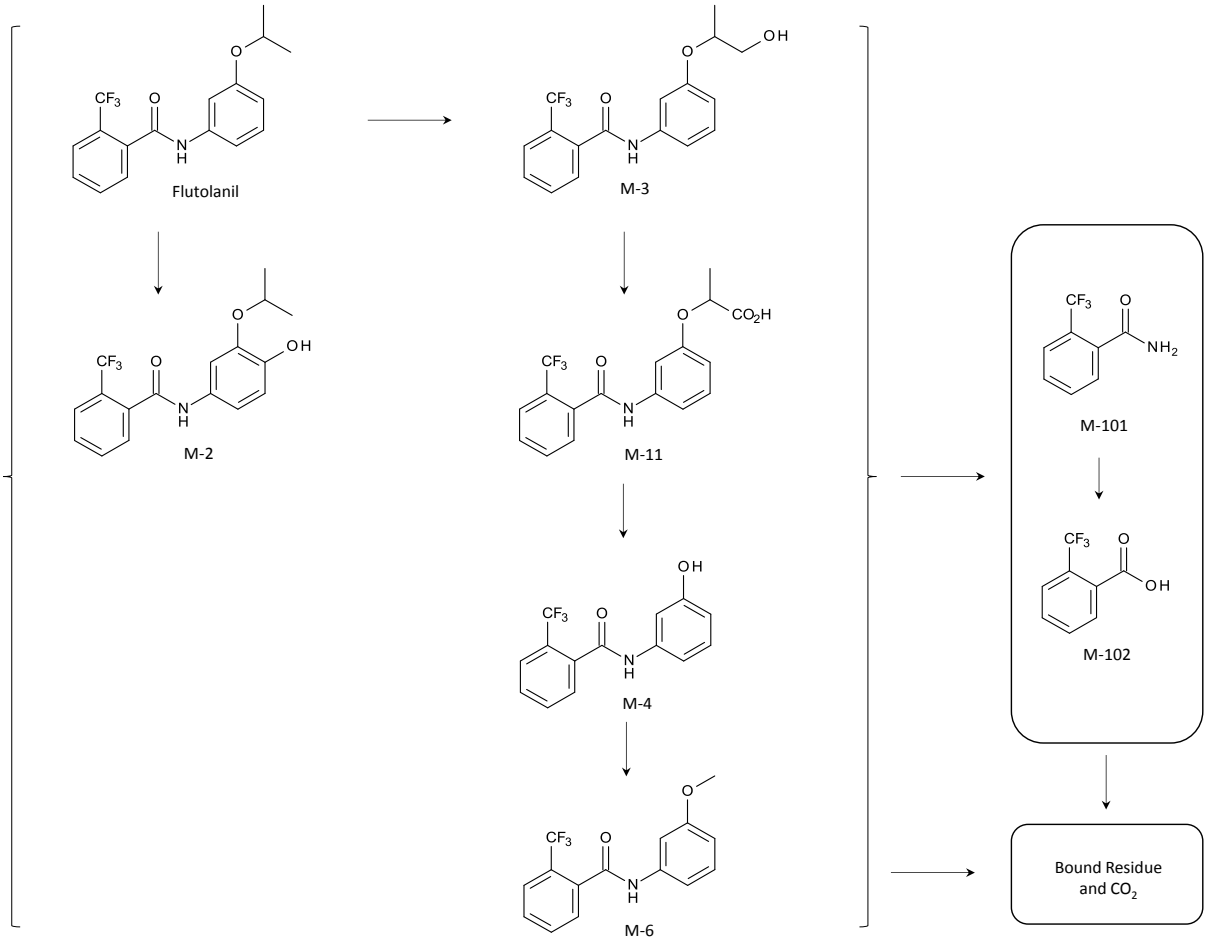


Figure 2.8.1-1 Aerobic route of degradation in soil

The route of degradation of flutolanil under dark aerobic conditions at 20ºC - 30ºC was investigated with [aniline ring-U-14C] labelled and [phenyl ring-U-14C] labelled compound in four reliable studies with five European soils, one US soil and two Japanese soils. The eight soils covered a range of pH (5.1–7.4), clay content (3.5-19.0%) and organic carbon content (0.6-4.9%). The aerobic degradation of flutolanil resulted in formation of bound residues (max. 27.9% AR after 105 days at 20ºC) and carbon dioxide (13.4% AR after 116 days at 25ºC). There were no major aerobic degradation metabolites at >10% or minor metabolites in soil >5% at 2 or more consecutive timepoints or >5% and increasing at the final timepoint in soil. Metabolite M4 was detected at max 3.0% and metabolite M11 was detected at max 4.9% AR (Takahashi, 2015).

The majority of the bound radioactivity was recovered in humin and humic acid fractions or associated in fulvic acid fraction. A degradation study under lower temperatures (10ºC) was conducted using Speyer soil having characteristics close to the one of the soils used in aerobic degradation study at 20ºC. Unextracted soil bound residues account for between 2 and 27% of the applied flutolanil at the end of the soil laboratory studies. Mineralization accounted for 28% AR at the end of the study.

The degradation rate of flutolanil under aerobic conditions was investigated in the same studies used to establish the route of degradation in soil. Calculated DT50 values were in the range 115-1000 days.

In the following tables, the acceptable persistence and modelling endpoints for flutolanil are summarised.
See the tables below for the summary of the degradation rates of flutolanil (laboratory and field).

Table B.2.8.1-1: Rate of degradation of flutolanil in soil (aerobic) laboratory studies.

Soil			Dark aerobic conditions.						
Name	Type	Year	pH (method)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_f / k_{dp}	DT_{50} (d) 20 °C pF2/10kPa)	St. (χ^2)	Method of calculation
Morgenroth, U. (1993),									
Speyer 2.2	loamy sand	1986	6.0 KCl	20 ± 2°C 100% of the field capacity.	115 / 383	-	115	1.75	SFO
Breda	sandy loam	1986	7.1 KCl	20 ± 2°C 100% of the field capacity.	383 / 1270	-	383	1.08	SFO
Westmaas	loam	1986	7.2 KCl	20 ± 2°C 100% of the field capacity.	151 / 502	-	151	0.873	SFO
St. Maartensbrug	sand	1986	7.4 KCl	20 ± 2°C 100% of the field capacity.	400 / 1330	-	400	2.04	SFO
Swanson, M. (1996)									
Wonder Lake / Millington Loam Bottom Soil	sandy loam	1993	7.4 unknown	25 ± 1°C 75% of the 1/3 bar field moisture capacity	116 / 820	-	442	3.81	DFOP
Takahashi, Y. (2015)									
F2.2 (Phenyl)	Loamy sand	2014	5.5 $CaCl_2$	20°C ± 2°C (40.2-59.8% of MWHC).	569 / 1890	-	not used in geometric mean calculation	1.51	SFO
F2.2 (Aniline)					547 / 1820	-		2.18	SFO
F2.2 (Aggregated Rep)					560 / 1860	-	560	1.70	SFO
Aizawa, H. (1982)									
Saitama (upland)	Loam	1981	4.8 KCl	30°C 60% MWHC	1000/>1000 700/2320	-	1000[a]	0.131/1.43	FOMC (persistence) SFO (modelling)
Okayama (upland)	Sandy loam	1981	5.3 KCl	30°C 60% MWHC	531 / 1770	-	1000 [a]	2.55	SFO

Soil			Dark aerobic conditions.						
Name	Type	Year	pH (method)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_f / k_{dp}	DT_{50} (d) 20 °C pF2/10kPa)	St. (χ^2)	Method of calculation
Geometric mean (n=8)							400		
Arithmetic mean						-			
pH dependence					No (R^2 < 0.5)				

[a] normalisation to 20°C and pF2 resulted in a degradation rate > 1000 days. The default maximum of 1000 days was applied.

The relationship between the soil pH (all converted to KCl) and the degradation rate was not correlated (R^2 < 0.5).

Table B.2.8.1-2: Rate of degradation of flutolanil in soil field studies. Bold values are used for exposure assessment

Soil									
Name	Type	Year	pH method	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_f / k_{dp}	DT_{50} (d) 20 °C pF2/10kPa)	St. (χ^2)	Method of calculation
Wicks, R. (1999) / Hardy, I.A.J., Agostini, F., & Jastrzebski, N. (2016b, c) and Hardy, I. & Jastrzebski, N. (2016a)									
Manningtree (tuber)	Sandy loam	1997	5.2 water	-	283 / 940	-	137	8.47	SFO
Ottersum (tuber)	Sandy loam	1997	7.0 water	-	**342** / 1140	-	171	10.7	SFO
Goch (tuber)	Silt loam	1997	6.5 water	-	184 / 1050	-	125	5.08	DFOP (persistence) SFO (modelling)
Niederkirchen (tuber)	Sandy loam	1997	7.6 water	-	259 / 859	-	166	14.6	SFO
Manningtree (spray)*	Sandy loam	1997	5.2 water	-	127 / 421	-	67.6	12.7	SFO
Ottersum (spray)	Sandy loam	1997	7.0 water	-	**211** / 701	-	116	16.3	SFO
Ginzburg, N & Hardy, I. (2007) / Hardy, I.A.J., Agostini, F., & Jastrzebski, N. (2016b,c)									
Amstenrade (FA-26-05-01/02)	Silt loam	2005	8.0 unknown	-	104 / 347	-	66.3	15.0	SFO
Ubachsberg (FA-26-05-01/01)	Loam	2005	7.7 unknown	-	86.0 / 286	-	60.4	15.7	SFO
Geometric mean (n=8)							**105**		
Arithmetic mean						-			
pH dependence					No				

* excluding day 0.

The relationship between the soil pH (water) and the degradation rate was not correlated ($R^2 < 0.5$). RMS determined whether the databases of DegT50matrix values from laboratory (Table B.2.8.1-1) and field (Table B.2.8.1-2) studies can be treated as separate databases or whether they should be pooled. From the DegT50 excel sheet that is related to the EFSA guidance document[1] to obtain DegT50, the conclusion was that the test confirms that the field studies show shorter DegT50 than the laboratory studies. Therefore, the field DegT50 results are used to derive the geometric mean modelling endpoint (see Table B.2.8.1-2). It should be noted that tuber and spray application field DT_{50} values are combined. However, based on comments of the co-RMS and applicant it was verified with the EFSA endpoint selector that these populations are statistically different (geomean tuber treatments is 148.5 days and geomean spray treatments is 74.9 days).
For PEC soil modelling, the maximum tuber non-normalised field DT50 is used (342 days). If an authorisation with a spray application is applied for, the maximum spray non-normalised field DT50 of 211 days should be used.

Soil accumulation studies were triggered because the $DisT_{90}$field in one or more soils is greater than one year. This study showed no leaching of flutolanil to deeper layers.

Under anaerobic conditions only very limited degradation of flutolanil was observed. Please refer to the next table for details.

Table B.2.8.1-3: Rate of degradation flutolanil in soil (anaerobic) laboratory studies.

Soil			Dark anaerobic conditions.						
Name	Type	Year	pH (water)	t. °C / % MWHC (during aerobic phase)	DT_{50}/ DT_{90} (d)	f. f. k_f / k_{dp}	DT_{50} (d) 20 °C pF2/10kPa)	St. (χ^2)	Method of calculation
Mallipudi, N. & Cooke, L. (2013)									
Sandy clay loam	Sandy clay loam	2011	6.9	20°C / 40%	958/3181	-	597	2.23	SFO
Loamy sand 2	Loamy sand	2011	5.9	20°C / 40%	1372/4556	-	1054	1.49	SFO
Roohi, A. (2016)									
Speyer 2.2	loamy sand	2015	5.9	20°C / pF2	> 1000	-	> 1000	-	SFO (anaerobic) and HS (aerobic/anaerobic)- Not statistically sound
Geometric mean (n=3)							857		
Arithmetic mean						-			
pH dependence					No				

[1] European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp., doi:10.2903/j.efsa.2014.3662

The three results that are shown are not acceptable according to FOCUS kinetics, since they are statistically not significant (k not different from zero). They are shown to confirm that anaerobic degradation is limited.

The main identified metabolite was M4 (maximum 3.5% AR at day 90 during the anaerobic phase. There were no major anaerobic degradation metabolites at >10% or minor metabolites in soil >5% at 2 or more consecutive timepoints or >5% and increasing at the final timepoint in soil.

Photodegradation does not play a role in the degradation of flutolanil. No measurable degradation of flutolanil occurred under the conditions of the study in dark and irradiated samples. No metabolites were found in irradiated samples exceeding 2% AR.

Summary sorption flutolanil

The adsorption/desorption characteristics of flutolanil were determined in a standard batch equilibrium experiment. For the results, see the table below.

Table B.2.8.1-4: Adsorption and desorption constants for flutolanil in soil

Soil ID	Texture	pH (water)	OC [%]	Adsorption			Desorption		
				K_f [mL/g]	K_{oc} [mL/g]	1/n	K_f [mL/g]	K_{oc} [mL/g]	1/n
Williams, M., (1992a)									
#110 Loam	loam	8.0	0.47	2.76	594	~~0.835~~	3.86	830	~~0.892~~
#90 Clay loam	clay loam	7.4	2.85	13.0	457	~~0.714~~	18.8	659	~~0.726~~
#86 Clay loam	clay loam	6.2	0.64	4.02	628	~~0.901~~	5.71	892	~~0.714~~
#126 Loamy sand	loamy sand	4.8	1.57	15.8	1005	~~0.926~~	20.8	1327	~~0.936~~
Geometric mean (n=4)	-	-	-	-	**643**	-	-	897	-
Arithmetic mean (n=4)	-	-	-	-	-	**0.9***	-	-	0.9*

* no acceptable Freundlich exponent (1/n) could be derived and therefore the default value is proposed by RMS. This default of 0.9 is set when Tier 3 OECD 106 has been performed, but no reliable endpoint could be determined.

The range of acceptable adsorption Kf constants for flutolanil is between 2.76 – 15.8, corresponding to a Kfoc range of 457 – 1005. The Freundlich values that were reported in Williams (1992a) are not used, because the range in concentrations is too low to derive the Freundlich exponent reliably. Therefore, the use of the default value is proposed by RMS. This default of 0.9 is set when Tier 3 OECD 106 has been performed, but no reliable endpoint could be determined.

There is a correlation between pH and adsorption for the investigated soils (R^2 = 0.717), but this relation is not visually substantiated by the data available. Please refer to the following figure.

Additionally, the substance has no acidic or basic substituents which could dissociate (i.e. no dissocation constant is available), making pH dependent behavior unlikely.

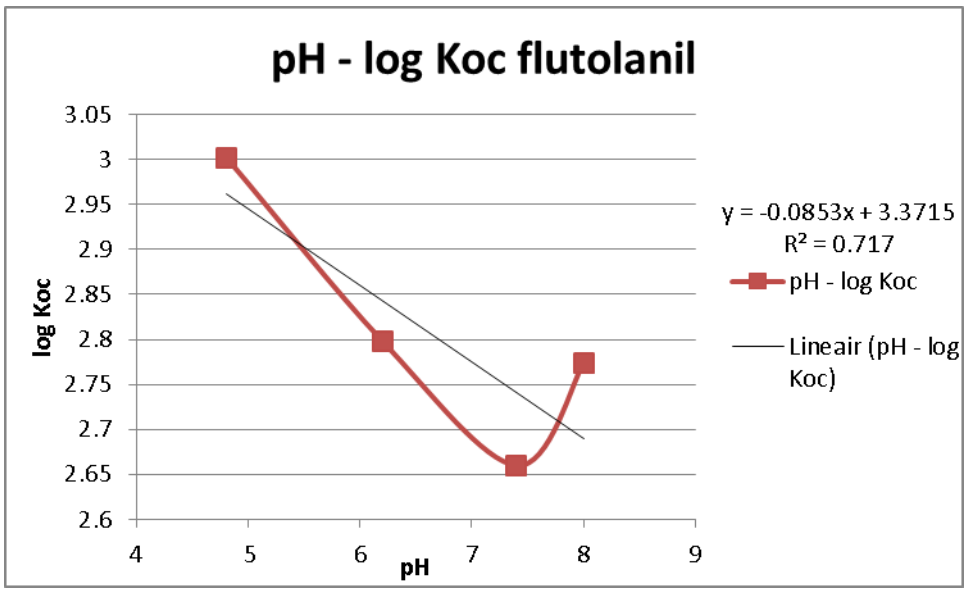


Figure 2.8.1-2 Relation between pH and sorption

Summary sorption desisopropylflutolanil (M4)

For the surface water metabolite desisopropylflutolanil (α,α,α-trifluoro-3'-hydroxy-o-toluanilide) (M4), sorption study results are available.

See the table below for details.

Table B.2.8.1-5: Adsorption and desorption constants for flutolanil surface water metabolite M4

Soil ID	Texture	pH (water)	OC [%]	Adsorption			Desorption		
				K_f [mL/g]	K_{oc} [mL/g]	1/n	K_f [mL/g]	K_{oc} [mL/g]	1/n
Williams, M., (1992b)									
#110 Loam	loam	8.0	0.47	1.36	293	~~0.859~~	1.74	375	~~0.702~~
#90 Clay loam	clay loam	7.4	2.85	11.3	396	~~0.750~~	14.9	522	~~0.756~~
#126 Loamy sand	loamy sand	4.8	1.57	4.98	317	~~0.752~~	8.27	527	~~0.684~~
Geometric mean (n=3)	-	-	-		**333**			469	
Arithmetic mean (n=3)	-	-	-	-	-	**0.9***	-	-	0.9*

[a] Due to poor correlation and a percent adsorbed of < 20%, the desorption isotherm for sand #92 was also calculated using the measured amount of ^{14}C-activity remaining on the soil.
* no acceptable Freundlich exponent (1/n) could be derived and therefore the default values are proposed by RMS. This default of 0.9 is set when Tier 3 OECD 106 has been performed, but no reliable endpoint could be determined.

There is no correlation between pH and adsorption for the investigated soils (R^2 = 0.008).

The range of acceptable adsorption Kf constants for M4 is between 1.36 – 11.3, corresponding to a narrow Kfoc range of 293 – 396. The Freundlich values that were reported in Williams (1992b) are not

used, because the range in concentrations is too low to derive the Freundlich exponent reliably. Therefore the use of the default value is proposed by RMS. This default of 0.9 is set when Tier 3 OECD 106 has been performed, but no reliable endpoint could be determined.

2.8.2 Summary of fate and behaviour in water and sediment

Flutolanil is hydrolytically stable in buffers at pH 5, pH 7 and pH 9, independent of the temperature.

The photolytic degradation of flutolanil in water has been investigated under sterile conditions in acetate buffer solutions at pH 7 for up to 30 days. Photolysis accelerates the degradation of flutolanil in aqueous buffer solutions at pH 7. The DT50 value based on individual replicate data of Tanaka (2016) was 231 days. The other photolysis study (Carpenter, 1991) did not present half lives according to FOCUS kinetics, but similar half lives were observed. Two known degradates M-101 and M-102 were identified as minor degradates, which accounted for 2.6 and 1.3% of AR after 24 days irradiation, several unknown degradates were detected but none of these accounted for greater than 2% of AR.

Flutolanil was found to be non-biodegradable in a non-GLP BOD study.

In four water / sediment systems (pH of water phase 6.8 - 8.3) flutolanil did not significantly mineralize. Flutolanil partitioned from the water phase into the sediment. Once in the sediment, parent continued to degrade over time. Flutolanil reached a maximum of 78.4% of applied radioactivity in the sediment at the end of the incubation period 98 days. Kinetic modelling analysis according to FOCUS Kinetics of the data from four aquatic sediment systems treated with flutolanil provided acceptable model fits, giving a geometric mean total system DegT50 value of **224** days. Trigger DT50 values for whole system, water and sediment were in the range 88.7-413, 4.49-50.4 and 91.9-1000 days, respectively, and trigger DT90 values were in the range 295-1480, 86.2->10000 and 305-3320 days, respectively.

No transformation products ≥10% AR were observed in the water or sediment layer for either radiolabel. Two major degradates of flutolanil were found: metabolite M-4, (α,α,α-trifluoro-3'-hydroxy-*o*-toluanilide) was found in the water at 5.2% AR%, without other timepoints at >5% and without an increasing tendency. However, the %AR for water + sediment (system) was >5% at two consecutive timepoints (max **6.8%**). Metabolite M-11, (2-[3'-(α,α,α-trifluoro-*o*-toluamido)phenoxy]propionic acid) was found >5% at two consecutive timepoints (5.4% at day 61 and 6.9% AR at day 105) in the water compartment, and consequently >5% in the whole system as well (max **8.3**%). Additionally, variousinor transformation products in the sediment were detected which reached maximum concentrations of < 5.0% AR.

In an aerobic mineralisation study (OECD 309) the fate of flutolanil was investigated in natural water at pH 8.2. The results indicated that flutolanil did not significantly mineralise (<1% applied radioactivity) over the study duration (90 days). Hence no metabolites were formed at >5% AR. DT_{50} and DT_{90} values for flutolanil in surface water were greater than one year.

2.8.3 Summary of fate and behaviour in air

The photochemical-oxidative half-life of flutolanil in air is 0.072 days (12hr day) or 0.036 (24hr day). The vapour pressure of flutolanil is 4.1 x 10^{-7} Pa, which is well below the triggers for volatilisation of 10^{-5} Pa from plants and 10^{-4} Pa from soil. Thus it would not be expected to be present in significant concentrations in air following use of the compound according to the proposed GAP.

2.8.4 Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products

Two publications of groundwater monitoring in the United Kingdom and the Netherlands which include monitoring for flutolanil have been included in this submission. Both publications confirm a low risk to groundwater from flutolanil. A surface water monitoring study for the Netherlands was included, indicating that flutolanil concentrations do not exceed ecotoxicological treshold values in surface water.

2.8.5 Definition of the residue in the environment requiring further assessment

The residue definition relevant for environmental risk assessment is as follows:

Soil	Flutolanil
Groundwater	Flutolanil
Surface water	Flutolanil
Sediment	Flutolanil
Air	Flutolanil

2.8.6 Summary of exposure calculations and product assessment

Exposure via Soil

The predicted environmental concentrations in soil (PEC_{soil}) for the active substance flutalonil were calculated based on a simple first tier approach (Microsoft® Excel spreadsheet) assuming even distribution of the compound in the upper 0-5 cm soil layer. A standard soil density of 1.5 g/cm^3 was assumed. The interception rates follow the recommendations of the FOCUS groundwater guidance paper (FOCUS 2014) for potatoes and flower bulbs. According to the use pattern, a single application of flutolanil at 368 g flutolanil/ha to potatoes and at 2760 g flutolanil/ha to flower bulbs was considered. The maximum PECsoil for application to flower bulbs is 4.520 mg/kg (assuming a soil layer of 5 cm, worst-case default) and 2.641 mg/kg (assuming a soil layer of 10 cm, conservative approach considering incorporation into the soil to a depth of 10-15 cm). The maximum PECsoil for potatoes is 0.603 mg/kg.

Details of the calculations are given in Document CP, B.8.2, for flutolanil.

Exposure via Groundwater

Predicted environmental concentrations in groundwater (PEC_{gw}) for flutolanil was calculated for the use in Europe, using the simulation models FOCUS-PEARL (version 4.4.4), PELMO (version 5.5.3) and MACRO (version 5.5.4). PEC_{gw} were evaluated as the 80^{th} percentile of the mean annual leachate

concentration at 1 m soil depth. Model parameters and scenarios consisting of weather, soil, and crop data were used as proposed by FOCUS.

Details of the calculations are given in Document CP, B.8.3. The results are summarised in the tables below.

Table B.2.8-6: FOCUS PEARL, PELMO and MACRO PEC_{gw} results of Flutolanil potato incorporation at 0.1 m. Values in bold exceed the 0.1 µg/L criterion.

Scenario	Flutolanil		
	PEARL	PELMO	MACRO
	[µg/L]	[µg/L]	[µg/L]
Chateaudun	<0.001	<0.001	<0.001
Hamburg	0.004	0.001	n.a.
Jokioinen	<0.001	<0.001	n.a.
Kremsmuenster	0.002	0.001	n.a.
Okehampton	0.003	0.003	n.a.
Piacenza	0.003	0.002	n.a.
Porto	<0.001	<0.001	n.a.
Sevilla	<0.001	<0.001	n.a.
Thiva	<0.001	<0.001	n.a.

n.a.= not assessed

Table B.2.8-7: FOCUS PEARL, PELMO and MACRO PEC_{gw} results of Flutolanil potato injection at 0.1 m. Values in bold exceed the 0.1 µg/L criterion.

Scenario	Flutolanil		
	PEARL	PELMO	MACRO
	[µg/L]	[µg/L]	[µg/L]
Chateaudun	<0.001	n.a.	n.a.
Hamburg	0.012	n.a.	n.a.
Jokioinen	<0.001	n.a.	n.a.
Kremsmuenster	0.007	n.a.	n.a.
Okehampton	0.009	n.a.	n.a.
Piacenza	0.009	n.a.	n.a.
Porto	<0.001	n.a.	n.a.
Sevilla	<0.001	n.a.	n.a.
Thiva	<0.001	n.a.	n.a.

n.a.= not assessed since this application method is not available in PELMO and MACRO

Table B.2.8-8: FOCUS PEARL, PELMO and MACRO PEC_{gw} results of Flutolanil flower bulbs incorporation at 0.15 m (onion used as a surrogate crop). Values in bold exceed the 0.1 µg/L criterion.

Scenario	Flutolanil		
	PEARL	PELMO	MACRO
	[µg/L]	[µg/L]	[µg/L]
Chateaudun	0.005	<0.001	<0.001
Hamburg	**0.345**	0.001	n.a.
Jokioinen	<0.001	<0.001	n.a.
Kremsmuenster	**0.216**	0.001	n.a.
Okehampton	n.a.	n.a.	n.a.
Piacenza	n.a.	n.a.	n.a.
Porto	0.025	<0.001	n.a.
Sevilla	n.a.	n.a.	n.a.
Thiva	<0.001	<0.001	n.a.

n.a.= not assessed

Exposure via Surface Water and Sediment

Predicted environmental concentrations of the active substance flutolanil and its metabolites M-4 and M-11 in surface water (PEC_{sw}) and sediment (PEC_{sed}) were calculated for the use in Europe, employing the tiered FOCUS Surface Water (SW) approach (FOCUS 2001, 2015). All relevant entry routes of a compound into surface water (principally a combination of spray drift and runoff/erosion or drain flow) were considered in these calculations.

The FOCUS tool SWASH (v 5.3), including the operational models FOCUS-MACRO (v 5.5.4), FOCUS-PRZM (v 4.3.1) and FOCUS-TOXSWA (v 4.4.3), were used in the modelling study for Step 3 simulations.

According to the use pattern, a single application of flutolanil at 368 g flutolanil/ha to potatoes and a single use for flower bulbs at 2760 g flutolanil/ha to were considered.

Details of the calculations are given in Document 3-CP, Section B.8.4, for flutolanil.

The maximum PECsw and PECsed for flutolanil and its metabolites are shown in the tables below.

Maximum PECsw and PECsed values for Flutolanil, M4 and M11 (FOCUS Steps 1-2, and SWASH (Step 3))

Crop Usage	Scenario	Flutolanil		M4		M11	
		PEC_{sw}	PEC_{sed}	PEC_{sw}	PEC_{sed}	PEC_{sw}	PEC_{sed}
		[µg/L]	[µg/kg]	[µg/L]	[µg/kg]	[µg/L]	[µg/kg]
Potato 368 g a.s./ha No interception Spring (Mar. - May)	Step 1	66.04	424.67	2.22	7.38	5.36	0.05
	Step 2	25.73	165.44	0.88	2.94	2.14	0.02
	Step 3	0.091	0.224	0.013	0.088	2.795	1.994
Tulip & iris 2760 g a.s./ha No interception Spring (Mar. - May)	Step 1	495.33	3.18E+03	16.63	55.37	40.16	0.40
	Step 2	192.97	1.24E+03	6.63	22.09	16.02	0.16
	Step 3	25.25	33.74	0.163	1.009	20.74	14.89

Other routes of exposure

There are no other routes of exposure if the product is used according to good agricultural practice.

2.9 Effects on non-target species

2.9.1 Summary of effects on birds and other terrestrial vertebrates

Test species	Time scale	Test material	Endpoint [95% CI, lower - upper]	Data point Author, year
Birds				
Bobwhite quail (*Colinus virginianus*)	Acute	Flutolanil Technical	**LD_{50} > 2000 mg a.s./kg bw** NOEL = 2000 mg a.s./kg bw LD_{10} = ND LD_{20} = ND	CA 8.1.1.1-01 [redacted] 1987a
Mallard duck (*Anas platyrhynchos*)	Acute	Flutolanil Technical	LD_{50} > 2000 mg a.s./kg bw NOEL = 2000 mg a.s./kg bw LD_{10} = ND LD_{20} = ND	CA 8.1.1.1-02 [redacted] 1987b
Bobwhite quail (*Colinus virginianus*)	Short-term dietary (5-days)	Flutolanil Technical	LC_{50} > 5243 ppm LD_{50} > 961 mg/kg bw/d	CA 8.1.1.2-01 [redacted] 1987c
Mallard duck (*Anas platyrhynchos*)	Short-term dietary (5-days)	Flutolanil Technical	LC_{50} > 5243 ppm LD_{50} > 1249 mg/kg bw/d	CA 8.1.1.2-02 [redacted] 1987d
Bobwhite quail (*Colinus virginianus*)	Long-term	Flutolanil Technical	**NOEC = 247.8 mg a.s./kg bw/day** EC_{10}^{*} = 525 [ND - 873] mg a.s./kg bw/day EC_{20} = ND EC_{50} = ND	CA 8.1.1.3-01 [redacted] 1993a CA 8.1.1.3-03. [redacted] 2016

Test species	Time scale	Test material	Endpoint [95% CI, lower - upper]	Data point Author, year
Mallard duck (*Anas platyrhynchos*)	Long-term	Flutolanil Technical	NOEC = 267.5 mg a.s./kg bw/day $NOEC_{ecologically\ relevant}$ = 687 mg a.s./kg bw/day EC_{10} = ND EC_{20} = ND EC_{50} = ND	CA 8.1.1.3-02 [redacted] 1996 CA 8.1.1.3-03. [redacted] 2016
Other terrestrial vertebrates				
Rat	Acute oral	Flutolanil 40SC	LD_{50} > 2000 mg/kg bw	CP 7.1.1/01 [redacted] (2007a)
Rat	Acute oral	Flutolanil Technical	**LD_{50} > 2000 mg/kg bw**	CA 5.2.1-03 [redacted], 2009
Rat	Short term oral 28 days	Flutolanil	NOAEL = 180 mg/kg/day (minor reduction in body weight gain with slight liver weight increase at ≥ 916 mg/kg/day)	CA 5.3.1/01 [redacted] 1977
Rat	Short term oral 90 days	Flutolanil technical	NOAEL = 37 mg/kg/day (increased liver and thyroid/parathyroid weight and increased albumin at ≥ 299 mg/kg/day).	CA 5.3.2/01 [redacted] 1986a
Mouse	Short term oral 90 days	Flutolanil technical	NOAEL = 680 mg/kg/day (reduced weight gain with increased liver weight at 8637 mg/kg/day)	CA 5.3.2/02 [redacted] 1987
Dog	Short term oral 90 days	Flutolanil technical	NOAEL = 80 mg/kg/day (increased liver weight with hepatocyte swelling and pallor at 400 mg/kg/day)	CA 5.3.2/03 [redacted] 1986b
Rat	Reproductive	Flutolanil Technical	$NOAEL_{parental}$ = 160 mg/kg/d for males, 190 mg/kg/d for females EC_{10} = ND EC_{20} = ND (increased liver weight) $NOAEL_{pup,\ reproduction}$ = ≥ 1614 mg/kg bw/d	CA 5.6.1-01 [redacted], 1991 CA 8.1.2.2-01 [redacted] 2016
Rat	Developmental 6-15 days gestation	Flutolanil Technical	Maternal: NOAEL ≥ 1000 mg/kg bw/day No LOAEL Embryofetal toxicity: NOAEL ≥ 1000 mg/kg bw/day No LOAEL EC_{10} = ND EC_{20} = ND	CA 5.6.2/01 [redacted] 1987, as amended 1992 CA 8.1.2.2-01 [redacted] 2016

Test species	Time scale	Test material	Endpoint [95% CI, lower - upper]	Data point Author, year
Rabbit	Developmental 6-18 days gestation	Flutolanil Technical	**NOAEL = 40 mg/kg bw/d** (resportions and deaths occurring in 5 different litters (out of 13 litters))	CA 5.6.2/02 [redacted] (1987)
Rabbit	Developmental 6-27 days gestation	Flutolanil	Maternal: NOAEL ≥ 1000 mg/kg bw/day No LOAEL Embryofetal toxicity: NOAEL ≥ 1000 mg/kg bw/day No LOAEL EC_{10} = ND EC_{20} = ND	CA 5.6.2/03 [redacted] 2012
Metabolite M-101				
Rat	Acute oral	2-(trifluoromethyl)-benzamide (M-101)	LD_{50} = > 300 mg metabolite/kg bw and < 2000 mg/kg bw	CA 5.8.1/02 [redacted] (2011)
Rat	Short term oral 28 days	2-(trifluoromethyl)-benzamide (M-101)	NOAEL ♂ = 4.2 mg metabolite/kg bw/d (organ weight changes, clinical chemistry) **NOAEL ecotoxicologically relevant ♂ = 17.6 mg metabolite/kg bw/d** (bodyweight decrease♂)	CA 5.8.1/03 [redacted] (2012)
Metabolite M-102				
Rat	Acute oral	2-(trifluoromethyl)-benzoic acid (M-102)	**LD_{50} > 2000 mg metabolite/kg bw**	CA 5.8.1/07 [redacted] (2016)
Rat	Short term oral 28 days	2-(trifluoromethyl)-benzoic acid (M-102)	**NOAEL ♂ = 252 mg metabolite/kg bw/d**	[redacted] (2010) CA 5.8.1/08

Endpoints in **bold** are the agreed endpoints retained for the risk assessment in line with the EFSA Conclusion (2008, 2013)
ND: could not be determined.
CI: Confidence intervals
* Endpoint not considered reliable

2.9.2 Summary of effects on aquatic organisms

Species	Test substance	Time-scale (Test type)	End point	Data point Author, year
Toxicity to Fish				

Species	Test substance	Time-scale (Test type)	End point		Data point Author, year
Oncorhynchus mykiss[1] (Rainbow trout)	Flutolanil Technical	Acute, 96h (static)	LC_{50} NOEC	5.4 mg/L (m.m.) 3.0 mg/L (m.m.)	CA 8.2.1-01 [redacted] 1987a
Lepomis macrochirus (Bluegill sunfish)	Flutolanil Technical	Acute, 96h (static)	LC_{50} NOEC	> 5.4 mg/L (m.m.) 2.5 mg/L (m.m.)	CA 8.2.1-02 [redacted] 1987b
Pimephales promelas (Fathead minnow)	Flutolanil Technical	Acute, 96h (static)	LC_{50} NOEC	**4.8 mg/L (m.m.)** 1.2 mg/L (m.m.)	CA 8.2.1-03 [redacted] 1990
Pimephales promelas (Fathead minnow)	Flutolanil Technical	Long-term, FELS, 30 days (flow-through)	NOEC $EC_{10, wet weight}$ EC_{20} EC_{50} MATC	**0.233 mg/L (m.m.)** 0.601 mg/L (m.m.) ND ND 0.337 mg/L (m.m.)	CA 8.2.2.1-01 [redacted] 1995 CA 8.2.2.1-02 [redacted] 2016
Toxicity to aquatic invertebrates					
Daphnia magna (Water flea)	Flutolanil Technical	Acute, 48h (static)	EC_{50}	> 6.8 mg/L (m.m.)	CA 8.2.4.1-01 Forbis, A.D. *et al*., 1990
Daphnia magna (Water flea)	Flutolanil Technical	Reproduction, 21 days (semi-static)	NOEC EC_{10} (95% CI) EC_{20} (95% CI) EC_{50} (95% CI) MATC	0.29 mg/L (m.m.) 2.03 (1.35-2.45) mg/L (m.m.) 2.37 (1.74-2.75) mg/L (m.m.) 3.18 (2.73-3.58) mg/L (m.m.) 0.76 mg/L (m.m.)	CA 8.2.5.1-01 Blakemore, G.C. & Burgess, D.,1991 CA 8.2.5.1-02 Palmer, D.A., 2016
Mysidopsis bahia (Shrimp)	Flutolanil	Acute, 48h (static)	LC_{50}	**0.13**[3] **(0.087-0.16) mg/L (m.m.)**	CA 8.2.4.2-01 Forbis, A.D., 1991
Mysidopsis bahia (Shrimp)	Flutolanil	Life-cycle, 28 days (flow-through)	NOEC EC10 (95%CI) Survial production young/female growth (dry weight) EC20 (95%CI) Survial production young/female growth (dry weight) EC50 (95%CI) Survial production young/female growth (dry weight)	0.0113 mg/L **0.00397 (0.00241-0.00560) mg/L (m.m.)** 0.0117 (0.0101-0.0129) mg/L (m.m.) 0.0165 (0.0063-0.0252) mg/L (m.m.) 0.00685 (0.00472-0.00896) mg/L (m.m.) 0.0136 (0.0122-0.0147) mg/L (m.m.) 0.0321 (0.0192-0.0430) mg/L (m.m.) 0.0195 (0.0158-0.0238) mg/L (m.m.) 0.0182 (0.0172-0.0191) mg/L (m..m) 0.115 (0.0812-0.237) mg/L (m.m.)	CA 8.2.5.2-01 Boeri, R.L., Kowalski, P.L., Ward, T.J., 1995
Chironomus riparius (Chironomid Midge)	Flutolanil	Long-term: Water spiked, 28 days (static)	NOEC EC_{10} EC_{20} EC_{50}	**1.0 mg/L (nom.)** ND ND > 1 mg/L (nom.)	CA 8.2.5.3-01 Desmares-Koopmans, D., 2003
Toxicity to algae					

Species	Test substance	Time-scale (Test type)	End point		Data point Author, year
Pseudokirchneriella subcapitata[2] (Green algae)	Flutolanil Technical	Chronic, 72h (static)	E_rC_{10} E_rC_{25} E_rC_{50} E_bC_{50} NOEC	0.49 mg/L (nom.) 2.30 mg/L (nom.) **> 3.2 mg/L (nom.)** 0.97 mg/L (nom.) 0.18 mg/L (nom.)	CA 8.2.6.1-01 Migchielsen, M.H.J., 2003

[1] Formerly known as *Salmo gairdneri*
[2] Formerly known as *Selenastrum capricornutum*
[3] only for adults, not for juvenile shrimps
ND: Could not be determined
CI: Confidence Intervals
Note: When more than one endpoints are available for a substance for the same taxonomic group and study type, the lowest endpoint is in **bold** and is the one used in the risk assessment

2.9.3 Summary of effects on arthropods

Summary of toxicity data on bees

Species	Test substance	Time-scale (Test type)	End point	Toxicity	Data point /Author, year
Honey bee (*Apis mellifera* L.)	Flutolanil Technical	48h, Acute oral	LD_{50}	**> 208.7 µg a.s./bee**	CA 8.3.1.1.1-01 Schmitzer, S., 2001
		48h, Acute contact	LD_{50}	**> 200 µg a.s./bee**	
	Flutolanil 40 SC[1]	10 d, Chronic oral	LDD_{50} (95% CI) LDD_{20} (95% CI) LDD_{10} (95% CI)	**35.1 µg a.s./bee/day** (29.0 – 42.7) 18.3 µg a.s./bee/day (13.2 – 22.7) 13.0 µg a.s./bee/day (8.4-17.0)	CA 8.3.1.2-01 Ruhland, S., 2016
	Flutolanil 40 SC[1]	22 d, Larval toxicity	NOED LD/ED_{10} (95% CI) LD/ED_{20} (95% CI) LD/ED_{50} (95% CI)	**10 µg a.s./larva** 9.4 (6.5-14.0) µg a.s./larva 10.6 (7.1-15.9) µg a.s./larva 11.7 (10.6-13.0) µg a.s./larva	CA 8.3.1.3-01 Scheller, K., 2016
	Monarch 40 SC[1]	8 d, Semi-field	NOEC	> 11200 g in 400 L/ha	CP 10.3.1.6-01 Kling, A., 2003

Note: Endpoints in **bold** are the agreed endpoints retained for the risk assessment in line with the EFSA Conclusion (2008)

[1] Flutolanil 40 SC and Monarch 40 SC are equivalent to the representative formulation MONCUT 40 SC

CI = Confidence Intervals

Effects on other arthropod species (Regulation (EU) N° 283/2013, Annex Part A, point 8.3.2 and Regulation (EU) N° 284/2013 Annex Part A, point 10.3.2)

Laboratory tests with standard sensitive species

Species	Test Substance	Endpoint	Toxicity
Typhlodromus pyri	EXP10066A	Mortality, LR_{50} Reproduction, ER_{50}	> 4500 g a.s./ha > 4500 g a.s./ha
Aphidius rhopalosiphi	EXP10066A	Mortality, LR_{50} Reproduction, ER_{50}	> 4500 g a.s./ha > 4500 g a.s./ha

Further laboratory tests, extended laboratory tests, aged residue tests

Species	Life stage	Test substance, substrate	Time scale	Dose (g/ha)	Endpoint	% effect	LR/ER_{50}
Poecilus cupreus	Adult	EXP10066A (quartz sand)	14 d	450 4500 (active substance, initial residues)	Mortality	0 6.7	LR_{50} > 4500 g a.s./ha
Pardosa sp.	Subadult and adult	EXP10066A (animals and quartz sand)	14 d	450 4500 (active substance, initial residues)	Mortality	0 6.7	LR_{50} > 4500 g a.s./ha
Aleochara bilineata	Adult (1-3 days old)	EXP10066A (quartz sand)	91 days (28-day exposure period followed by 63-day extraction period)	450 4500 (active substance, initial residues)	Reproduction	2.2 42.7	ER_{50} > 4500 g a.s./ha NOEC = 650 g a.s./ha
Aleochara bilineata	Adult (1-4 days old)	EXP10066A (quartz sand)	86 days (28-day exposure followed by 58-day extraction period)	4500 7800 11200	Reproduction	20.3 15.2 21.9	ER_{50} > 11200 g a.s./ha NOEC = 11200 g a.s./ha

2.9.4 Summary of effects on non-target soil meso- and macrofauna

Effects on non-target soil meso- and macro fauna; effects on soil nitrogen transformation (Regulation (EU) N° 283/2013, Annex Part A, points 8.4, 8.5, and Regulation (EU) N° 284/2013 Annex Part A, points 10.4, 10.5)

Test organism	Test substance	Application method of test a.s./ OM	Time scale	End point	Toxicity
Earthworms					
Eisenia fetida	EXP10066A	Mixed into soil / 10%	Chronic	Growth, reproduction, behaviour	NOEC = 12.9 mg a.s./kg soil dw
Eisenia fetida	EXP10066A	Mixed into soil / 5%	Chronic	Growth, reproduction, behaviour	NOEC 25 (corr. **12.5**) mg a.s./kg soil dw
Other soil macroorganisms					
Folsomia candida	EXP100066A	Treated surface / 10%	Chronic	Mortality, reproduction	LC_{50} could not be determined $NOEC_{survival}$ < 10.4 mg a.s./kg soil dw $NOEC_{reproduction}$ = 37.6 (corr. **18.8**) mg a.s./kg soil dw
Hypoaspis aculeifer	EXP100066A	Mixed into soil / 5%	Chronic	Mortality, reproduction	LC_{50} > 407 mg a.s./kg soil dw NOEC = 407(corr. **203.5**) mg a.s./kg soil dw

Field studies:

1. Effect of EXP10066A on decomposition of the organic matter was investigated. First application was conducted in arable field (mustard) in Germany with 15000 g a.s./ha, followed by second application with 11300 g a.s./ha. At the test termination after 244 days, 22.6 to 30% decomposition reduction was observed.

2. Effect of Moncut 40SC on decomposition of the organic matter was investigated. The product was applied on bare soil at a dose rate of 670.5 g a.s./ha. Test duration was 616 days. Moncut 40SC induced significant decomposition reduction only at a second sampling date (90 days, 11.6 % reduction).

2.9.5 Summary of effects on soil nitrogen transformation

Nitrogen transformation	EXP10066A	0.71% effect at day 42 at 2.09 mg a.i./kg soil (1392 g a.i./ha)

2.9.6 Summary of effects on terrestrial non-target higher plants

Application of EXP10066A at a rate of 11200 g a.s./ha did not cause significant effects on plant growth (tested on six terrestrial non-target plant species representing six plant families). NOER was determined to be 11200 kg a.s./ha.

2.9.7 Summary of effects on other terrestrial organisms (flora and fauna)

2.9.8 Summary of effects on biological methods for sewage treatment

Effects on biological methods for sewage treatment (Regulation (EU) N° 283/2013, Annex Part A, point 8.8)

Test type/organism	Endpoint
Activated sludge	EC_{50} >1000 mg a.s./L.

2.9.9 Summary of product exposure and risk assessment

2.9.9.1 *Birds and mammals*

2.9.9.1.1 Birds Tier 1 Risk Assessment from dietary exposure

Avian first tier acute assessment for the proposed uses of MONCUT 40 SC in flower bulbs – presence of weeds scenario (Leafy vegetables)

Crop stage	Indicator spp.	Shortcut value	MAF	TWA	Endpoint (mg/kg bw)	DDD (mg/kg bw)	TER
Application rate: 2.76 kg a.s./ha (single, pre-emergence application to flower bulbs)							
leaf development BBCH 10-19	Medium herbivorous/ granivorous bird "pigeon"	55.5	1.0	1.0	2000	153.18	13.06
BBCH 10 - 19	Small insectivorous bird “wagtail”	26.8				73.97	27.04
Metabolite M-4: Application rate: 0.279 kg a.s./ha							
leaf development BBCH 10-19	Medium herbivorous/ granivorous bird "pigeon"	55.5	1.0	1.0	200	15.47	12.93
BBCH 10 - 19	Small insectivorous bird “wagtail”	26.8				7.47	26.77

MAF: multiple application factor TWA: time weighted average factor
DDD: daily dietary dose n.a.: not applicable
Note: calculations conducted using unrounded values; TER values in **bold** are lower than the trigger value of 10

Avian first tier long term assessment for the proposed uses of MONCUT 40 SC in flower bulbs – presence of weeds scenario (Leafy vegetables)

Crop stage	Indicator spp.	Shortcut value	MAF	TWA	Endpoint (mg/kg bw)	DDD (mg/kg bw)	TER
Application rate: 2.76 kg a.s./ha (single, pre-emergence application to flower bulbs)							
leaf development BBCH 10-19	Medium herbivorous/ granivorous bird "pigeon"	26.7	1.0	0.53	247.8	39.06	7.46
BBCH 10 - 19	Small insectivorous bird “wagtail”	11.3				16.53	15.0
Metabolite M-4: Application rate: 0.279 kg a.s./ha							
leaf development BBCH 10-19	Medium herbivorous/ granivorous bird "pigeon"	22.7	1.0	0.53	24.78	3.94	7.38
BBCH 10 - 19	Small insectivorous bird “wagtail”	11.3				1.67	14.8

MAF: multiple application factor TWA: time weighted average factor
DDD: daily dietary dose n.a.: not applicable
Note: calculations conducted using unrounded values; TER values in **bold** are lower than the trigger value of 5

2.9.9.1.2 Risk assessment for potato-eating birds

Exposure estimate of MONCUT 40 SC and acute TER_A values for birds for an application in seed potatoes

Active substance	Relevant potato-eating species	Concentration on potato	PT	FIR/bw	ETE	LD_{50}	TER_A	Trigger value
Flutolanil	Common crane	92.4	1	0.277	25.59	> 2000	> 78.14	10

ETE = Estimated Theoretical Exposure (mg/kg bw/day) TER = Toxicity Exposure Ratio
PT= Fraction of diet obtained in treated fields
FIR/bw = Food intake rate/body weight

Exposure estimate of MONCUT 40 SC and chronic TER_L values for birds for and application in seed potatoes

Active substance	Relevant potato-eating species	Concentration on potato	PT	FIR/bw	ETE	NOEL	TER_L	Trigger value
Flutolanil	Common crane	92.4	1	0.277	25.59	247.8	9.7	5

ETE = Estimated Theoretical Exposure (mg/kg bw/day) TER = Toxicity Exposure Ratio
PT= Fraction of diet obtained in treated fields
FIR/bw = Food intake rate/body weight

2.9.9.1.3 Mammals Tier 1 Risk Assessment from Dietary Exposure

Mammal first tier acute assessment for the proposed uses of MONCUT 40 SC in flower bulbs presence of weeds scenario (Leafy vegetables)

Crop stage	Indicator spp.	Shortcut value	MAF	TWA	Endpoint (mg/kg bw)	DDD (mg/kg bw)	TER
Application rate: 2.76 kg a.s./ha (single, pre-emergence application to flower bulbs)							
All season	Large herbivorous mammal "lagomorph"	35.1	1.0	1.0	2000	96.9	20.6
BBCH 10-49	Small omnivorous mammal "mouse"	17.2				47.5	41.6
Metabolite M-4: Application rate: 0.279 kg a.s./ha							
All season	Large herbivorous mammal "lagomorph"	35.1	1.0	1.0	200	9.79	20.4
BBCH 10-49	Small omnivorous mammal "mouse"	17.2				4.79	42

MAF: multiple application factor TWA: time weighted average factor
DDD: daily dietary dose n.a.: not applicable
Note: calculations conducted using unrounded values; TER values in **bold** are lower than the trigger value of 10

Mammal first tier acute assessment for the proposed uses of MONCUT 40 SC in flower bulbs – presence of weeds scenario (Leafy vegetables as surrogate)

Crop stage	Indicator spp.	Shortcut value	MAF	TWA	Endpoint (mg/kg bw)	DDD (mg/kg bw)	TER
Application rate: 2.76 kg a.s./ha (single, pre-emergence application to flower bulbs)							
All season	Large herbivorous mammal "lagomorph"	14.3	1.0	0.53	40	20.92	**1.9**
BBCH 10-49	Small omnivorous mammal "mouse"	7.8				11.41	**3.5**
Metabolite M-4: Application rate: 0.279 kg a.s./ha							
All season	Large herbivorous mammal "lagomorph"	14.3	1.0	0.53	4	2.11	**1.9**
BBCH 10-49	Small omnivorous mammal "mouse"	7.8				1.15	**3.5**

MAF: multiple application factor TWA: time weighted average factor
DDD: daily dietary dose n.a.: not applicable
Note: calculations conducted using unrounded values; TER values in **bold** are lower than the trigger value of 5

Mammal first tier acute assessment for the proposed uses of MONCUT 40 SC in bare soils, potatoes and flower bulbs

Crop stage	Indicator spp.	Shortcut value	MAF	TWA	Endpoint (mg/kg bw)	DDD (mg/kg bw)	TER
Flower bulbs - application rate: 2.76 kg a.s./ha (single, pre-emergence application to flower bulbs)							
BBCH <10	Small omnivorous mammal "mouse"	14.3	1.0	0.53	40	20.9	**1.9**
Potatoes - application rate: 0.368 kg a.s./ha (single, pre-emergence application to flower bulbs)							
BBCH <10	Small omnivorous mammal "mouse"	14.3	1.0	0.53	40	2.79	14.3

Risk assessment for potato-eating mammal

Exposure estimate of MONCUT 40 SC and acute TER_A values for mammals for an application in seed potatoes

Active substance	Relevant potato-eating species	Concentration on potato	PT	FIR/bw	ETE	LD_{50} (mg/kg bw/d)	TER_A	Trigger value
Flutolanil	Badger	92.4	1	0.193	17.875	> 10000	> 559	10
	Boar			0.17	15.708		> 637	

ETE = Estimated Theoretical Exposure (mg/kg bw/day) TER = Toxicity Exposure Ratio
PT= Fraction of time spent foraging in treated fields
FIR/bw = Food intake rate/body weight

Exposure estimate of MONCUT 40 SC and long-term TER_A values for mammals for an application in seed potatoes

Active substance	Relevant potato-eating species	Concentration on potato	PT	FIR/bw	ETE	NOAEL (mg/kg bw/d)	TER_A	Trigger value
Flutolanil	Badger	92.4	1	0.193	17.833	40	**2.24**	5
	Boar			0.17	15.708		**2.55**	

ETE = Estimated Theoretical Exposure (mg/kg bw/day) TER = Toxicity Exposure Ratio
PT= Fraction of diet obtained in treated fields
FIR/bw = Food intake rate/body weight

2.9.9.1.4 Risk assessmsent from exposure via drinking water

Drinking water assessment for the proposed worst-case use of MONCUT 40 SC

Time-scale	Crop scenario (Maximum effective application rate)	Endpoint	Ratio	Trigger value
Birds				
Acute	Flower bulb (1 × 2760 g/ha)	LD_{50} > 2000 mg a.s./kg bw	11.1	3000
Long-term		NOEL = 248 mg a.s./kg bw/d	1.38	
Mammals				
Acute	Flower bulb (1 × 2760 g/ha)	LD_{50} > 2000 mg a.s./kg bw	< 1.38	3000
Long-term		NOEL = 160 mg a.s./kg bw/d	17.3	
		NOEL = 40 mg a.s./kg bw/d	69.2	

2.9.9.1.5 Risk assessment from secondary poisoning

Calculation of TER_{LT} for secondary poisoning from flutolanil of earthworm-eating birds and mammals

21 day TWA PEC_{soil}[a] (mg/kg)	2.68		
K_{ow}	1479.1		
f_{oc} (default value)	0.02		
K_{oc}	652.2		
BCF_{worm}	1.43		
PEC_{worm} (mg/kg)	3.83		
DDD (mg/kg bw/d)	4.02		
Endpoint (mg/kg bw/d)	248	160	40
TER_{LT}	61.6	32.6	8.14

[a] For flutolanil the plateau soil $PEC_{accumulation}$ is used (see Document M - CP 9.1.3) for the higher application rate and at 10 cm planting depth)

Summary

A chronic risk to mammals is identified for the proposed uses in flower bulbs and potatoes.

Aquatic organisms

The risk assessment has been conducted in line with EFSA (2013) and presented in B.9.4 (PPP).

Summary of the risk assessment for flutolanil on aquatic organisms

First-tier risk assessment for flutolanil on potatoes (dose 0.368 kg a.s./ha)

The FOCUS Step 1 PEC_{sw} value of flutolanil was found to be lower than the acute $RAC_{sw, ac}$ value for the chronic $RAC_{sw, ch}$ values for chironomids and algae, indicating that the chronic risks to chironomids and algae are considered acceptable.

The FOCUS Step 2 PEC_{sw} values of flutolanil was found to be lower than the acute $RAC_{sw, ac}$ value for fish, indicating that the acute risk to fish are considered acceptable.

After assessing all scenarios in FOCUS Step 3, PEC_{sw} values of flutolanil were found to be lower than the chronic $RAC_{sw, ch}$. Therefore, the risk of flutolanil is considered acceptable for the use in potatoes.

First-tier risk assessment for flutolanil on flower bulbs (dose 2.76 kg a.s./ha)

The FOCUS Step 2 PEC_{sw} values of flutolanil were found to be lower than the chronic $RAC_{sw, ch}$ value for algae. The chronic risk to algae is considered acceptable.

The acute and chronic risks for fish and the chronic risks for chironomids were considered acceptable after assessing all scenarios in FOCUS Step 3, except for the chronic risk of flutolanil to fish for the application in flower bulbs for the scenario D3 (ditch) and D6 (ditch), and further for all flower bulb scenarios for the acute and chronic risk of flutolanil to aquatic invertebrates, and therefore, a risk for flutolanil remains for the use in flower bulbs

Summary of the risk assessment for metabolites on aquatic organisms

First-tier risk assessment for metabolites on potatoes (dose 0.368 kg a.s./ha)

Metabolite M-4

The Step 1 PEC_{sw} value of M-4 was found to be lower than the chronic $RAC_{sw, ch}$ values for chironomids and algae and the acute $RAC_{sw, ac}$ value for fish. The chronic risks to chironomids and algae and the acute risk to fish are considered acceptable.

The FOCUS Step 2 PEC_{sw} values of M-4 were found to be lower than the chronic $RAC_{sw, ac, ch}$ values for fish, indicating that the chronic risk to fish is considered acceptable for the use in potatoes.

After assessing all scenarios in FOCUS Step 3, PEC_{sw} values of M-4 were found to be lower than the acute RAC_{sw} for aquatic invertebrates but not for the chronic RAC_{sw} for the scenarios D4 Stream and D6 Ditch (E and L) for aquatic invertebrates. Therefore, the risk from M-4 is considered unacceptable for the use in potatoes.

Metabolite M-11

The FOCUS Step 1 PEC_{sw} value of M-11 was lower than the chronic $RAC_{sw, ch}$ value for algae and chironomids, indicating that the chronic risk to algae and chironomids is considered acceptable.

The FOCUS Step 2 PEC_{sw} values of M-11 were found to be lower than the acute and chronic risks for fish, indicating that the acute and chronic risk to fish are considered acceptable. However, the FOCUS Step 3 PEC_{sw} for M-11 for scenario D4 pond is higher than PEC_{sw} of FOCUS step 2 which resulted in a chronic risk for fish for the metabolite M-11 for the scenario D4 Pond for the use in potatoes. Comparison of the FOCUS Step 3 PEC_{sw} for the M-11 metabolite with the RAC indicated an unacceptable acute and chronic risk for aquatic invertebrates for the scenarios D3 Ditch, D4 Pond, D4 Stream and D6 Ditch (E andL) for the application in potatoes. Therefore, a risk from M-11 remains for the use in potatoes.

First-tier risk assessment for metabolites on flower bulbs (dose 2.76 kg a.s./ha)

Metabolite M-4

The FOCUS Step 1 PEC_{sw} values of M-4 were found to be lower than the chronic $RAC_{sw, ch}$ value for algae, indicating that the chronic risk to algae is considered acceptable.

The FOCUS Step 2 PEC_{sw} values of M-4 were found to be lower than the chronic $RAC_{sw, ch}$ value for chironomids, indicating that the chronic risk to chironomids is considered acceptable.

The acute and chronic risks for fish and the acute risk for aquatic invertebrates were considered acceptable after assessing all scenarios in FOCUS Step 3 but not for the chronic risk for aquatic invertebrates for the the scenarios D4 Stream and D6 Ditch (E and L). Therefore, the risk from M-4 is considered unacceptable for the use in flower bulbs.

Metabolite M-11

The chronic risk for algae was considered acceptable after assessing all scenarios in FOCUS Step 3, but not for the acute and chronic risks for fish (scenario D3 Ditch, D4 Pond, D4 stream and D6 Ditch (E and L)) and the acute (scenario D3 Ditch, D4 Pond, D4 Stream, D6 Ditch (E and L)) and chronic (all scenario scenarios except R1 Pond) risks for aquatic invertebrates, as well as the chronic risk for chironomids (scenario D3 Ditch, D4 Pond). Therefore, a risk from M-11 remains for the use in flower bulbs.

Endocrine disruption

The results of the fish short term reproduction assay indicate a potential endocrine effect, based on effects on vitellogenin (concentration-related reduction), fecundity, secondary sexual characteristics in males and histological alterations of both male and female gonads. These seem to indicate a potential anti-androgenic or possibly steroidogenic mechanism of action, however, assays addressing these aspects in humans (or mammals) present in the mammalian data set were negative. Further data are needed to investigate the potential endocrine activity of flutolanil in fish. A data gap is set for an extended one generation test (medaka) and/or any other pertinent information relating to mechanism of action or molecular interactions relevant to the potential for endocrine disruption in fish and to determine whether or not these potential actions may be considered adverse at the population level.

2.9.9.2 Arthropods

2.9.9.2.1 Bees

Acute Risk Assessment

The acute risk to honey bees from the use of flutolanil was assessed using the worst-case maximum single application rate for the proposed uses and the LD_{50} values to calculate the Exposure Toxicity Ratio (ETR) according to EFSA Journal 2013 as follows:

$$ETR_{\text{acute adult oral}} = \frac{\text{Application Rate (AR) (kg a.s./ha)} \times \text{Shortcut Value (SV)}}{\text{Acute } LD_{50} \text{ (µg a.s./bee)}}$$

Exposure Toxicity Ratio (ETR) was calculated for the acute oral exposure and was evaluated against a trigger value of ETR > 0.2. The shortcut value used for this type of spray application to bare soil was 10.6 (side-ward application) as no emerged crops will be exposed to down-ward spraying of MONCUT 40SC. Values below or equal to the trigger meet the protection goal and are considered to indicate an acceptable risk to bees in the field. The calculated ETR value is presented in **Table 9.6.1.2-1**.

Table 9.6.1.2-1 Exposure toxicity ratios for honeybees based on oral acute laboratory study

Test substance	Route	Toxicity (µg a.s./bee)	Application rate (kg a.s./ha)	SV	ETR	ETR Trigger value
Flutolanil	Oral	208.7	2.76	10.6	0.140	> 0.2

Hazard quotient (HQ) for acute contact exposure of adult honey bees in the field margin was calculated:

$$\text{Hazard Quotient } (HQ_C) = \frac{\text{Maximum single application rate (g a.s./ha)}}{\text{Acute contact } LD_{50} \text{ (µg a.s./ha)}}$$

Table 9.6.1.2-2 Hazard quotient for honeybees based on laboratory acute contact toxicity study

Test substance	Route	Toxicity (µg a.s./bee)	Application rate (g a.s./ha)	Hazard quotient	Trigger value
Flutolanil	Contact	200	2760	13.8	HQ (suw) > 85

HQ(suw) = HQ trigger for sideward/upwards spray application

The oral ETR value and contact hazard quotient for flutolanil are below 0.2 and 85, respectively, indicating that the acute exposure risk to bees from flutolanil following the highest application rate according to the proposed uses, is acceptable.

No further consideration of the acute risk to bees is required.

Chronic Risk Assessment

The chronic adult oral and larval development risks to honey bee will be evaluated in accordance with the EFSA Guidance Document (EFSA Journal 2013; 11(7):3295) These long-term assessments are considered to address potential exposure via nectar and pollen from the treated crop and flowering weeds and encompass potential exposure from systemic activity. The chronic adult assessment did not pass in the screening step, thus, a tier 1 assessment of the potential chronic risk to bees from the proposed uses is required.

Table 9.6.1.2-3 Tier 1 chronic risk assessment for adult honey bee

category	scenario	BBCH	Honeybee	
			ETR	trigger
Bulb flowers (attractive nectar and pollen)				
chronic	treated crop	< 10	**0.035**	0.03
chronic	weeds	< 10	0.02	0.03
chronic	field margin	< 10	0.00	0.03
chronic	adjacent crop	< 10	0.00	0.03
chronic	next crop	< 10	**0.031**	0.03
Potatoes (only attractive pollen)				
chronic	treated crop	< 10	0.00	0.03
chronic	weeds	< 10	0.00	0.03
chronic	field margin	< 10	0.00	0.03
chronic	adjacent crop	< 10	0.00	0.03
chronic	next crop	< 10	0.00	0.03

As shown in the Table above, the chronic adult risk assessment according to EFSA (2013) indicates a potential chronic risk to adult honey bees from the proposed use of Monocut 40SC in bulb flowers,

from the crop itself and from a potential following crop, however, the proposed use in potatoes shows an acceptable risk.

The Tier 1 risk assessment for chronic exposure to adult bees can be refined considering the available field study with Monarch 40 SC, a formulation which is slightly different from Monocut 40 SC but contains the same a.s. level and the same formulation type. The semi-field test was performed under worst-case circumstances versus the proposed use of Monocut 40SC in blub flowers, as it was applied only two weeks before full flowering and at a rate significantly higher (>4x) than the proposed use rate. There were no effects on mortality of adult bees flying in the crop (*Phacelia*) in the 8 days of observation. Nor were there any effectson the number of adult bees in each of the tested colonies during the entire time of observation. Considering these data, and the fact that the trigger value was very close to acceptable (ratio of 1.2), the RMS considers the chronic risk to honey bees from the proposed use of Monocut 40 SC in bulb flowers acceptable.

Larval Risk Assessment

The chronic adult oral and larval development risks to honey bee will be evaluated in accordance with the EFSA Guidance Document (EFSA Journal 2013; 11(7):3295) These long-term assessments are considered to address potential exposure via nectar and pollen from the treated crop and flowering weeds and encompass potential exposure from systemic activity. The larval risk assessment did not pass in the screening step for the proposed use in bulb flowers (it did pass for the proposed use in potatoes), thus, a tier 1 assessment of the potential risk to larval bees from the proposed uses is required.

Table 9.6.1.2-4 Tier 1 chronic risk assessment for larval honey bee

category	scenario	BBCH	Honeybee	
			ETR	trigger
Bulb flowers (attractive nectar and pollen)				
larva	treated crop	< 10	0.09	0.2
larva	weeds	< 10	0.05	0.2
larva	field margin	< 10	0.00	0.2
larva	adjacent crop	< 10	0.00	0.2
larva	next crop	< 10	0.09	0.2

As shown in the Table above, according to the Tier 1 risk assessment (EFSA, 2013), the potential risk to larval honey bees from the proposed uses of Monocut 40SC is acceptable.

Assessment of the risk from exposure via contaminated water

The risk assessment was performed according to EFSA, 2013, wherever data was available. Note that the Fate section does not calculate PECrunoff, as there is no agreed methodlogy in the Fate section for this calculation. Thus, the PECpuddle was not calculated and no risk assessment could be performed for puddle water. As inputs, the water solubility of flutolanil (8 mg/L, see Table B.2.9-1) and the highest Step 3 PECsw (0.02525 mg/L, see Table 9.4-9) were used. Note that as there was no safe

use for bulb flowers using this PEC, it is likely that refinements will be performed, perhaps resulting in a lower PECsw.

According to these inputs the risk to bees from surface water passed in the screening step. The risk to bees from puddle water could not be calculated. The risk to bees from guttation water is presented in a Tier 1 step, as it is not known to what degree guttation water is likely to form on bulb flowers or potatoes during the potential exposure period. The Tier 1 assessment is shown below.

Table 9.6.1.2-5 Tier 1 risk assessment for honey bee exposure via guttation water

	water cons. (µL)	ETR	Trigger
acute	11.4	0.00	0.2
chronic	11.4	0.002	0.03
larvae	111	0.06	0.2

As shown in the Table above, the potential risk to honey bees from guttation water is assumed to be low. Considering the above, the risk to honey bees from exposure via water from the proposed uses of Monocut 40SC is expected to be low.

Assessment of the risk from exposure to metabolites

Only one metabolite is found in plants at TRR >10%, that being metabolite M-4.

	Molecular weight	Mole fraction	%TRR[1]	AR_{EQ} (kg a.s./ha)	$EXP_{metabolite}$
Flutolanil	323.3			2.76	
M-2 (+ conjugates)	339.3	1.04949	0.16	0.345	0.000579318
M-4 (+ conjugates)	281.2	0.86978	33.65		0.100998986
M-101	189.1	0.584998	1.00		0.002018245
M-102	190.1	0.588061	0.62		0.001257862

[1] Found in the outer leaf of mature cabbage (radiolabel: [Phenyl-U-^{14}C]-Flutolanil)

The risk assessment for potential exposure to metabolite M-4 was conducted according to EFSA (2013), assuming that the metabolite was 10x more toxic than the parent. This resulted in the following results, shown in Table 9.6.1.2-4, below.

Table 9.6.1.2-6 Tier 1 risk assessment for honey bee exposure to metabolite M-4

category	scenario	BBCH	Honeybee	
			ETR	trigger
Bulb Flowers (attractive nectar and pollen)				
acute	treated crop	< 10	0.028	0.2
acute	weeds	< 10	0.014	0.2
acute	field margin	< 10	0.001	0.2
acute	adjacent crop	< 10	0.001	0.2
acute	next crop	< 10	0.028	0.2
chronic	treated crop	< 10	**0.090**	0.03
chronic	weeds	< 10	**0.048**	0.03
chronic	field margin	< 10	0.004	0.03
chronic	adjacent crop	< 10	0.003	0.03
chronic	next crop	< 10	0.085	0.03
larva	treated crop	< 10	0.275	0.2
larva	weeds	< 10	0.137	0.2
larva	field margin	< 10	0.014	0.2

category	scenario	BBCH	Honeybee	
			ETR	trigger
larva	adjacent crop	< 10	0.010	0.2
larva	next crop	< 10	**0.275**	0.2
Potato (attractive pollen only)				
acute	treated crop	< 10	0.000	0.2
acute	weeds	< 10	0.002	0.2
acute	field margin	< 10	0.000	0.2
acute	adjacent crop	< 10	0.000	0.2
acute	next crop	< 10	0.004	0.2
chronic	treated crop	< 10	0.000	0.03
chronic	weeds	< 10	0.006	0.03
chronic	field margin	< 10	0.001	0.03
chronic	adjacent crop	< 10	0.000	0.03
chronic	next crop	< 10	0.011	0.03
larva	treated crop	< 10	0.000	0.2
larva	weeds	< 10	0.018	0.2
larva	field margin	< 10	0.002	0.2
larva	adjacent crop	< 10	0.001	0.2
larva	next crop	< 10	0.037	0.2

As shown in the Table above, the risk to honey bees from exposure to metabolite M-4 is considered acceptable for the proposed use in potato, however, there is a chronic risk to adult bees from use in the crop and from weeds in the treated field, and to larvae from the next crop. However, the results of the semi-field test do not show any significant effects on adult bees, nor any brood effects, despite a worst-case exposure profile in a highly attractive crop. The honey bees in the semi-field study were exposed to the metabolite at higher rates, in the same way they were exposed to flutolanil at higher rates than proposed in the GAP. The assumption of 10x greater toxicity is also considered conservative, as the parent molecule is a fungicide, and is not highly toxic in and of itself. Considering all the available data, the RMS finds the risk to honey bees from the metabolite, M-4, acceptable.

2.9.9.2.2 Non-target terrestrial arthropods

The risk assessment has been conducted in line with ESCORT 2 (Candolfi *et al*., 2000)[2] and presented in B.9.6.

In tier 1 assessment, acceptable risk to non-target terrestrial arthropods was concluded for all proposed applications, see the table below.

[2] M.P. Candolfi, K.L. Barrett, P.J. Campbell, R. Forster, N. Grandy, M-C. Huet, G. Lewis, P. A. Oomen, R. Schmuck and H. Vogt (2000) Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. From the ESCORT 2 workshop (European Standard Characteristics Of non-target arthropod Regulatory Testing)

In-field and Off-field HQs for non-target arthropods exposed to MONCUT 40 SC on potatoes and flower bulbs

Species	LR_{50} (g a.s./ha)	In-field PER (g a.s./ha)	$HQ_{in\text{-}field}$	Off-field PER (g a.s./ha)	$HQ_{off\text{-}field}$	Trigger
Aphidius rhopalosiphi	> 4500	2760	< 0.613	76.45	< 0.017	2
Typhlodromus pyri	> 4500		< 0.613		< 0.017	2

2.9.9.3 *Non-target soil meso- and macrofauna*

The risk assessment for non-target soil meso- and macrofauna has been conducted in line with the Terrestrial Guidance Document (SANCO/10329/2002) and presented in B.9.8.

Earthworms

In tier 1 assessment, unacceptable long-term risk to earthworms was concluded for use in flower bulbs (see the table below). Long-term risk to earthworms is acceptable for use in potatoes.

Long term TER values for earthworms exposed to MONCUT 40 SC

Organism	Species	Toxicity endpoint	Appl. rate (g a.s./ha)	PEC_{soil} (mg/kg)	Endpoint [mg/a.s. kg dw soil]	TER_{LT}	Trigger value
Earthworm	*Eisenia fetida*	Long-term	1 × 368 (potatoes)	0.603	12.5	20.7	5
Earthworm	*Eisenia fetida*	Long-term	1 × 2760 (bulbs incorp. to 10 cm)	2.641	12.5	**4.73**	5

Other non-target soil meso- and macrofauna (other than earthworms)

For *Folsomia candida* the tier 1 TER_{LT} values for flutolanil (see table below) are above the trigger value of 5 for use in potato and bulbs incorporated in soil at 10 cm, demonstrating an acceptable chronic risk following application in accordance with the proposed uses.

For *Hypoaspis aculeifer* the tier 1 TER_{LT} values for flutolanil are above the trigger value of 5, demonstrating an acceptable chronic risk following application in accordance with the proposed uses. No further consideration is necessary.

Long term TER values for non-target soil macro-organisms exposed to MONCUT 40 SC (other than earthworms)

Species	Application rate (g a.s./ha)	Toxicity * (mg a.s./kg dw soil)	$PEC_{soil\ accum}$ (mg/kg dw soil)	TER_{LT}	Trigger
Folsomia candida	1 × 368	18.8	0.603	31.2	5
	1 × 2760 (bulbs incorp. to 10 cm)	18.8	2.680	7.01	
	1 × 368	> 203.5	0.603	337	

Species	Application rate (g a.s./ha)	Toxicity * (mg a.s./kg dw soil)	$PEC_{soil\ accum}$ (mg/kg dw soil)	TER_{LT}	Trigger
Hypoaspis aculeifer	1 × 2760 (bulbs incorp. to 10 cm)	> 203.5	2.680	75.9	5

2.9.9.4 *Soil nitrogen transformation*

The risk to soil nitrogen transformation has been assessed in accordance with the Terrestrial Guidance Document (SANCO/10329/2002) and presented in B.9.10.

Risk from use in potato is acceptable since the exposure is 3.5 times lower than the threshold. However, unacceptable risk is concluded for use in flower bulbs, as the threshold is exceeded by 1.28.

2.9.9.5 *Terrestrial non-target higher plants*

The risk to terrestrial non-target higher plants has been assessed in accordance with the Terrestrial Guidance Document (SANCO/10329/2002) and presented in B.9.12.

Risk to non-target terrestrial plants is acceptable for all proposed uses, see the table below.

MONCUT 40 SC TER values for non-target plants

Test Substance	Species	NOER (g a.s./ha)	PER (g a.s./ha)	TER_{LT}	Trigger value
EXP10066A* Seedling emergence	Tomato *Solanum lycopersicon*	11200	76.5	146.5	5
	Cucumber *Cucumis sativus*				
	Radish *Raphanus sativus*				
	Soybean *Glycine max*				
	Oat *Avena sativa*				
	Onion *Allium cepa*				

* EXP10066A is equivalent to the representative formulation MONCUT 40 SC

2.10 Classification and labelling

Proposed classification according to Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification 1)	Reason for no classification 2)
2.1.	Explosives	No classification	None	Not classified	Conclusive but not sufficient for classification
2.2.	Flammable gases	Not applicable	-	-	Not applicable
2.3.	Flammable aerosols	Not applicable	-	-	Not applicable
2.4.	Oxidising gases	Not applicable	-	-	Not applicable
2.5.	Gases under pressure	Not applicable	-	-	Not applicable
2.6.	Flammable liquids	Not applicable	-	-	Not applicable

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.7.	Flammable solids	No classification	None	Not classified	Conclusive but not sufficient for classification
2.8.	Self-reactive substances and mixtures	No classification	None	Not classified	Conclusive but not sufficient for classification
2.9.	Pyrophoric liquids	Not applicable	-	-	Not applicable
2.10.	Pyrophoric solids	No classification	None	Not classified	Conclusive but not sufficient for classification
2.11.	Self-heating substances and mixtures	No classification	None	Not classified	Conclusive but not sufficient for classification
2.12.	Substances and mixtures which in contact with water emit flammable gases	No classification	None	Not classified	Conclusive but not sufficient for classification
2.13.	Oxidising liquids	Not applicable	-	-	Not applicable
2.14.	Oxidising solids	No classification	None	Not classified	Conclusive but not sufficient for classification
2.15.	Organic peroxides	No classification	None	Not classified	Conclusive but not sufficient for classification
2.16.	Substance and mixtures corrosive to metals	No classification	None	Not classified	Conclusive but not sufficient for classification
3.1.	Acute toxicity - oral	No classification	none	Not classified	Conclusive but not sufficient for classification
	Acute toxicity - dermal	No classification	none	Not classified	Conclusive but not sufficient for classification
	Acute toxicity - inhalation	No classification	none	Not classified	Conclusive but not sufficient for classification
3.2.	Skin corrosion / irritation	No classification	none	Not classified	Conclusive but not sufficient for classification
3.3.	Serious eye damage / eye irritation	No classification	none	Not classified	Conclusive but not sufficient for classification
3.4.	Respiratory sensitisation	No classification	none	Not classified	Conclusive but not sufficient for classification
3.4.	Skin sensitisation	No classification	none	Not classified	Conclusive but not sufficient for classification
3.5.	Germ cell mutagenicity	No classification	none	Not classified	Conclusive but not sufficient for classification
3.6.	Carcinogenicity	No classification	none	Not classified	Conclusive but not sufficient for classification

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
3.7.	Reproductive toxicity	No classification	none	Not classified	Conclusive but not sufficient for classification
3.8.	Specific target organ toxicity –single exposure	No classification	none	Not classified	Conclusive but not sufficient for classification
3.9.	Specific target organ toxicity – repeated exposure	No classification	none	Not classified	Conclusive but not sufficient for classification
3.10.	Aspiration hazard	No classification	none	Not classified	Conclusive but not sufficient for classification
4.1.	Hazardous to the aquatic environment	H400 H410	M=1 M=10	No Annex VI available	Not applicable
5.1.	Hazardous to the ozone layer	Not applicable	-	-	Not applicable

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Signal word: Warning

Hazard statements: H410: Very toxic to aquatic life with long lasting effects

Precautionary statements:

P501: Dispose of contents/container to hazardous or special waste collection point

P273: Avoid release to the environment

P391: Collect spillage

Proposed notes assigned to an entry:

Notes in accordance with CLP Regulation, Annex VI, Section 1.1.3

2.11 Relevance of metabolites in groundwater

Not required for flutolanil, since there are no major soil metabolites

2.12 Consideration of isomeric composition in the risk assessment

2.12.1 Identity and physical chemical properties

Flutolanil is not an isomeric compound. Further consideration of the isomeric composition in the risk assessment is therefore not required.

2.12.2 Methods of analysis

Flutolanil is not an isomeric compound. No analytical methods with respect to the isomeric composition are therefore required.

2.12.3 Mammalian toxicity

Flutolanil is not an isomeric compound. Further consideration of the isomeric composition in the risk assessment is therefore not required.

2.12.4 Residues and Consumer risk assessment

Flutolanil is not an isomeric compound. Further consideration of the isomeric composition in the risk assessment is therefore not required.

2.12.5 Environmental fate

Flutolanil is not an isomeric compound. Further consideration of the isomeric composition in the risk assessment is therefore not required.

2.12.6 Ecotoxicology

Flutolanil is not an isomeric compound. Further consideration of the isomeric composition in the risk assessment is therefore not required.

2.13 Residue definitions

2.13.1 Definition of residues for exposure/risk assessment

To be specified for the following matrices:

Food of plant origin:

Residue definition for risk assessment:

1. Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil
2. Metabolite M-101

Food of animal origin:

Poultry:

1. Flutolanil
2. Metabolite M-101

Ruminants: Sum of flutolanil and metabolite M-4 (free and conjugated), expressed as flutolanil.

Soil: flutolanil

Groundwater: flutolanil

Surface water: flutolanil, M4, M11

Sediment: flutolanil, M4, M11

Air: flutolanil

2.13.2 Definition of residues for monitoring

To be specified for the following matrices:

Food of plant origin: Flutolanil

Food of animal origin:

Poultry: flutolanil

Ruminants: metabolite M-4 (free and conjugated)

Soil: flutolanil

Groundwater: flutolanil

Surface water: flutolanil

Sediment: flutolanil

Air: -

Volume 1

Level 3

- Active substance -

Summary and consideration with respect to the approval criteria of Regulation (EC) No 1107/2009

Identification of data gaps, proposed conditions, risk management measures, issues that could not be finalized and critical areas of concern

Proposed decisions

3 Proposed decision with respect to the application

3.1 Background to the proposed decision

3.1.1 Proposal on acceptability against the decision making criteria – Article 4 and Annex II of Regulation (EC) No 1107/2009

3.1.1.1 Article 4				
		Yes	No	
i)	It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorisation in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses.			Inconclusive. Additional information (which can be submitted during the peer review) is needed to finalise the evaluation. Please refer to tables 3.1.4, 3.1.5 and 3.1.7.
3.1.1.2 Submission of further information				
		Yes	No	
i)	It is considered that a complete dossier has been submitted	X		
ii)	It is considered that in the absence of a full dossier the active substance may be approved even though certain information is still to be submitted because: (a) the data requirements have been amended or refined after the submission of the dossier; or (b) the information is considered to be confirmatory in nature, as required to increase confidence in the decision.			*Not applicable*
3.1.1.3 Restrictions on approval				
		Yes	No	
	It is considered that in line with Article 6 of Regulation (EC) No 1107/2009 approval should be subject to conditions and restrictions.			Inconclusive. Additional information (which can be submitted during the peer review) is needed to finalise this.

3.1.1.4 Criteria for the approval of an active substance				
Dossier				
		Yes	No	
	It is considered the dossier contains the information needed to establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).	X		
	It is considered that the dossier contains the information necessary to carry out a risk assessment and for enforcement purposes (relevant for substances for which one or more representative uses includes use on feed or food crops or leads indirectly to residues in food or feed). In particular it is considered that the dossier: (a) permits any residue of concern to be defined; (b) reliably predicts the residues in food and feed, including succeeding crops (c) reliably predicts, where relevant, the corresponding residue level reflecting the effects of processing and/or mixing; (d) permits a maximum residue level to be defined and to be determined by appropriate methods in general use for the commodity and, where appropriate, for products of animal origin where the commodity or parts of it is fed to animals; (e) permits, where relevant, concentration or dilution factors due to processing and/or mixing to be defined.	X		Risk assessment for consumer was sucesfully perform taking into account all available data. No chronic and acute risk have been identified for the requested uses. Based on the available data a safe MRL has been proposed.
	It is considered that the dossier submitted is sufficient to permit, where relevant, an estimate of the fate and distribution of the active substance in the environment, and its impact on non-target species.	X		*[*
Efficacy				
		Yes	No	
	It is considered that it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection	x		It should be mentioned that planting density of potatoes can vary by EU member state or whether the potato is being grown for consumption as ware potatoes or for the generation of seed potatoes,

	practice and having regard to realistic conditions of use is sufficiently effective.			the representative use in potatoes supported for the renewal of flutolanil is at a planting rate of 4 tonnes potatoes/ha since this is considered representative of the majority of intended EU uses. Especially for seed potatoes which are often planted at higher densities the proposed GAP is unlikely to be realistic for all member states, as several memberstates report higher planting densities of up to 5 or 7 tons per hectare. Planting densities compatible with the proposed GAP also occur. The GAP is realistic for ware and starch potatoes, which is the majority of the potato acreage.
Relevance of metabolites				
		Yes	No	
	It is considered that the documentation submitted is sufficient to permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.	X		No major soil metabolites for flutolanil
Composition				
		Yes	No	
	It is considered that the specification defines the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereo-isomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.	X		The minimum degree of purity, identity and maximum content of impurites have been sufficiently specified. No isomers are present. The content of impurities has been sufficiently addressed.
	It is considered that the specification is in compliance with the relevant Food and Agriculture Organisation specification, where such specification exists.	X		
	It is considered for reasons of protection of human or animal health or the environment, stricter specifications than that provided for by the FAO specification should be adopted.		X	
Methods of analysis				
		Yes	No	
	It is considered that the methods of analysis of the active substance, safener or synergist as manufactured and of determination of impurities of toxicological, ecotoxicological or environmental concern or which are present in quantities greater than 1 g/kg in the active substance, safener or synergist as manufactured, have been validated and shown to be sufficiently	X		See Volume 3, section 5 for evaluations of the submitted methods. Sufficient analytical methods with respect to the active substance are available.

	specific, correctly calibrated, accurate and precise.			
	It is considered that the methods of residue analysis for the active substance and relevant metabolites in plant, animal and environmental matrices and drinking water, as appropriate, shall have been validated and shown to be sufficiently sensitive with respect to the levels of concern.	X		Sufficient methods for the determination of residues of the active substance have been submitted. These methods have been validated with relevant guidelines.
	It is confirmed that the evaluation has been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		
Impact on human health				
Impact on human health - ADI, AOEL, ARfD				
		Yes	No	
	It is confirmed that (where relevant) an ADI, AOEL and ARfD can be established with an appropriate safety margin of at least 100 taking into account the type and severity of effects and the vulnerability of specific groups of the population.	X		ADI = 0.09 mg/kg bw/day, based on is the 104 week study with rats AOEL = 0.26 mg/kg bw/day, based on the 90-day study with rats ARfD = 0.4 mg/kg bw/day AAOEL = 0.28 mg/kg bw/day
Impact on human health – proposed genotoxicity classification				
		Yes	No	
	It is considered that, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as mutagen category 1A or 1B.**		x	Flutolanil was shown to be non-mutagenic in a series of in vitro and in vivo tests and is therefore not classified for mutagenicity. The weak positive shown in one in vitro chromosome aberration test using hamster lung cells was negated by the later testing and regarded as spurious.
Impact on human health – proposed carcinogenicity classification				
		Yes	No	
i)	It is considered that, on the basis of assessment of the carcinogenicity testing carried out in accordance with the data requirements for the active substances, safener or synergist and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No		x	Based on chronic studies in mouse, rat and dog there was no evidence that flutolanil caused any neoplastic change.

	1272/2008, **as carcinogen category 1A or 1B.**			
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			*not applicable*
Impact on human health – proposed reproductive toxicity classification				
		Yes	No	
i)	It is considered that, on the basis of assessment of the reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, **the substance SHOULD BE classified or proposed for classification**, in accordance with the provisions of Regulation (EC) No 1272/2008, **as toxic for reproduction category 1A or 1B.**		x	No signs of malformations were observed in oral developmental studies in rat and rabbit. Based on the occurrence of a positive trend of resportions and deaths a LOAEL of 200 mg/kg bw/day was determined for embryofetal toxicity
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			*not applicable*
Impact on human health – proposed endocrine disrupting properties classification				
		Yes	No	
i)	It is considered that **the substance SHOULD BE classified or proposed for classification** in accordance with the provisions		x	The potential of flutolanil and any major metabolites to interact with endocrine systems in mammals has been reviewed, to facilitate an

	of Regulation (EC) No 1272/2008, as **carcinogenic category 2 and toxic for reproduction category 2 and on that basis shall be considered to have endocrine disrupting properties**			assessment of whether flutolanil may be judged to be an endocrine disrupter (ED) within the framework of European legislation. The evidence shows that flutolanil does not interact with molecular endpoints known to cause endocrine activity. Flutolanil also had no endocrine activity in mammalian assays specific for endocrine disruption and in other regulatory studies with endpoints relevant for endocrine disruption. This weight of evidence indicates that it does not interact with mammalian endocrine systems in studies designed to detect effects relevant for human health.
ii)	It is considered that **the substance SHOULD BE classified or proposed for classification** in accordance with the provisions of Regulation (EC) No 1272/2008, as **toxic for reproduction category 2 and** in addition the RMS considers the substance **has toxic effects on the endocrine organs and on that basis shall be considered to have endocrine disrupting properties**			*not applicable*
iii)	Linked to either i) or ii) immediately above. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			*not applicable*
Fate and behaviour in the environment				
Persistent organic pollutant (POP)				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a persistent organic pollutant (POP) as laid out in Regulation 1107/2009 Annex II Section 3.7.1.		x	Water = Yes DT_{50} values derived from the OECD 309 study exceed the trigger value of 2 months (DT50>1000 days). The OECD 308 studies performed under dark conditions do not exceed the trigger value of 2 months: Trigger DT50 values for water were in the range 4.49-50.4 days (at 20°C), and trigger DT90 values were in the range 86.2->10000 days (at 20°C)

				Soil = yes Maximum DT_{50} values of flutolanil exceed the 6 months trigger. The geometric mean degT50 value is 105 days (at 20°C), which is above the 6 months trigger. Sediment = yes Trigger DT50 values for sediment were in the range 91.9-1000 days (at 20°C), and trigger DT90 values were in the range 305-3320 days (at 20°C). BCF = 100 l/g (<5000) Air degradation of flutolanil: DT_{50} = 0.072 days (12 hour day) (<2 days) flutolanil: DT_{50} = 0.036 days (24 hour day) (<2 days)
Persistent, bioaccumulative and toxic substance (PBT)				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a persistent, bioaccumulative and toxic (PBT) substance as laid out in Regulation 1107/2009 Annex II Section 3.7.2.		x	P=Yes B= No T= No Marine water data not available. Estuarine water DT_{50} values derived from the OECD 309 study exceed the trigger value of 2 months. The OECD 308 studies performed under dark conditions do not exceed the trigger value of 2 months: Trigger DT50 values for water were in the range 4.49-50.4 days (at 20°C), and trigger DT90 values were in the range 86.2->10000 days (at 20°C) Estuarine Sediment: Trigger DT50 values for sediment were in the range 91.9-1000 days (at 20°C), and trigger DT90 values were in the range 305-3320 days (at 20°C). Soil: Maximum DT_{50} values of flutolanil exceed the 6 months trigger. The geometric mean degT50 value is 105 days (at 20°C) , which is above the 6 months trigger. BCF =100 ml/g (<5000) Lowest aquatic toxicity endpoint = 0.233 mg/L Air degradation of flutolanil: DT_{50} = 0.072 days (12 hour day) (<2 days) flutolanil: DT_{50} = 0.036 days (24 hour day) (<2 days)

Very persistent and very bioaccumulative substance (vPvB).				
		Yes	No	
	It is considered that the active substance **FULFILS** the criteria of a a very persistent and very bioaccumulative substance (vPvB) as laid out in Regulation 1107/2009 Annex II Section 3.7.3.		X	See **(POP)** and **(PBT)** criteria for water, sediment and soil half life values. BCF = 100 ml/g (<5000)
Ecotoxicology				
		Yes	No	
	It is considered that the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. The RMS is content that the assessment takes into account the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.		X	There is an unacceptable risk to mammals for the proposed uses in flower bulbs and potatoes. There is an unacceptable risk for aquatic organisms for flutolanil (for the use in flower bulbs) and the metabolite M-11 (for the use in potatoes and flower bulbs). Unacceptable risk to earthworms was concluded for uses in flower bulbs. Unacceptable risk for soil nitrogen transformation was concluded for uses in flower bulbs.
	It is considered that, on the basis of the assessment of Community or internationally agreed test guidelines, the substance **HAS** endocrine disrupting properties that may cause adverse effects on non-target organisms.			The results of a fish short-term reproduction assay indicate a potential endocrine effect, based on effects on vitellogenin (concentration-related reduction in females), fecundity, secondary sexual characteristics in males and histological alterations of both male and female gonads. These seem to indicate a potential anti-androgenic or steroidogenic mechanism of action, however, assays addressing these aspects in humans (or mammals) present in the mammalian data set were negative. Further data are needed to investigate the potential endocrine activity of flutolanil in fish. A data gap is set for an extended one generation test (medaka) and/or any other pertinent information relating to mechanism of action or molecular interactions relevant to the potential for endocrine disruption in fish and in order to

				determine whether these potential interactions might be considered adverse at the population level.
	Linked to the consideration of the endocrine properties immediately above. It is considered that the exposure of non-target organisms to the active substance in a plant protection product under realistic proposed conditions of use is negligible.		x	
	It is considered that it is established following an appropriate risk assessment on the basis of Community or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist: — will result in a negligible exposure of honeybees, or — has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour.	x		Acute and chronic studies in honey bees are available. Risk assessments performed according to SANCO and EFSA (2013), and did not show a risk to honey bee populations. A semi-field study in Phacelia supported this conclusion.
Residue definition				
		Yes	No	
	It is considered that, where relevant, a residue definition can be established for the purposes of risk assessment and for enforcement purposes.	X		See level 2 for detail assessment
Fate and behaviour concerning groundwater				
		Yes	No	
	It is considered that it has been established for one or more representative uses, that consequently after application of the plant protection product consistent with realistic conditions on use, the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		For the use in potatoes, flutolanil PEC_{GW} values are < 0.1 µg/L. For the use in tulips & iris, flutolanil PEC_{GW} values are < 0.1 µg/L for the scenarios Chateaudun, Jokioinen, Porto and Thiva. For Hamburg and Kremsmuenster, groundwater concentrations above the parametric limit of 0.1 µg/L are expected.

3.1.2 Proposal – Candidate for substitution

Candidate for substitution				
		Yes	No	
	It is considered that the active substance shall be approved as a candidate for substitution		X	

3.1.3 Proposal – low risk active substance

Low-risk active substances				
		Yes	No	
	It is considered that the active substance **shall be considered of low risk.** In particular it is considered that the substance **should NOT be classified or proposed for classification** in accordance with Regulation (EC) No 1272/2008 as at least one of the following: — carcinogenic, — mutagenic, — toxic to reproduction, — sensitising chemicals, — very toxic or toxic, — explosive, — corrosive. In addition it is considered that **the substance is NOT**: — persistent (half-life in soil more than 60 days), — has a bioconcentration factor higher than 100, — is deemed to be an endocrine disrupter, or — has neurotoxic or immunotoxic effects.		X	

3.1.4 List of studies to be generated, still ongoing or available but not peer reviewed

Data gap	Relevance in relation to representative use(s)	Study status		
		No confirmation that study available or on-going.	Study on-going and anticipated date of completion	Study available but not peer-reviewed
3.1.4.1 Identity of the active substance or formulation				
No data gap.				
3.1.4.2 Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation				
No data gap.				
3.1.4.3 Data on uses and efficacy				
No data gap.				
3.1.4.4 Data on handling, storage, transport, packaging and labelling				
No data gap.				
3.1.4.5 Methods of analysis				
No data gap.				
3.1.4.6 Toxicology and metabolism				

3.1.4.7 Residue data				
3.1.4.8 Environmental fate and behaviour				
Public literature search fate. RMS requests notifier to include searches with (proquest) dialog databases		X		
Public literature search fate. RMS requests notifier to add a summary/abstract for RMS and other member states to evaluate the relevance of the 8 relevant (or unclear) publications.		X		
3.1.4.9 Ecotoxicology				
Further data is needed to support/refine the mammalian long-term risk assessment.		x		
Further data is needed to support the aquatic risk assessment with metabolites M-4 and M-11.		x		
Further data is necessary to determine whether potential interaction with the endocrine system in fish exists and may be considered adverse at the population level.		x		
Further data is needed to support the earthworm risk assessment.		x		
Further data is needed to support the soil		x		

microorganisms risk assessment.				

3.1.5 Issue that could not be finalized

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

Area of the risk assessment that could not be finalised on the basis of the available data	**Relevance in relation to representative use(s)**
Risk for wild mammals	There is an unacceptable risk for wild mammals from the proposed uses in flower bulbs and potatoes.
Risk for aquatic organisms	There is an unacceptable risk for aquatic organisms for flutolanil (for the use in flower bulbs) and the metabolites M-4 M-11 (for the use in potatoes and flower bulbs). A potential interaction with the endocrine system was determined from the fish short term reproduction assay. Further information is required to eliucidate these effects and determine the potential for adversity at the population level.
Risk to non-target soil meso- and macro fauna (other than earthworms)	An unacceptable risk to earthworms was concluded for uses in flower bulbs.
Risk for soil nitrogen transformation	An unacceptable risk for soil nitrogen transformation was concluded for uses in flower bulbs.
Toxicity studies for mammalian toxicology	The formulation composition of the representative formulation MONCUT 40SC changed over time. Although the composition of the representative product since the inclusion of flutolanil in Annex I of Dir 91/414/EEC is provided in Volume 4, it has to be made clear by the notifier which formulation is the representative formulation used for the acute toxicity studies as this remains unclear.
Risk for children (bystanders)	For bystanders the exposure to children resulting from drift still exceeds the AAOEL when using drift reduction (140% of the AAOEL). The exposure to flutolanil as a result of spray drift is thus not acceptable and the applicant is requested to provide a refined risk assessment.

3.1.6 Critical areas of concern

An issue is listed as a critical area of concern:
(a) where the substance does not satisfy the criteria set out in points 3.6.3, 3.6.4, 3.6.5 or 3.8.2 of Annex II of Regulation (EC) No 1107/2009 and the applicant has not provided detailed evidence that the active substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical methods, taking into account risk mitigation measures to ensure that exposure of humans and the environment is minimised, or
(b) where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

Critical area of concern identified	**Relevance in relation to representative use(s)**
	[specify if concern relates to all or specific representative use/use scenario/product or to all uses/products]

3.1.7 Overview table of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in 3.3.1, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)
All columns are grey as the material tested in the toxicological studies has not been demonstrated to be representative of the technical specification.

Representative use		potatoes (X^1)	flower bulbs(X^1)
Operator risk	Risk identified		
	Assessment not finalised		
Worker risk	Risk identified		
	Assessment not finalised		
Bystander risk	Risk identified		**X**
	Assessment not finalised		**X**
Consumer risk	Risk identified		
	Assessment not finalised		
Risk to wild non target terrestrial vertebrates	Risk identified	x	x
	Assessment not finalised	x	x
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	x	x
	Assessment not finalised	x	x
Risk to aquatic organisms	Risk identified	x	x
	Assessment not finalised	x	x
Groundwater exposure active substance	Legal parametric value breached		x
	Assessment not finalised		
Groundwater exposure metabolites	Legal parametric value breached		
	Parametric value of 10µg/L[(a)] breached		
	Assessment not finalised		
Comments/Remarks			

The superscript numbers in this table relate to the numbered points indicated within chapter 3.1.5 and 3.1.6. Where there is no superscript number, see level 2 for more explanation.
(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

3.1.8 Area(s) where expert consultation is considered necessary

It is recommended to organise a consultation of experts on the following parts of the assessment report:

Area(s) where expert consultation is considered necessary	Justification
Fate and behavior 3-CP	Tulip and iris The selected FOCUS crop for tulip and iris was onions. This crop does not cover all scenarios, and hence no PECgw values are available for flower bulbs in Okehampton, Piacenza and Sevilla. RMS does not consider it necessary to select a different crop to represent flower bulbs in order to have all scenarios included. Alternatively, winter cereals could be simulated to represent flower bulbs as default crop, but this is too conservative in RMS's opinion. Do notifier and other MS agree on this approach?
Residues	Discuss the proposed residue definitions (both for monitoring and risk assessment) in plant and animal commodities.
Ecotoxicology	Weight of evidence for the risks to mammals from the "presence of weeds scenario" for the use in tulip and iris. Potential for endocrine disruption in fish (all uses). The RMS has set a data gap for more information to address this based upon the results of the FSTRA. Agreement with this data gap and the appropriate data that might be requested should be discussed with the MS experts.

3.1.9 Critical issues on which the co-RMS did not agree with the assessment by the RMS

Points on which the co-rapporteur Member State did not agree with the assessment by the rapporteur member state. Only the points relevant for the decision making process should be listed.

Issue on which Co-RMS disagrees with RMS	Opinion of Co-RMS	Opinion of RMS

3.2 Proposed decision

[redacted]

3.3 Rational for the conditions and restrictions to be associated with the approval or authorisation(s), as appropriate

3.3.1 Particular conditions proposed to be take into account to manage the risks identified

[redacted]

Proposed condition/risk mitigation measure	Relevance in relation to representative use(s)
	[specify if measure relates to a specific representative use/use scenario/product or to all uses/products]

Appendices

Appendix 1 Guidance documents used in this assessment

EFSA Journal 2014;12(5):3662 [67 pp.].

Appendix 2 Reference list

EFSA Journal 2015;13(7):4175 [54 pp.].