European Commission

Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation)

CLOMAZONE

Volume 1

Clomazone (ISO); 2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one
EC: -
CAS: 81777-89-1

Rapporteur Member State: Denmark
Co-Rapporteur Member State: Germany

September 2018

Version History

When	What
2005/March	Initial DAR
2005/June	Revised Vol. 1
2018/January	Draft RAR
2018/October	Revised vol. 1 according to ECHA accordance check.

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Level 1

CLOMAZONE

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 THIS DRAFT ASSESSMENT REPORT WAS PREPARED

1.1.1 Purpose for which the draft assessment report was prepared

In accordance with Commission Regulation (EU) 1107/2009 and Commission Regulation (EU) 844/2012, two dossiers to support renewal of clomazone were submitted by the 30 April 2016.

A joint dossier was submitted by the Clomazone AIR Task force (CATF) consisting of FMC Chemical sprl. (FMC) and ADAMA Ltd (ADAMA). FMC being the original notifier at the Annex I inclusion. Another joint dossier was submitted by Oxon Italia S.p.A., Albaugh Europe Sàrl and Sapec Agro S.A (OAS).

This RAR reviews new data generated since the first approval of clomazone or data already available during the first EU evaluation but not peer reviewed. In addition, already EU review data are summarised for the sake of completeness.

No new MRLs were proposed by the notifiers.

A proposal for Classification and Labelling is included within Vol. 1.

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

DK acting as Rapporteur Member State (RMS) has evaluated all sections of the dossier. The draft Renewal Assessment Report (dRAR) was subjected to quality assurance by the Co-RMS Germany.

1.1.3 EU Regulatory history for use in Plant Protection Products

Clomazone is an existing active substance, the renewal of which is part of the AIR III renewal programme.

FMC, the sole notifier of the 1st EU review, submitted in November 2003 a dossier to include Clomazone in Annex I of Directive of 91/414/EEC. Denmark was the Rapporteur Member State (RMS). Clomazone was approved by Commission Directive 2007/76/EC of 20 December 2007 (entry into force: 11 November 2008) and taken over by Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 as regards the list of approved active substances. The expiration date of the approval of clomazone is 31 October 2018. There was no requirement on confirmatory data at the approval.

The following documents of the previous evaluation process resulting in the first approval of clomazone are considered to provide relevant review information on already accepted data or a reference to where such information and data can be found:

EC review report and related documents

- EC review report on Clomazone SANCO/2823/07-rev. 2, 10 September 2007, referring to the DAR (August 2007), the Final Addendum to the DAR (June 2007), the EFSA peer review report (April 2007) and the EFSA Scientific Report (2007)
- Draft Assessment Report (DAR) on Clomazone, August 2005
- Final Addendum to the Draft Assessment Report (DAR) on Clomazone, June 2007
- EFSA peer review report on Clomazone, 27 July 2007 containing
  - Comments on the draft assessment report

- Reporting table
- PRAPeR Experts' Meeting Reports
- Evaluation table

• EFSA Scientific Report (2007) 109, 1-73, Conclusion regarding the peer review of the pesticide risk assessment of the active substance clomazone including
- Listing of end points agreed at the first approval

EU MRL review, finalised in 2011

• EFSA Journal 2011; 9(8):2345; Review of the existing maximum residue levels (MRLs) for clomazone according to Article 12 of Regulation (EC) No 396/2005.

1.1.4 Evaluations carried out under other regulatory contexts

There are currently no JMPR evaluations published of clomazone. There is also no FAO specification.

1.2 APPLICANT INFORMATION

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

Clomazone AIR Task Force (CATF)

Applicant 1

Name:	FMC Chemical, sprl
Address:	Boulevard de la Plaine, 9 B-1050 Brussels Belgium
Contact:	[redacted]
Address:	c/o Cheminova / FMC Thyborønvej 78 DK-7673 Harboøre Denmark
Telephone number:	[redacted]
Fax:	[redacted]
Email:	[redacted]
Alternative contact:	[redacted]
Name:	FMC Corporation
Address:	2929 Walnut St Philadelphia, PA 19104, USA
Telephone number:	[redacted]
Fax:	[redacted]
Email:	[redacted]

Applicant 2

Name:	ADAMA Agan Ltd.
Address:	Northern Industrial Zone POB 262 7752009 Ashdod Israel

Contact:	[redacted]
Address:	ADAMA Agricultural Solutions Ltd. Airport City, Golan Street, 7019900 Israel
Telephone number:	[redacted]
Fax:	[redacted]
Email:	[redacted]
Alternative contact:	[redacted]
Address:	ADAMA Deutschland GmbH 1 Edmund-Rumpler-Str. 6 51149 Köln Germany
Telephone number:	[redacted]
Email:	[redacted]

Second clomazone task force (OAS)

Applicant 3

Name:	Oxon Italia SpA
Address:	Via Sempione 195 20016 Pero (Milan) Italy
Contact:	[redacted]
Telephone No.:	[redacted]
Telefax No.:	[redacted]
Email:	[redacted]

Applicant 4

Name:	Albaugh Europe Sàrl
Address:	World Trade Center Lausanne Avenue Gratta-Paille 2 1018 Lausanne Switzerland
Contact:	[redacted]
Telephone No.:	[redacted]
Email:	[redacted]

Applicant 5

Name:	Sapec Agro S.A.
Address:	Avenida do Rio Tejo Herdade das Praias

2910-440- Setubal
Portugal

Contact: [redacted]

Telephone No.: [redacted]

Telefax No.: [redacted]

Email: [redacted]

1.2.2 Producer or producers of the active substance

Producer (Applicant 1, FMC)

Name: FMC Corporation
Address: 2929 Walnut St
Philadelphia, PA 19104
USA

Contact: [redacted]
Telephone number: [redacted]
Fax: [redacted]
Email: [redacted]

Producer (Applicant 2, ADAMA)

Name: ADAMA Agan Ltd.
Address P.O. Box 262, Ashdod, 7710201
Israel

Contact: [redacted]
Telephone number: [redacted]
Email: [redacted]

Producer (Applicant 3)

Name: Albaugh Europe Sàrl
Address: World Trade Center Lausanne
Avenue Gratta-Paille 2
1018 Lausanne
Switzerland
Contact: [redacted]
Telephone No.: [redacted]
Email: [redacted]

Producer (Applicant 4)

Name: Oxon Italia SpA
Address: Via Sempione 195
20016 Pero (Milan)
Italy
Contact: [redacted]
Telephone No.: [redacted]

Telefax No.: [redacted]
Email:

Producer (Applicant 5)

Name: Sapec Agro S.A.

Address: Avenida do Rio Tejo
Herdade das Praias
2910-440- Setubal
Portugal

Contact: [redacted]

Telephone No.: [redacted]

Telefax No.: [redacted]

Email: [redacted]

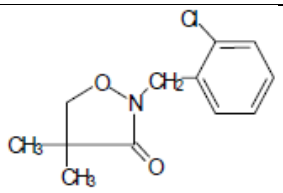
1.2.3 Information relating to the collective provision of dossiers

To support the approval of renewal of clomazone, FMC Chemical sprl and ADAMA Agan Ltd. submitted a joint CA (Chemical Active) dossier consisting of the data package of both companies. In the data package of FMC also data generated by Cheminova are included, which is now a subsidiary of FMC. Also Oxon S.p.A., Albaugh Europe Sàrl and Sapec Agro S.A. formed a task force and submitted a joint CA dossier.

In October 2015 FMC were contacted by JSC International on behalf of the three companies mentioned above regarding the potential for a joint submission. This was by request of the RMS on the pre-submission meetings with the two respective task forces. By then the cooperation between FMC and ADAMA were already well advanced and FMC/ADAMA considered the timing extremely late to allow an effective cooperation. Date of submission was 30. April 2016.

1.3 IDENTITY OF THE ACTIVE SUBSTANCE

1.3.1 Common name proposed or ISO-accepted and synonyms	Clomazone (ISO); 2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one
1.3.2 Chemical name (IUPAC and CA nomenclature)	
IUPAC	2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one
CA	2-(2-chlorophenyl)methyl-4,4-dimethyl-3-isoxazolidinone
1.3.3 Producer's development code number	FMC 57020
1.3.4 CAS, EEC and CIPAC numbers	
CAS	81777-89-1
EEC	NA
CIPAC	509
1.3.5 Molecular and structural formula, molecular mass	
Molecular formula	$C_{12}H_{14}ClNO_2$

Structural formula	
Molecular mass	239.7 g/mol
1.3.6 Method of manufacture (synthesis pathway) of the active substance	Confidential (see confidential Vol 4 of RAR)
1.3.7 Specification of purity of the active substance in g/kg	960 g/kg
1.3.8 Identity and content of additives (such as stabilisers) and impurities	
1.3.8.1 Additives	None
1.3.8.2 Significant impurities	Confidential (see confidential Vol 4 of the RAR)
1.3.8.3 Relevant impurities	None
1.3.9 Analytical profile of batches	Confidential (see confidential Vol 4 of the RAR)

1.4 INFORMATION ON THE PLANT PROTECTION PRODUCT

B.1.1.1. Applicant	Name: FMC Chemical, sprl Address: Boulevard de la Plaine, 9 B-1050 Brussels Belgium Contact: [redacted] Address: c/o Cheminova / FMC Thyborønvej 78 DK-7673 Harboøre Denmark Telephone number: [redacted] Fax: Email:
B.1.1.2. Producer of the plant protection product	Name: FMC Corporation Address: 2929 Walnut St Philadelphia, PA 19104 USA Contact: [redacted] Telephone number: Fax: Email:
B.1.1.3. Trade name or proposed trade name and producer's development code number of the plant protection product	CENTIUM® 36 CS Development code No.: FMC-Clomazone 360 CS
B.1.1.4. Detailed quantitative and qualitative information on the composition of the plant protection product	

<table>
<tr><td>B.1.1.4.1. Composition of the plant protection product</td><td>
Technical and pure active substance
<table>
<tr><td>Content of technical active substance :</td><td>375 g / L</td><td>(32.0 % w / w)</td></tr>
<tr><td>limits :</td><td>± 18.8 g / L</td><td>(± 5 % w / w)</td></tr>
<tr><td>Content of pure active substance:</td><td>360 g/L</td><td>(30.7% w/w)</td></tr>
<tr><td>Limits:</td><td>± 18 g/L</td><td>(± 5 % w/w)</td></tr>
</table>
Free (non-encapsuled) and total active substance content
<table>
<tr><th>Active substance</th><th>Content [%w/w]</th></tr>
<tr><td>Total Clomazone content</td><td>30.51</td></tr>
<tr><td>Free Clomazone content</td><td>0.7378</td></tr>
</table>
</td></tr>
<tr><td>B.1.1.4.2. Information on the active substances</td><td>
ISO common name: Clomazone
CAS No.: 81777-89-1
EC No.: NA
CIPAC No.: 509
Salt, ester, anion/cation present: Not relevant
</td></tr>
<tr><td>B.1.1.4.3. Information on safeners, synergists and co-formulants</td><td>Confidential</td></tr>
<tr><td>B.1.1.5. Type and code of the plant protection product</td><td>CS (capsule suspension)</td></tr>
<tr><td>B.1.1.6. Function</td><td>Herbicide</td></tr>
<tr><td>B.1.1.7. Field of use envisaged</td><td>Agriculture</td></tr>
<tr><td>B.1.1.8. Effects on harmful organisms</td><td>Pre-emergence control of broadleaved weed species</td></tr>
</table>

1.4.1 Applicant	Name: Albaugh Europe Sàrl Address: World Trade Center Lausanne Avenue Gratta-Paille 2 1018 Lausanne Switzerland Person to contact: [redacted] Telephone No.: [redacted] Email: [redacted]

1.4.2 Producer of the plant protection product	Name: Albaugh Europe Sàrl Address: World Trade Center Lausanne Avenue Gratta-Paille 2 1018 Lausanne Switzerland Person to contact: [redacted] Telephone No.: [redacted] Email: [redacted]
1.4.3 Trade name or proposed trade name and producer's development code number of the plant protection product	Trade name: Clomate Development code No.: ALB 36 CL Alternative names: ALB 360 CS Clomazone 360 g/L
1.4.4 Detailed quantitative and qualitative information on the composition of the plant protection product	
1.4.4.1 Composition of the plant protection product	**Pure active substance(s)** Content of pure active substance: 360 g/L (30.25% w/w)[1] Limits: (±5%)[2] 342 - 378g/L (28.7 – 31.8% w/w)[1] **Technical active substance(s)** Content of technical active substance: 375 g/L* (31.5% w/w)[1] Limits: (±5%)[2] 356.3–393.8 g/L(29.9 – 33.1% w/w 1 - Based on density of 1.19 g/mL 2 - Manual on development and use of FAO and WHO specifications for pesticides (November 2010 - second revision of the First Edition)
1.4.4.2 Information on the active substances	ISO common name: Clomazone CAS No.: 81777-89-15 EC No.: NA CIPAC No.: 509 Salt, ester, anion/cation present: Not relevant
1.4.4.3 Information on safeners, synergists and co-formulants	Confidential
1.4.5 Type and code of the plant protection product	Capsule suspension (CS)
1.4.6 Function	Herbicide

1.4.7 Field of use envisaged	Agricultural and horticultural crops
1.4.8 Effects on harmful organisms	Pre-emergence control of broadleaved weed species.

1.5 DETAILED USES OF THE PLANT PROTECTION PRODUCT

1.5.1 Details of representative uses

Crop and/or situation (a)	Member State	Product Name	F G 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 a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	g a.i./hl min max (g/hl)	Water l/ha min max	g a.i./ha min max (*) (g/ha)		
Potato	N-EU and S-EU residue zone	FMC-Clomazone 360 CS	F	Herbicide, Broadleaved weeds and annual grasses	Capsule suspension	360 g/L	Broadcast soil directed spray, tractor mounted	Pre-emergence (crop BBCH 00-09)	a) 1 b) 1	not applicable	22.5-60	150-400	a) 90 b) 90	F	also use of first EU review
Winter oilseed rape	N-EU and S-EU residue zone	FMC-Clomazone 360 CS	F	Herbicide, Broadleaved weeds and annual grasses	Capsule suspension	360 g/L	Broadcast soil directed spray, tractor mounted	Pre-emergence (crop BBCH 00-09)	a) 1 b) 1	not applicable	30-80	150-400	a) 120 b) 120	F	also use of first EU review
Spring oilseed rape*	N-EU and S-EU residue zone	FMC-Clomazone 360 CS	F	Herbicide, Broadleaved weeds and annual grasses	Capsule suspension	360 g/L	Broadcast soil directed spray, tractor mounted	Pre-emergence (crop BBCH 00-09)	a) 1 b) 1	not applicable	30-80	150-400	a) 120 b) 120	F	also use of first EU review

Crop and/or situation (a)	Member State	Product Name	F G 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 a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	Kg a.i./hl min max (g/hl)	Water l/ha min max	Kg a.i./ha min max (*) (g/ha)		
Potato	Central EU	ALB 360 CL	F	Dicotyledonous weeds	CS	360 g/L	Overall spray	BBCH 00-09(Following the last ridging and before soil cracking or pre-emergence)	1	NA	0.022-0.054	200-500	0.108	-	
Oilseed rape	Central EU	ALB 360 CL	F	Dicotyledonous weeds	CS	360 g/L	Overall spray	BBCH 00-09 (Pre-emergence)	1	NA	0.030-0.060	200-400	0.119	-	
Potato	Southern EU	ALB 360 CL	F	Dicotyledonous	CS	360 g/L	Overall spray	BBCH00-09 (Following	1	NA	0.022-0.054	200-500	0.108	-	

				weeds				the last ridging and before soil cracking or pre-emergence)							
Oilseed rape	Southern EU	ALB 360 CL	F	Dicotyledonous weeds	CS	360 g/L	Overall spray	BBCH 00-09 (Pre-emergence)	1	NA	0.030-0.060	200-400	0.119	-	

* For uses where the column „Remarks“ in 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 classification (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 N° 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 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

For the Annex I renewal of clomazone, the representative uses are in potato, and in winter and spring oilseed rape, for protection against broadleaved weeds and annual grasses.

Following normal harvest of an autumn or spring treated crop no restrictions apply. Waiting period for replacement crops in case of crop failure can be different and will be handled on national level.

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

Details on other uses than the representative uses have not been submitted.

1.5.4 Overview on authorisations in EU Member States

FMC was the only one to provide the below list.

Member State	Product Name	Formulation	License Number
Austria	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	3802
Austria	CENTIUM 36 CS	Clomazone 360 g/l CS	2733
Austria	Circuit Sync Tec	Clomazone 40 + Metazachlor 300 CS	3707
Austria	Colzor Sync Tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	3726
Austria	COMMAND 48 EC	Clomazone 480 EC	2524
Austria	Nero 424 EC	Pethoxamid 400 g/l + Clomazone 24 g/l EC	3363
Austria	Novitron Dam Tec	Clomazone 30 + Aclonifen 500 WG	3781
Austria	Reactor 360 CS	Clomazone 360 g/l CS	3548
Austria	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	3483
Austria	Tribeca Sync Tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	3726-901
Belgium	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	10600 P/B
Belgium	CENTIUM 36 CS	Clomazone 360 g/l CS	8925P/B
Belgium	Novitron Dam tec	Clomazone 30 + Aclonifen 500 WG	10338P/B
Belgium	PERTUS	Clomazone 360 g/l CS	'10014P/B
Belgium	Quantum Power	Pethoxamid 400 g/l + Clomazone 24 g/l EC	'10235P/B
Belgium	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	10274P/B
Belgium	Toutatis Dam Tec	Clomazone 30 + Aclonifen 500 WG	10561P/B
Bulgaria	Alcance Sync Tec	Clomazone 43 + pendimethalin 298 CS	1350
Croatia	Reactor 360 CS	Clomazone 360 g/l CS	'UP/I-320-20/12-01/263
Cyprus	Alcance Sync Tec	Clomazone 43 + pendimethalin 298 CS	3233
Czech	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	5056-0
Czech	CENTIUM 36 CS	Clomazone 360 g/l CS	4475-3
Czech	Cetus	Clomazone 60 + Metribuzin 233 ZC	4765-0
Czech	Circuit Sync Tec	Clomazone 40 + Metazachlor 300 CS	5118-0
Czech	Cirrus CS	Clomazone 360 g/l CS	4475-1

Member State	Product Name	Formulation	License Number
Czech	Clomanova	Clomazone 360 g/l CS	'4707-3
Czech	Colzor Sync Tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	5119-0
Czech	COMMAND 36 CS	Clomazone 360 g/l CS	4475-0
Czech	Commpas	Clomazone 360 g/l CS	'4707-1
Czech	CULMINATE EXTRA	Clomazone 30 + Pendimethaline 333 CS	4994-0
Czech	Gamit 36 CS	Clomazone 360 g/l CS	4475-2
Czech	Nero 424 EC	Pethoxamid 400 g/l + Clomazone 24 g/l EC	'4970-0
Czech	PERTUS	Clomazone 360 g/l CS	'4707-2
Czech	Quantum Power	Pethoxamid 400 g/l + Clomazone 24 g/l EC	'4970-1
Czech	Reactor 360 CS	Clomazone 360 g/l CS	'4707-0
Czech	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	4994-1
Denmark	CENTIUM 36 CS	Clomazone 360 g/l CS	421-2
Denmark	Novitron Dam Tec	Clomazone 30 + Aclonifen 500 WG	421-7
Denmark	Reactor 360 CS	Clomazone 360 g/l CS	'11-36
France	Alcance Sync Tec	Clomazone 43 + pendimethalin 298 CS	2160817
France	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	2150007
France	CENTIUM 36 CS	Clomazone 360 g/l CS	2000299
France	Cirrus 36 CS / Gamit 36 CS	Clomazone 360 g/l CS	2030010
France	Nero / Dousco	Pethoxamid 400 g/l + Clomazone 24 g/l EC	2150078
France	PERTUS, DOGON, RUEDA	Clomazone 360 g/l CS	2100214
France	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	2140023
France	Toutatis Dam Tec	Clomazone 30 + Aclonifen 500 WG	2150481
Germany	CENTIUM 36 CS	Clomazone 360 g/l CS	024798-00
Germany	CHA 6710	Clomazone 360 g/l CS	'007232-00
Germany	Cirrus WP	Clomazone 500 WP	024202-00
Germany	Echelon	Clomazone 500 WP	024202-60/00
Germany	Nero 424 EC	Pethoxamid 400 g/l + Clomazone 24 g/l EC	007575-00
Germany	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	007363/00
Greece	Alcance Sync Tec	Clomazone 43 + pendimethalin 298 CS	70168
Greece	CENTIUM 36 CS	Clomazone 360 g/l CS	70101
Hungary	COMMAND 48 EC	Clomazone 480 EC	15605/2003 (04.2/6675-1/2012)
Hungary	Metric	Clomazone 60 + Metribuzin 233 ZC	02.5/1092/3/2009 MgSzHK
Hungary	Nero 424 EC	Pethoxamid 400 g/l + Clomazone 24 g/l EC	04,2/2293-1/2014
Hungary	Reactor 360 CS	Clomazone 360 g/l CS	'04.2/3350-1/2011 MgSzH
Ireland	CENTIUM 36 CS	Clomazone 360 g/l CS	5674

Member State	Product Name	Formulation	License Number
Ireland	Gamit 36 CS	Clomazone 360 g/l CS	PCS No. 05357
Ireland	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	5483
Italy	Alcance Sync Tec	Clomazone 43 + pendimethalin 298 CS	15142
Italy	CENTIUM 36 CS	Clomazone 360 g/l CS	14643
Italy	CIRCUIT ACCESS	Clomazone 360 g/l CS	16505
Italy	CIRCUIT ACCESS	Clomazone 360 g/l CS	16484
Italy	Cirrus CS	Clomazone 360 g/l CS	15181
Italy	COMMAND 36 CS	Clomazone 360 g/l CS	11649
Italy	Gamit 36 CS	Clomazone 360 g/l CS	15039
Italy	Metric	Clomazone 60 + Metribuzin 233 ZC	14432
Luxembourg	CENTIUM 36 CS	Clomazone 360 g/l CS	L01456-083
Luxembourg	LINGO	Clomazone 45 + Linuron 250 ZC	L01882-118
Luxembourg	Metric	Clomazone 60 + Metribuzin 233 ZC	L01881-118
Luxembourg	PERTUS	Clomazone 360 g/l CS	'L01905-091
Luxembourg	Quantum Power	Pethoxamid 400 g/l + Clomazone 24 g/l EC	'L01989-091
Malta	Alcance Sync Tec	Clomazone 43 + pendimethalin 298 CS	2015-08-05 P01
Netherlands	CENTIUM 360 CS	Clomazone 360 g/l CS	12148 N
Netherlands	PERTUS	Clomazone 360 g/l CS	'13953 N
Netherlands	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	14751 N
Poland	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	R108/2016
Poland	AVATAR 293 ZC	Clomazone 60 + Metribuzin 233 ZC	R-23/2014
Poland	COMMAND 36 CS	Clomazone 360 g/l CS	R-4/2014
Poland	COMMAND 48 EC	Clomazone 480 EC	R-11/2014
Poland	COMMAND TOP 375 CS	Clomazone 30 + Napropamide 345 CS	R6/2015
Poland	HARRIER 295 ZC	Clomazone 45 + Linuron 250 ZC	R11/2015
Poland	KILOF 480 EC	Clomazone 480 EC	MRiRW nr. R-33/2013 h.r.z dnia 18.07.2013 r
Poland	Nero 424 EC	Pethoxamid 400 g/l + Clomazone 24 g/l EC	'R-77/2014
Poland	Reactor 360 CS	Clomazone 360 g/l CS	'R-128-2013
Poland	Reactor 480 EC	Clomazone 480 EC	'R -154/2014
Poland	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	R-74/2015
Poland	Szpada 480 EC	Clomazone 480 EC	R-35/2014
Portugal	CENTIUM 36 CS	Clomazone 360 g/l CS	611
Romania	COMAND	Clomazone 480 EC	1595
Slovakia	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	16-11-1790

Member State	Product Name	Formulation	License Number
Slovakia	Cetus	Clomazone 60 + Metribuzin 233 ZC	14-11-1412
Slovakia	Circuit Sync Tec	Clomazone 40 + Metazachlor 300 CS	15-11-1679
Slovakia	Cirrus CS	Clomazone 360 g/l CS	12-11-1250
Slovakia	Colzor Sync Tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	16-11-1777
Slovakia	COMMAND 36 CS	Clomazone 360 g/l CS	12-11-1251
Slovakia	Nero 424 EC	Pethoxamid 400 g/l + Clomazone 24 g/l EC	'14-11-1414
Slovakia	Reactor 360 CS	Clomazone 360 g/l CS	'11-11-1191
Slovenia	CENTIUM 36 CS	Clomazone 360 g/l CS	3433-422/2007/9
Slovenia	CULMINATE EXTRA	Clomazone 30 + Pendimethaline 333 CS	U34330-4/2014/1
Slovenia	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	34330-263/2014/2
Spain	Alcance syn tec	Clomazone 43 + Pendimethalin 298 CS	ES-00138
Spain	COMMAND 36 CS	Clomazone 360 g/l CS	22.646
Spain	Nero	Clomazone 24 + Pethoxamid 400 EC	ES-00113
Sweden	CENTIUM 36 CS	Clomazone 360 g/l CS	4778
UK	Altiplano Dam Tec	Clomazone 35 + Napropamide 400 WG	17189
UK	CENTIUM 36 CS	Clomazone 360 g/l CS	MAPP 17327
UK	Circuit Sync Tec	Clomazone 40 + Metazachlor 300 CS	17118
UK	Cirrus CS	Clomazone 360 g/l CS	17328
UK	CLEANCROP CHICANE	Clomazone 360 g/l CS	17330
UK	CLEANCROP COVERT	Clomazone 360 g/l CS	17340
UK	Colzor Sync Tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	17113
UK	Colzor Sync tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	18092
UK	Gamit 36 CS	Clomazone 360 g/l CS	17314
UK	Stallion Sync Tec	Clomazone 30 + Pendimethaline 333 CS	17243
UK	Tribeca Sync Tec	Clomazone 24 + Metazachlor 150 + Napropamide 150 CS	17312

Level 2

CLOMAZONE

2 SUMMARY OF ACTIVE SUBSTANCE HAZARD AND OF PRODUCT RISK ASSESSMENT

Summary of methodology proposed by the applicant for literature review and for all sections

CATF:

The systematic literature review is a stepwise approach basically involving the following core steps:

- Developing the review protocol
- Searching for scientific peer-reviewed open literature
- Selecting of studies for inclusion or exclusion from the review of the active substance. This selection is done in a stepwise approach involving
  - a rapid assessment by analysis of the study title and abstract, followed by
  - a detailed assessment by analysis of the full-text document.
- Inclusion of the selected studies (classified as relevant or of unclear relevance in the previous steps) in the dossier, followed by a reliability assessment and drawing conclusions for use of the results in exposure and risk assessments. These steps of the assessment are done in the CA and/or CP documents relevant for the corresponding data point established for the selected study.

A single concept search strategy was used that captures all data requirements of interest in one search. Initially, general criteria for identifying clearly irrelevant references that can be excluded from the dossier were defined and used for the rapid assessment for relevance by screening of titles and abstracts. For the subsequent detailed assessment for relevance by full-text analysis, specific relevance criteria have been developed for a concerned data point or group of data points.

Relevance criteria for detailed assessment:

Data requirement(s) (indicated by the correspondent OECD data point number(s))	**Criteria for relevance**
Relevance criteria for toxicological and metabolism studies (data points CA5, CP7)	
Studies on absorption, distribution, metabolism and excretion in mammals (CA 5.1)	1. Defined test material 2. *In vivo* tests in relevant test species for toxicological testing (i.e. rat, mouse, rabbit, dog) 3. In vitro tests 4. Specific endpoint can be clearly related to this data requirement
Acute toxicity (CA 5.2 and CP 7.1) Short term toxicity (CA 5.3) Long term toxicity and carcinogenicity (CA 5.5) Reproductive toxicity (CA 5.6) Neurotoxicity (CA 5.7)	1. Defined test material 2. Relevant test species for toxicological testing (i.e. rat, mouse, rabbit, dog, guinea pig) 3. Relevant (physiological) route of exposure 4. Several dose levels tested (at least 3), preferably including a negative control, to establish a dose-response 5. Number of animals per group sufficient to establish a statistical significance 6. Description of the observations, examinations, analysis performed, or necropsy 7. Specific endpoint can be clearly related to the data requirement

Genotoxicity testing (CA 5.4)	1. Defined test material 2. *In vitro* tests 3. *In vivo* tests in relevant species 4. Specific endpoint can be clearly related to this data requirement
Other toxicological studies (CA 5.8)	1. Defined test material 2. *In vitro* tests 3. *In vivo* tests in relevant species 4. Relevant (physiological) route of exposure 5. Specific endpoint can be clearly related to this data requirement
Medical data (CA 5.9)	1. Defined test material 2. Epidemiological studies 3. Poisonings, clinical cases 4. Relevant (physiological) route of exposure
Data on exposure (CP 7.2)	1. Defined test material 2. Field studies 3. Calculations 4. Specific endpoint can be clearly related to this data requirement
Dermal Absorption (CP 7.3)	1. Defined test material 2. Field studies

Relevance criteria for the section residue behaviour (data points CA6, CP8)	
Storage stability of residues (CA 6.1 and CP 8)	Content of publication addresses data requirements for stability of residues of the active substance (defined test material) in representative substrates (water-, oil-, protein- or starch-containing materials) to ensure that the residue situation of a sample remains accurately quantifiable from the time of sampling to analysis
Metabolism, distribution and expression of residues in plants (CA 6.2.1 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for the metabolism, distribution and expression of residues of the active substance (defined test material with one or more radiolabelled forms) in plants in order to: 1. provide an estimate of total terminal residues in the relevant portion of crops at harvest following treatment as proposed; 2. identify the major components of the total terminal residue and indicate the distribution of residues between relevant crop parts; 3. quantify components of the residue and to establish the efficiency of extraction procedures for these components; 4. decide on the definition and expression of a residue.
Metabolism, distribution and expression of residues in livestock (CA 6.2.2 – 6.2.5 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for the metabolism, distribution and expression of residues of the active substance (defined test material with one or more radiolabelled forms) in livestock (poultry, ruminant, pig, fish) in order to: 1. identify the major components of the total terminal residue in edible animal products; 2. quantify the rate of degradation and excretion of the total residue in certain animal products (milk or eggs) and excreta; 3. to indicate the distribution of residues between relevant edible animal products; 4. quantify the major components of the residue and to show the efficiency of extraction procedures for these components; 5. generate data from which a decision on the need for livestock feeding studies (...) can be made; 6. decide on the definition and expression of a residue.
Magnitude of residue trials in plants (CA 6.3 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for the presence of residues of the active substance (defined test material) on and in plants and plant products in order to determine the level of residues and, where appropriate, the decline of residues, and to assess the consequences of these residues on the health of man. Details on the application, e.g. application level shall be given.
Feeding studies (CA 6.4 and CP 8[Error! Bookmark not defined.Error! Bookmark not defined.])	Content of publication addresses data requirements for feeding studies to determine the residue of the active substance (defined test material) in products of animal origin (ruminants, poultry, pigs, fish) which will result from residues in feeding stuff or fodder crops in order to assess the consequences of these on the health of humans.

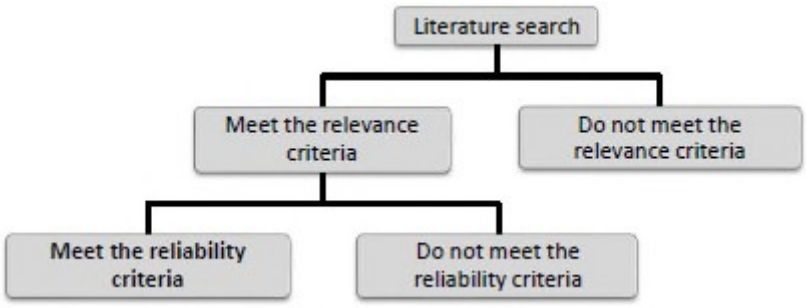
Effects of processing (CA 6.5 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for effects of industrial processing and/or household preparation on: 1. the nature of the active substance (defined test material) in order to show whether or not breakdown or reaction products arise during processing, which may require a separate risk assessment 2. the magnitude of the active substance (defined test material) in order to determine the quantitative distribution of residues in processed commodities, to estimate processing factors and to allow a more realistic estimation of dietary intake of residues.
Residues in rotational crops (CA 6.6 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for residues of the active substance in crops grown in rotation to a treated crop to allow the determination: 1. of the nature and extent of potential residue accumulation of the active substance (defined test material with one or more radiolabelled forms) in rotational crops from soil uptake, 2. of the magnitude of residues of the active substance (defined test material) in rotational crops under realistic field conditions the consequences of these residues on the health of humans.
Estimation of the potential and actual exposure through diet and other sources (CA 6.9 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for the consumer exposure assessment. This involves the possible presence of residues according to the residue definition established for risk assessment (defined test material) from other sources than plant protection uses (biocides, veterinary drug) and their aggregate exposure and the cumulative exposure to more than one active substance.
Residue level in pollen and bee products (CA 6.10.1 and CP 8[Error! Bookmark not defined.])	Content of publication addresses data requirements for residue levels of the active substance (defined test material) in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom in order to assess the consequences of these on the health of humans.
Further issues	1. Content of publication addresses problematic issues currently under discussion for the active substance and its metabolites (defined test material) and possible unknown metabolites and the corresponding consequences of these on the health of humans. 2. Studies which may be helpful for the interpretation of other studies present in the dossier but do not fit under a specific residue relevant endpoint or studies whose relevance for hazard and risk characterisation remained unclear.
Relevance criteria for the section environmental fate and behaviour (data points CA7, CP9)	
CA 7 and CP 9	1. Adequate information on persistence, degradation/dissipation or metabolism in the environment 2. Adequate information on mobility, absorption or desorption in soil or sediment 3. Field or monitoring data on concentrations in the environment from a European region 4. Relevance for hazard and risk characterisation remained unclear

Relevance criteria for the section ecotoxicology (data points CA8, CP10)	
Effects on birds (CA 8.1.1 and CP 10.1.1) Effects on other terrestrial vertebrates (CA 8.1.2 and CP 10.1.2) Effects on aquatic organisms (CA 8.2 and CP 10.2) Effects on bees (CA 8.3.1 and CP 10.3.1) Effects on non-target arthropods other than bees (CA 8.3.2 and CP 10.3.2) Earthworms –Sublethal effects (CA 8.4.1 and CP 10.4.1) Effects on non-target soil meso- and macrofauna (other than earthworms) (CA 8.4.2 and CP 10.4.2) Effects on soil nitrogen transformation (CA 8.5 and CP 10.5) Effects on terrestrial non-target higher plants (CA 8.6 and CP 10.6) Effects on other terrestrial organisms (flora and fauna) CA 8.7 and CP 10.7) Effects on biological methods for sewage treatment (CA 8.8)	**Relevance check based on information given in the title and the abstract:** 1. Ecotoxicological studies conducted with the active substance, metabolites or product containing the active substance (defined test material) addressing any of the data requirements. 2. Field studies relevant for European conditions (climate, species, …) 3. Papers dealing with the effects on mammals were not included in the relevance assessment because this was considered to be covered in the section toxicology (see toxicology). However, studies on other non-target vertebrate species (e.g. fish, birds, other mammals than the relevant species for toxicological testing) or studies which are not covered by the data requirements of the section toxicology, e.g. field studies, avoidance studies, were considered in the relevance and reliability check. **Relevance check based on full-text:** 1. Literature reviews were excluded 2. Literature coping with combined and/or mixture toxicity were excluded (no tests were conducted with the active substance and/or a solo formulation).

Publications that (potentially) provide data for establishing or refining risk assessment parameters were only found for the sections 'Environmental fate and behaviour' and 'Ecotoxicology'. In all other sections (e.g. 'Residue behaviour', 'Toxicology'), no publication was clearly relevant to the risk assessment. The classification of the relevant studies was carried out in dependence on the Klimisch evaluation scheme. 26 full text-documents have been found relevant and are included in the CA/CP documents.

OAS

The search strategy was based on a single concept search.



The selection process resulted in three categories of publication:

- Publications which meet the relevance criteria are assessed to be reliable and where the endpoints will have an impact on the risk assessment.
- Publications which meet the relevance criteria but are assessed to be non-reliable are referenced and a justification for not meeting the reliability criteria.
- Publications not meeting the relevance criteria.

The following relevance criteria were applied:

Data requirement	Criteria for relevance
Toxicological and metabolism studies	1. Well defined test material (including its purity and impurity profile) 2. Relevant test species (to the mammalian toxicological assessment - preferred species are rodents - rats and mice, the dog is the preferred non-rodent species) 3. Number of animals per group sufficient to establish a statistical significance 4. Several dose levels tested (at least 3), preferably including a negative control, to establish a dose-response 5. Relevant route of administration in terms of risk assessment (oral, dermal or by inhalation) 6. Description of the observations, examinations, analysis performed, or necropsy 7. In addition: studies which may be helpful for the interpretation of other studies present in the dossier, but do not fit under a specific toxicological endpoint

Data requirement	Criteria for relevance
Residues studies	1. Representative use 2. The application rates within the range of good of agricultural practices proposed 3. The measurement of all the components of the residue in the residue definition
Environmental fate and behaviour studies	1. Contains information on active substance 2. Paper includes sufficient detail eg. information on test system characteristics 3. Paper includes new or useful information. If it confirms GLP and guideline study results, paper would be considered to provide no new information and regulatory studies would be used instead 4. Information provided that would satisfy data requirements, answer specific point under EC regulation 1107/2009 (eg. information on isomers) or could be used for the risk assessment
Ecotoxicological studies	1. Well defined test material 2. Relevant test species used 3. Relevance to standard test guidelines

The reliability assessment for relevant studies was done according to Klimisch et al (1997).

A review of the published literature for clomazone and its potentially relevant metabolites revealed 3 articles that were considered relevant and reliable to the risk assessment of human health, animal health or the environment and will be included in the dossier.

2.1 IDENTITY

2.1.1 Summary of identity

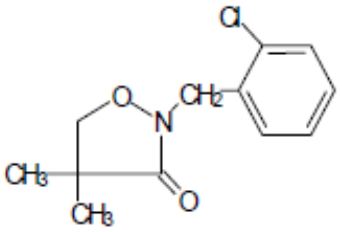
Clomazone is a selective systemic herbicide and belongs to the chemical family of Isoxazolidiones (HRAC class F4)

Chemical name (IUPAC): 2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one

Molecular formula: $C_{12}H_{14}ClNO_2$

Mass: 239.7 g/mole

Structure formula:



Impurities: No relevant or significant impurities

Isomers: Clomazone is not a mixture of isomers

2.2 PHYSICAL AND CHEMICAL PROPERTIES [EQUIVALENT TO SECTION 7 OF THE CLH REPORT TEMPLATE]

2.2.1 Summary of physical and chemical properties of the active substance

The information on the physicochemical properties represents the information as submitted by the two notifiers of the active substance, namely CATF and OAS.

The technical Clomazone can be both solid and liquid at room temperature. Hence, both physical states are considered at the relevant endpoints.

Table 1: Summary of physicochemical properties of the active substance - CATF

Property	**Value**	**Reference**	**Comment (e.g. measured or estimated)**
Physical state at 20°C and 101,3 kPa	<u>Pure material (99.7 %) (DAR 2005):</u> Physical state: solid at room temperature Colour: Neutral value scale according to the Munsell book of colours Odour: No odour <u>Technical material (98.4%)</u> (from DAR 2005) Determination > 35°C: Physical state: Homogenous liquid Colour: Colourless Determination < 25°C: Physical state: Solid Colour: Translucent white Odour: no odour	CATF: <u>FMC:</u> CA 2.3/a* (filed in CA 2.1/a): Alvarez, M. (1993), report no.: 164AF93263 Company no.: – Evaluated in DAR (2005) for clomazone, B.2.1.7 ref no. IIA 2.4	Visual
Melting/freezing point	33.0 – 34.7 °C (99.7%) (DAR 2005)	CATF: <u>FMC:</u> Alvarez, M. (1993), report no.: 164AF93263	Measured

Property	Value	Reference	Comment (e.g. measured or estimated)
		Company no.:- Evaluated in DAR (2005) for clomazone, B.2.1.1, ref no. IIA 2.1	
Boiling point	281.7 °C (99.1 %) (DAR 2005)	CATF: <u>FMC:</u> Brachet, A: (2003), Report no.: P-17-02-38 Company no.:- Evaluated in DAR (2005) for clomazone, B.2.1.2 ref no. IIA 2.1	Measured
Relative density	Not a requirement according to 283/2014		
Vapour pressure	20°C (Purity 99.0%) 1.91×10^{-3} Pa 25°C (99.7%) 5.04×10^{-2} Pa	CATF: <u>FMC:</u> KCA 2.2/02: Elliot, T. (2016), report no.: 81622 Company no.: 2014PCP-CLZ1576 CATF: <u>CHE:</u> KCA 2.2/01 (filed in KCA 2.1/03): Wolley, S. M.; Mullee, D. M. (2007), report no.: 0545/0535 Company no.: 75 CAZ	Measured
Surface tension	52.2 mN/m (0.1 %, 20°C, 99.0%) Clomazone is regarded as a surface-active substance.	<u>FMC:</u> KCA 2.12/03 (filed in KCA 2.1/02): Apps, G. (2016) report no.: CEMS-6686 Company no.: 2014PCP- CLZ161	Measured
Water solubility	1.212 g/L at 20°C (pH 7) (Purity 99.0%) Water solubility is not pH dependent	CATF: <u>FMC:</u> KCA 2.5/01: Apps, G., (2016), report no. CEMS-6689 Company no. 2014PCP-CLZ1561	Measured
Partition coefficient n-	**Clomazone**	CATF:	Measured

Property	Value	Reference	Comment (e.g. measured or estimated)
octanol/water	log P_{ow} = 2.49 (21.4 – 21.9°C, pH 7, 99.5%) Partition coefficient for Clomazone is not pH dependent **Residue definition** **CLZ-M01:** log P_{ow} = 1.8 (25°C, pH 7, 98.6%) **CLZ-M02:** log P_{ow} = 2.3 (25°C, pH 7, 99.1%) **CLZ-M03:** log P_{ow}= 0.6 (25°C, pH 4, 97.0%) log P_{ow}= - 0.7 (25°C, pH 7, 97.0%) log P_{ow}= - 0.6 (25°C, pH 9, 97.0%) **CLZ-M04:** log Pow = 1.3 (25°C, pH 4, 99.8%) log P_{ow}= - 0.7 (25°C, pH 7, 99.8%) log P_{ow}= - 0.9 (25°C, pH 9, 99.8%) **CLZ-M05:** log P_{ow} =2.1 (25°C, pH 7, 99.4%)	ADM: KCA 2.7/01: Lange, J., (2008), report no. COS12552 Company no.: 90010643 1) CATF: FMC, ADM: KCA 2.7/04: González-Benítez, J.M. (2016) report no.: CEMS-7548 Company no.: 2015PCP-CLZ2218 2) CATF: FMC, ADM: KCA 2.7/05: González-Benítez, J.M. (2016) report no.: CEMS-7549 Company no.: 2015PCP-CLZ2219 3) CATF: FMC, ADM: KCA 2.7/06: González-Benítez, J.M. (2016) report no.: CEMS-7550 Company no.: 2015PCP-CLZ2220 4) CATF: FMC, ADM: KCA 2.7/07: González-Benítez, J.M. (2016) report no.: CEMS-7551 Company no.: 2015PCP-CLZ2221	

Property	Value	Reference	Comment (e.g. measured or estimated)
		5) CATF: FM C, ADM: KCA 2.7/08: González-Benítez, J.M. (2016) report no.: CEMS-7468 Company no.:	
Henry's law constant	3.78 × 10^{-4} Pa m^3 mol^{-1} (20°C) (calculated)		calculated
Flash point	110°C (96.6 %)	CATF: ADM: KCA 2.10/01 (filed in KCA 2.6/03): Comb, A.L., (2008), report no. AGM0349 Company no.: 90010614	Measured
Flammability	Not highly flammable	CATF: ADM: KCA 2.9/01: Bodsch, J., (2008), report no. CPE12399 Company no.: 90010644	Tested
Explosive properties	Not explosive (96.6%)	CATF: ADM (solid): KCA 2.11/01: Krack, M., (2008), report no. 20080664.03 Company no.: 90010645 CHE (liquid): KCA 2.11/02 (filed in KCA 2.9/02): Tremain, S. P. (2007), report no. 0545/0537 Company no.: 41 CAZ	Tested on solid and liquid.
Self-ignition temperature	Auto flammability: 374 °C (96.8%)	CATF: FMC: KCA 2.9/04 (filed in KCA 2.1/02): Apps, G. (2016) report no.: CEMS-	Measured

<table>
<tr><th>Property</th><th>Value</th><th>Reference</th><th>Comment (e.g. measured or estimated)</th></tr>
<tr><td></td><td></td><td>6686
Company no.: 2014PCP- CLZ161</td><td></td></tr>
<tr><td>Oxidising properties</td><td>Not oxidising (96.6%)</td><td>CATF:
ADM:

KCA 2.13/02:
Krack, M. (2009)
report no.: 20080664.05
Company no.: 90012148</td><td>Tested</td></tr>
<tr><td>Granulometry</td><td>Not relevant</td><td></td><td></td></tr>
<tr><td>Solubility in organic solvents and identity of relevant degradation products</td><td>Organic solvent solubility g/L at 20°C (purity 99.0%)

Methanol >250
Dichloromethane >250
Ethyl acetate >250
Toluene >250
Acetone >250
n-heptane 201± 5</td><td>CATF:
FMC:
KCA 2.6/01:
Apps, G., (2016),
report no. CEMS-6690
Company no.: 2014PCP-CLZ1575</td><td>Measured</td></tr>
<tr><td>Dissociation constant</td><td>No dissociation in water</td><td>CATF:
ADM:

KCA 2.8/01:
Bodsch, J., (2009),
report no. CDC12552
Company no.: 90010638</td><td>Tested</td></tr>
<tr><td>Viscosity</td><td>Not a requirement according to Regulation 283/2013</td><td></td><td></td></tr>
<tr><td>Spectra (UV/VIS, IR, NMR, MS), molar extinction at relevant wavelengths, optical purity</td><td>UV/Vis Spectra for 190 -750 nm
Purity (99.0%)
8.0x10^{-5} M clomazone

<table>
<tr><th>Solvent</th><th>λ /nm</th><th>Absorbance (A)</th><th>Molar absorption coefficient (Ɛ L x mol^{-1} x cm^{-1})</th></tr>
<tr><td rowspan="2">Aqueous solution</td><td>195.5</td><td>2.349</td><td>28437.1</td></tr>
<tr><td>210.0</td><td>1.201</td><td>14539.4</td></tr>
<tr><td rowspan="2">Acidified aqueous solution</td><td>201.5</td><td>1.267</td><td>15338.4</td></tr>
<tr><td>210.0</td><td>1.190</td><td>14406.2</td></tr>
<tr><td rowspan="2">Basic aqueous solution</td><td>197.5</td><td>1.990</td><td>24091.1</td></tr>
<tr><td>210.0</td><td>1.202</td><td>14551.5</td></tr>
</table></td><td>CATF:

FMC

KCA 2.4/01:
Apps, G., (2015),
report no. CEMS-6687
Company no.: 2014PCP-CLZ1650</td><td>Measured</td></tr>
</table>

Property	Value	Reference	Comment (e.g. measured or estimated)
	No absorbance from about 290 nm and above MS, IR, NMR details awaiting applicant:		

Table 2: Summary of physicochemical properties of the active substance - OAS

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Pure (99.95%): uncoloured crystal homogenous product with a faint odour Technical grade (96.8%; 20°C): Pale yellow viscous liquid, Munsell code 5Y 9/2. No odour detected	OAS: 1) de Ryckel, B., 2010 (22129) 2) Comb, A.L., 2016 (JR27CN)	Visual
Melting/freezing point	32.8°C (99.95 %)	OAS: de Ryckel, B., 2010 (22129)	Measured
Boiling point			Study not accepted
Relative density	Not a requirement according to 283/2014		
Vapour pressure	20°C (Purity 99.0%) 2.7×10^{-2} Pa	OAS: Demangel, B., 2010 (10-901050-001)	Measured
Surface tension	45.98 mN/m (0.9918 g/L, 20°C, 99.9%) Clomazone is regarded as a surface-active substance.	OAS: Silva, S., 2016a (AI/261/16)	Measured
Water solubility	1.09 g/L at 20°C (pH 7) (Purity 99.95%) Water solubility is not pH dependent	OAS: de Ryckel, B., 2010 (22129)	Measured
Partition coefficient n-octanol/water	**Clomazone** (purity 99.95%) Log P_{ow} at 20°C pH 5 buffer log P_{ow} 2.60 ± 0.01 pH 7 buffer log P_{ow} 2.58 ± 0.00 pH 9 buffer log P_{ow} 2.54 ± 0.01 Partition coefficient is not pH dependent	OAS: Clomazone : de Ryckel, B., 2010 (22129)	Measured Data on CLZ-M03, CLZ-M04

Property	Value	Reference	Comment (e.g. measured or estimated)
	Residue definition **CLZ-M01:** log P_{ow} = 1.610 (25°C, pH 7, 99.8%) **CLZ-M02:** log P_{ow} = 2.504 (25°C, pH 7, 97.5%) **CLZ-M03:** missing **CLZ-M04:** missing **CLZ-M05:** missing	CLZ-M01: Silva, S., 2016b (AI/262/16) CLZ-M02 : Silva, S., 2016c (AI/263/16)	and CLZ-M05 are missing
Henry's law constant	5.9×10^{-3} Pa m^3 mol^{-1} (20°C) (calculated)		calculated
Flash point	158°C (96.8%)	OAS: Comb, A.L., 2016 (JR27CN)	measured
Flammability			Data missing as technical active can be solid
Explosive properties	Not explosive (96.8%)	OAS: Comb, A.L., 2016 (JR27CN)	Tested on liquid. Data missing on solid.
Self-ignition temperature	Auto flammability: 380 °C (96.8%)	OAS: Comb, A.L., 2016 (JR27CN)	Measured
Oxidising properties			Statement was not accepted
Granulometry	Not relevant		
Solubility in organic solvents and identity of relevant degradation products	20°C (purity 99.95%) n-heptane: 161.84 ± 13.8 g/L toluene: >250 g/L dichloromethane > 250 g/L acetone > 250 g/L methanol > 250 g/L ethyl acetate > 250 g/L	OAS: de Ryckel, B., 2010 (22129)	Measured
Dissociation constant	No dissociation in water	OAS	Statement
Viscosity	Not a requirement according to Regulation 283/2013		
Spectra (UV/VIS, IR, NMR, MS), molar extinction at relevant	*UV/Vis Spectra for 205-805 nm, 25°C* Purity (99.95%) Acidi c:	OAS: de Ryckel, B., 2010 (22129)	Measured IR and NMR data

Property	Value	Reference	Comment (e.g. measured or estimated)
wavelengths, optical purity	ε = 13866.0 L.mol^{-1}.cm^{-1} Neutral: Wavelength 210.3 nm ε = 13454.5 L.mol^{-1}.cm^{-1} Alkaline: Wavelength 222.0 nm ε = 3731.1 L.mol^{-1}.cm^{-1} Wavelength 259.1 nm ε = 325.9 L.mol^{-1}.cm^{-1} Wavelength 272.6 nm ε = 178.2 L.mol^{-1}.cm^{-1} Wavelength 298.8 nm ε = 31.0 L.mol^{-1}.cm^{-1} No absorbance from 350 to 805 nm Mass Spectra Characteristic ion: 89. 125 and 204 m/z. The mass spectrum is consistent with the structure of clomazone. IR and NMR spectra and details not provided		missing

2.2.1.1 Evaluation of physical hazards [equivalent to section 8 of the CLH report template]

2.2.1.1.1 Explosives *[equivalent to section 8.1 of the CLH report template]*

Table 3: Summary table of studies on explosive properties

Method	Results	Remarks	Reference
EEC A.14, OPPTS 830.6313	Not explosive Preliminary-test with thermal stability showed an energy release of 980J/g in the temperature range of 215-390°C. In the final test thermal sensitivity and mechanical sensitivity (shock + friction) were negative.	Clomazone technical Purity: 96.6% Batch no.: D-20071015-1	CATF: ADM: KCA 2.11/01: Krack, M., (2008), report no. 20080664.03 Company no.: 90010645
EEC A.14	Not explosive Thermal sensitivity and mechanical sensitivity (shock) were negative. The friction test was not performed since it is a liquid	Clomazone technical Purity: 98.2% Batch.: C1212 liquid	CATF: CHE: KCA 2.11/02 (filed in KCA 2.9/02): Tremain, S. P. (2007),

Method	Results	Remarks	Reference
			report no. 0545/0537 Company no.: 41 CAZ
EC A.14	Not explosive Thermal sensitivity and mechanical sensitivity (shock) were negative. The friction test was not performed since it is a liquid	Clomazone technical Purity: 96.8% Batch: 14640C1016 (liquid)	OAS: Comb, A.L., 2016 (JR27CN)

2.2.1.1.1.2 Short summary and overall relevance of the provided information on explosive properties
Three studies were provided on explosive properties of technical clomazone. All were acceptable and negative. Clomazone is not considered explosive.

2.2.1.1.1.2 Comparison with the CLP criteria
Thermal sensitivity and mechanical sensitivity (shock + friction) were negative in test. According to the CLP criteria Clomazone is not explosive.

2.2.1.1.1.2 Conclusion on classification and labelling for explosive properties
Clomazone is not classifiable as explosive

2.2.1.1.2 Flammable gases (including chemically unstable gases) ***[equivalent to section 8.2 of the CLH report template]***

Not relevant

2.2.1.1.3 Oxidising gases ***[equivalent to section 8.3 of the CLH report template]***

Not relevant

2.2.1.1.4 Gases under pressure ***[equivalent to section 8.4 of the CLH report template]***

Not relevant

2.2.1.1.5 Flammable liquids ***[equivalent to section 8.5 of the CLH report template]***

Table 4: Summary table of studies on flammable liquids

Method	Results	Remarks	Reference
EEC A. 9 Pensky-Martens Closed cup	Flash point 110 °C	Clomazone technical Purity: 96.6% Batch.: D-20071015-1 Solid at 20oC	CATF: ADM: KCA 2.10/01 (filed in KCA 2.6/03): Comb, A.L., (2008), report no. AGM0349 Company no.: 90010614
EEC A. 9 Closed cup	Result: 147 ± 2 °C	Clomazone technical Purity: 98.2% Batch.: C1212 liquid	CATF: CHE: KCA 2.10/03 (filed in KCA 2.9/02): Tremain, S. P. (2007),

Method	Results	Remarks	Reference
			report no. 0545/0537 Company no.: 41 CAZ
EC A.9 (Pensky-Martens closed cup tester)	Measured at 1016 mbar Flash point 158°C	Clomazone Purity: 96.8% Batch: 14640C1016 (liquid)	OAS: Comb, A.L., 2016 (JR27CN)

2.2.1.1.5.2 Short summary and overall relevance of the provided information on flammable liquids
Three studies on flash point were provided. Liquid clomazone is not highly flammable.

2.2.1.1.5.2 Comparison with the CLP criteria
Flash point is or above 110°C. Hence, not flammable according to CLP.

2.2.1.1.5.2 Conclusion on classification and labelling for flammable liquids
Clomazone should not be labelled flammable.

2.2.1.1.6 Flammable solids *[equivalent to section 8.6 of the CLH report template]*

Table 5: Summary table of studies on flammable solids

Method	Results	Remarks	Reference
EEC A.10	Result: Clomazone is not highly flammable.	Clomazone technical Purity: 96.6% Batch: D-20071015-	CATF: ADM: KCA 2.9/01: Bodsch, J., (2008), report no. CPE12399 Company no.: 90010644

2.2.1.1.6.2 Short summary and overall relevance of the provided information on flammable solids
One acceptable study was provided on flammability of solids. The technical material was not highly flammable.

2.2.1.1.6.2 Comparison with the CLP criteria
Not flammable

2.2.1.1.6.2 Conclusion on classification and labelling for flammable solids
Clomazone should not be labelled flammable.

2.2.1.1.7 Self-reactive substances *[equivalent to section 8.7 of the CLH report template]*

Not tested/Not relevant

2.2.1.1.8 Pyrophoric liquids *[equivalent to section 8.8 of the CLH report template]*

Not tested/Not relevant

2.2.1.1.9 Pyrophoric solids *[equivalent to section 8.9 of the CLH report template]*

Not tested/Not relevant

2.2.1.1.10 Self-heating substances *[equivalent to section 8.10 of the CLH report template]*

Table 6: Summary table of studies on self-heating substances

Method	Results	Remarks	Reference
EEC A.15	Self-heating: 382 ± 5°C	Clomazone technical	CATF: CHE:

Method	Results	Remarks	Reference
		Purity: 98.2% Batch.: C1212 liquid	KCA 2.9/02: Tremain, S. P., (2007), report no. 0545/0537 Company no.: 41 CAZ
EEC A.15 BS 4056	Self-heating: 390 °C	Clomazone technical Purity: 96.6%, Batch: D-20071015-1 Solid at 20°C with low melting temp.	CATF: ADM: KCA 2.9/03 (filed in KCA 2.6/03): Comb, A.L. (2008), report no. AGM0349 Company no.:
EEC A.15	Self-heating: 374°C	Clomazone technical Purity: 96.8% Batch: JLHP305001	CATF: FMC: KCA 2.9/04 (filed in KCA 2.1/02): Apps, G. (2016) report no.: CEMS-6686 Company no.: 2014PCP-CLZ161
EC A.15 (BS 4056)	Auto-ignition temperature 380°C	Clomazone Purity: 96.8% Batch: 14640C1016 (liquid)	OAS: Comb, A.L., 2016 (JR27CN)

2.2.1.1.10.2 Short summary and overall relevance of the provided information on self-heating substances

Four studies on auto-ignition were provided. They show a self-heating temperature range of 374-390°C. However, the substance has a low melting temperature (<160°C) and should not be considered for classification in this hazard class according to the CLP Guidance.

2.2.1.1.10.2 Comparison with the CLP criteria

The substance has a low melting temperature (<160°C) and should not be considered for classification in this hazard class according to the CLP Guidance.

2.2.1.1.10.2 Conclusion on classification and labelling for self-heating substances

Not relevant

2.2.1.1.11 Substances which in contact with water emit flammable gases *[equivalent to section 8.11 of the CLH report template]*

Not relevant

2.2.1.1.12 Oxidising liquids *[equivalent to section 8.12 of the CLH report template]*

Table 7: Summary table of studies on oxidising liquids

Method	Results	Remarks	Reference
EEC A.17 (liquids)	Result: The substance has no oxidising properties in the sense of EEC A.21. The mean pressure rise time was	Clomazone technical Purity: 96.6% Batch: D-20071015-1	CATF: ADM: KCA 2.13/02:

Method	Results	Remarks	Reference
	higher than for the reference. Hence, not oxidising.		Krack, M. (2009) report no.: 20080664.05 Company no.: 90012148

2.2.1.1.12.2 Short summary and overall relevance of the provided information on oxidising liquids
One acceptable study was submitted. The mean pressure rise time was higher than for the reference. Hence, not oxidising.

2.2.1.1.12.2 Comparison with the CLP criteria
The mean pressure rise time was higher than for the reference. Hence, not oxidising.

2.2.1.1.12.2 Conclusion on classification and labelling for oxidising liquids
Clomazone is not classifiable as an oxidising liquid

2.2.1.1.13 Oxidising solids *[equivalent to section 8.13 of the CLH report template]*

Table 8: Summary table of studies on oxidising solids

Method	Results	Remarks	Reference
EEC A.17 (solids)	Result: The test item has no oxidising properties.	Clomazone technical Purity: 96.8% Batch: JLHP305001 Non acceptable The preliminary test did actually indicate oxidising properties. Therefore the Train test should have been performed. The preliminary test cannot exclude oxidising properties. If the preliminary test does not show oxidising properties you should continue to the Train test. Only when the preliminary test show oxidising properties you should not do the Train test. A suspected false positive result in the Train test can be repeated using an inert substance - Not in the preliminary test.	FMC: KCA 2.13/01 (filed in KCA 2.1/02): Apps, G. (2016) report no.: CEMS-6686 Company no.: 2014PCP-CLZ1611
Statement	Not expected to be oxidising	Non Acceptable Clomazone contains O which is chemically bonded to N (not only C or H). Hence, it	OAS: Demangel, B., 2010 (10-901050-001)

Method	Results	Remarks	Reference
		does not meet the criteria set out in Appendix 6 of the United Nations 'Recommendations on the Transport of Dangerous Goods Manual of Tests and Criteria'.	

2.2.1.1.13.2 Short summary and overall relevance of the provided information on oxidising solids
No acceptable study or statement was submitted.

2.2.1.1.13.2 Comparison with the CLP criteria
Data were inconclusive

2.2.1.1.13.2 Conclusion on classification and labelling for oxidising solids
Data were inconclusive

2.2.1.1.14 Organic peroxides *[equivalent to section 8.14 of the CLH report template]*

Not relevant

2.2.1.1.15 Corrosive to metals *[equivalent to section 8.15 of the CLH report template]*

Not tested

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

OAS Task Force: The product 'Clomazone 360 g/L CS' is a Capsule Suspension formulation. The appearance of the product is a free-flowing homogenous liquid, opaque cream colour. A conclusion on explosive and oxidising properties is not yet possible. The formulation has no self-ignition temperature when tested up to 438°C. The product is not considered to be flammable. In aqueous solution it has a pH of 9.78. The viscosity is dependent on shear rate. Hence, the product is a non-Newtonian liquid. The surface tension is 51.3 mN/m and the product is therefore considered surface active. The formulation and the encapsulation was found to be stable under accelerated and ambient temperature storage conditions in HDPE containers. The technical characteristics are acceptable for a Capsule Suspension formulation and comply with the current and relevant FAO requirements for a CS product except for the lacking evidence on explosive and oxidising properties.

FMC: The product 'FMC-Clomazone 360 CS' is a capsule suspension (CS). The appearance of the product is that of an opaque brown liquid with a slight chemical odour. It has no oxidising properties. It has an auto-ignition temperature of 392^{o}C. The product is not considered to be flammable. Both, the 1 % aqueous dilution and the neat formulation have a pH value of 8.99. The viscosity is dependent on shear rate. Hence, the product is a non-Newtonian liquid. The surface tension is 43.5 and 50.4 mN/m for the product and dilution, respectively. The product is therefore considered surface active. The formulation proved to be stable for 14 days at 54^{o}C and after freeze/thaw storage. A shelf life study is awaiting submission in 2017. The technical characteristics of "FMC-Clomazone 360 CS" are acceptable for a capsule suspension formulation except for the lacking evidence on explosive properties and storage at ambient temperature.

2.3 DATA ON APPLICATION AND EFFICACY

2.3.1 Summary of effectiveness

Clomazone can be applied pre-emergence in a wide range of crops and is active on a wide range of broadleaved and grass weeds.

2.3.2 Summary of information on the development of resistance

Worldwide only 2 cases of resistance against herbicides of class F4 to which clomazone belongs are recorded, one in the USA and one in Australia.In Europe no case of clomazone resistance has been found so far. Risk of resistance to clomazone developing in the weed flora is considered low.

2.3.3 Summary of adverse effects on treated crops

Clomazone can cause bleaching on treated crops but these symptoms are temporary and rarely result in loss of plants or yield losses. In tolerant crops such as oilseed rape clomazone is absorbed by roots and shoots, but the acropetal translocation is reduced and the compound is rapidly metabolized to non-herbicidal active forms by oxidation, hydroxylation and conjugation processes. In case of failure of crops treated with clomazone waiting periods must be respected to avoid damage to the following crop.

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

Not relevant.

2.4 FURTHER INFORMATION

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

Handling and storage:

Clomazone

Additional hazards when processed:	Ensure good ventilation of the work station.
Precautions for safe handling:	Avoid contact with skin and eyes. Smoking is forbidden. Do not breathe vapours.
Hygiene measures:	Always wash hands after handling the product. Do not drink, eat or smoke in the workplace.
Storage conditions:	Store in a cool, well-ventilated place. Protect from moisture. Keep away from sources of ignition. Keep out of the reach of children. Keep away from food, drink and animal feeding stuffs. To maintain quality, maximum storage temperatures should not exceed 55°C.
Packaging materials:	Original packaging.

'FMC-Clomazone 360 CS'

Additional hazards when processed:	Vapour extraction. Avoid any direct contact with the product. Work in a well-ventilated area.
Hygiene measures:	Always wash hands after handling the product. Do not drink, eat or smoke in the workplace. Always take a shower after work. Separate working clothes from town clothes. Launder separately. Do not eat, drink or smoke when using this product.
Storage conditions:	Store in a cool, well-ventilated place. Protect from freezing. Keep out of the reach of children. Keep away from food, drink and animal feeding stuffs.
Packaging materials:	Original packaging.

Transport

Clomazone

UN-No (ADR, IMDG, IATA):	3082
Transport document description:	UN 3082 ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (Clomazone (81777-89-1)), 9, III, (E)
Transport hazard class:	9
Packaging group (ADR, IMDG, IATA):	III

'FMC-Clomazone 360 CS'

'FMC-Clomazone 360 CS' is not regulated for transport.

2.4.2 Summary of procedures for destruction or decontamination

Accidental release measures

Clomazone

Emergency procedures:	Avoid contact with skin and eyes Do not breathe vapours Do not smoke.
Protective equipment:	In case of important spillage: Do not attempt to take action without suitable protective equipment.
Environmental precautions:	Do not allow product to spread into the environment Contain the spilled material by bunding (product is hazardous for the environment).

Methods and material for containment and cleaning up

For containment:	Recover the product with absorbent material.
Methods for cleaning up:	Clean and neutralize spill area, tools and equipment by washing with bleach, soap and water.
Other information:	Dispose of in accordance with relevant local regulations.

'FMC-Clomazone 360 CS'

Emergency procedures:	Avoid contact with skin and eyes Do not breathe vapours Do not smoke.
Protective equipment:	Do not attempt to take action without suitable protective equipment.
Environmental precautions:	Do not allow product to spread into the environment Contain the spilled material by bunding (product is hazardous for the environment).

Methods and material for containment and cleaning up

For containment:	Liquid spill: take up in sand, earth, vermiculite.
Methods for cleaning up:	Clean and neutralize spill area, tools and equipment by washing with bleach, soap and water.
Other information:	Clean and neutralize spill area, tools and equipment by washing with bleach, soap and water Absorb rinsate and add to the collected waste. Waste must be classified and labelled prior to recycling or disposal.

2.4.3 Summary of emergency measures in case of an accident

Clomazone

First-aid measures after inhalation:	Move the affected person to the fresh air. If the person feels unwell: Call a doctor.
First-aid measures after skin contact:	Remove all contaminated clothing and footwear. Wash with soapy water.
First-aid measures after eye contact:	Rinse immediately with plenty of water Consult an ophthalmologist if irritation persists.
First-aid measures after ingestion:	If the person is fully conscious, make him/her drink plenty of water. Never give an unconscious person anything to drink. If the person is fully conscious, try to induce vomiting. Consult a doctor/medical service.

'FMC-Clomazone 360 CS'

First-aid measures after inhalation:	Move the affected person to the fresh air In the event of coughing and slight breathlessness: Call a doctor.
First-aid measures after skin contact:	Remove all contaminated clothing and footwear. Wash with soapy water.
First-aid measures after eye contact:	Rinse immediately with plenty of water for 15 minutes. If irritation persists, consult an eye specialist.

First-aid measures after ingestion: Rinse mouth out with water. If the person is fully conscious, make him/her drink plenty of water. Never give an unconscious person anything to drink. Ask for medical advice.

2.5 METHODS OF ANALYSIS

2.5.1 Methods used for the generation of pre-authorisation data

Technical material and formulations

Task force Oxon, Albaugh, Sapec and Task force FMC Chemical, sprl and ADAMA Agan Ltd have submitted data to show that the described methods to analyze clomazone in the technical material and formulations are validated according to SANCO/3030/99 rev. 4. Both the total and the free content of clomazone were determined in the two representative products (capsule suspensions).

Methods for risk assessment

Task force FMC Chemical, sprl and ADAMA Agan Ltd submitted a method used in the stability and homogeneity test with clomazone technical in experimental diet. LOQ is 100ppm. Specificity was not determined. The method was however considered fit for purpose.

Task force FMC Chemical, sprl and ADAMA Agan Ltd and Task force Oxon, Albaugh, Sapec submitted methods which were used in the physical and chemical properties tests. All methods were considered fit for purpose.

Residues
All the methods used for the generation of pre-authorisation data for clomazone in potatoes and oilseed rape are validated according to SANCO/3029/99. LOQ in all methods is 0.01 mg/kg. After clean-up resides were determined with LC-MS or GC-MS.

2.5.2 Methods for post control and monitoring purposes

Residues
Task force FMC Chemical, sprl and ADAMA Agan Ltd has submitted data showing that multi-method DFG S19 was independent validated for the determination of clomazone in potatoes and oilseed rape according to SANCO/825/00 rev.1.

Task force Oxon, Albaugh, Sapec has submitted data showing that multi-method QuEChERS was independent validated for the determination of clomazone in potatoes and oilseed rape according to SANCO/825/00 rev.1.

For both methods is LOQ 0.01 mg/kg in both matrices and LC-MS/MS is used for the determination of residues. The methods have also been independent validated for matrices with high acid content, matrices with high water content and dry matrices.

Soil and water
Task force FMC Chemical, sprl and ADAMA Agan Ltd submitted two methods for the determination of clomazone in soil. The data showed that both methods were validated according to SANCO/825/00 rev. 8.1. LOQ was 0.005 mg/kg which is below the LC_{50} for the most sensitive soil living organism. The task force submitted a study and a validation study for a method for determination of clomazone in water. The established method fulfils the requirements of SANCO/825/00 rev.8.1 and is suitable for monitoring of residues of clomazone in water. The limit of quantification was established at 0.1 µg/L.

Task force Oxon, Albaugh, Sapec also submitted a method for the determination of clomazone in soil. The data showed that the method was validated according to SANCO/825/00 rev. 8.1. LOQ was 0.01 mg/kg. The task force submitted a study and a validation study for a method for determination of clomazone in water. The established method fulfils the requirements of SANCO/825/00 rev.8.1 and is suitable for monitoring of residues of clomazone in water. The limit of quantification was established at 0.05 µg/L.

Air
Task force FMC Chemical, sprl and ADAMA Agan Ltd submitted two methods for the determination of clomazone in air. The data showed that both methods were validated according to SANCO/825/00 rev. 8.1. LOQ was below the calculated LOQmax.

Task force Oxon, Albaugh, Sapec also submitted a method for the determination of clomazone in air. The data showed that the method was validated according to SANCO/825/00 rev. 8.1. LOQ was below the calculated LOQmax.

Body fluids and tissue
Task force FMC Chemical, sprl and ADAMA Agan Ltd submitted a method for the determination of clomazone in body fluids. The method was validated according to SANCO/825/00 rev. 8.1 in bovine blood and human urine. LOQ of the method was 0.01 mg/L. For tissue, a reference was made to a

primary method for food of animal origin. This method was validated in liver, kidney and muscle and LOQ was 0.01 mg/kg for all matrices.

Task force Oxon, Albaugh, Sapec did not submit any method for body fluids or tissue.

2.6 EFFECTS ON HUMAN AND ANIMAL HEALTH

2.6.1 Summary of absorption, distribution, metabolism and excretion in mammals *[equivalent to section 9 of the CLH report template]*

Table 9: Summary table of toxicokinetic studies

Method	Results	Remarks	Reference
Single oral gavage high dose of 50 mg/kg [^{14}C]-methylene-clomazone (4 male and 4 female Sprague Dawley rats) Purity: Not stated for unlabelled clomazone 99.3 % for 14C-methylene labelled clomazone (radiochemical purity, specific activity: 26.81 mCi/mM) Batch no.: E710-97b	Excretion ~94% after 168 hours. The majority of the radioactivity excreted within 24 hours in urine and faeces with renal/faeces ratios of 74/19. No accumulation or sex-linked differences in metabolism and elimination. The kidneys were the predominant excretion organs.	The study is a non-guideline and non-GLP study. The principles of the method used are similar to OECD TG 417 (2010). The study is considered to contribute to the overall picture of the ADME of clomazone. Although all end-points aren't covered, the study is considered acceptable.	[redacted] 1983 P-0682
Single oral gavage high dose of 50 mg/kg [^{14}C]-carbonyl-clomazone (5 male Sprague Dawley rats) and 50 plus 500 (2×) plus 1000 (2×) mg/kg [^{14}C]-carbonyl-clomazone (1 male Sprague Dawley rats) Purity: Not stated for unlabelled clomazone 99.1 % for 14C-carbonyl labelled clomazone (radiochemical purity) Batch no.: E710-97b	Absorption and excretion almost complete ~97% after 168 hours. The majority of the radioactivity was excreted within 24 hours in urine and faeces with renal / faeces ratios of 62/35. No potential for accumulation. The kidneys were the predominant excretion organs. 500 mg/kg bw had no significant impact on the excretion pattern but 1000 mg / kg bw resulted in delayed excretion (rise in radioactive residues in the 24-48h urine fraction).	The study is a non-guideline and non-GLP study. The first part is similar to OECD TG 417 (2010), while the second part cannot be considered according to guideline, but the study does provide some information on absorption, metabolism and distribution. The study is considered acceptable.	[redacted] 1983 P-0683
Single oral gavage high dose of 50 mg/kg [^{14}C]-methylene-and [^{14}C]-carbonyl-clomazone (4 male and 4 female Sprague Dawley rats) Purity: Not stated for unlabelled clomazone 99.3 % (radiochemical) for 14C-methylene labelled clomazone and 14C-carbonyl labelled clomazone Batch no.: E710-976	Extensive metabolisation of clomazone. Clomazone and 11 metabolites were identified in excreta. The metabolites were hydroxylated derivatives of the parent compound, mono-, di- and trihydroxylated metabolites, and additional metabolites were formed by oxidation and opening of the heterocyclic ring	The study is a non-guideline and non-GLP study. The principles of the main method used are similar to OECD TG 417 (2010). The study is considered to contribute to the overall picture of the ADME of clomazone. The study is considered acceptable.	[redacted] 1984 P-0897
Single and repeated oral gavage low dose of 5 mg/kg, single high dose of 900 mg/kg and i.v.	Rapid and complete absorption ~ 87% low dose and ~100% high dose. Very low residue levels	The study is a non-guideline and non-GLP study. The	[redacted] 1984 PC-0017

Method	Results	Remarks	Reference
dose of 3 mg/kg [^{14}C]-methylene-clomazone (5 male and 5 female Sprague Dawley rats in each group) Purity: 99 % (reported) for unlabelled clomazone 99.8 % (radiochemical) for 14C-methylene labelled clomazone. Batch no.: E710-976	were observed in tissues and organs after 7 days except at the high dose. ~70% were excreted in urine and ~30% in faeces. 15 metabolites were identified in excreta and practically no parent compound. Low potential for accumulation. Elimination was complete and reached ~100% after 7 days. Repeated dosing did not significantly change the absorption, elimination and distribution of parent compound	methods used are similar to OECD TG 417 (2010). The study is considered to contribute to the overall picture of the ADME of clomazone. The study is acceptable.	
Single and repeated oral gavage low dose of 5 mg/kg, single high dose of 900 mg/kg and i.v. dose of 3 mg/kg [^{14}C]-methylene-clomazone (5 male and 5 female Sprague Dawley rats in each group) Purity: Not stated for unlabelled clomazone 99.8 % (radiochemical) for 14C-methylene labelled clomazone. Batch no.: E710-976	See above	The study is a continuation of the previous study.	[redacted] 1984 P-0898
Blood level of radioactivity following a single oral dose of radiolabelled FMC 57020 to 4 female rats Batch No.: not stated Purity: unlabelled: 99% (reported), labelled: 99.8% (analytical)	Radioactivity in blood was rapidly increased with t_{max} of 2.5 to 4 hours and 5 to 8 hours in single and multiple low dose groups, respectively. Clomazone was readily bioavailable. Evidence of some degree of enterohepatic circulation. No evidence of accumulation.	It is not possible to see if the absorption peaks at 8 h for the repeated dose, as the first data point thereafter is at 24h.	[redacted] 1984 P-4013
Position Paper: Clomazone pharmacokinetics in rats including estimated fraction of dose absorbed following oral administration	The position paper summarises the available toxicokinetic information in the rat and supports the adequacy of available data. It is confirmed that the results of the submitted *in vivo* rat metabolism studies are sufficient for evaluation of pharmacokinetic behaviour of clomazone. It is concluded, that no new pharmacokinetic study with an oral versus intravenous administration of test substance is necessary. Based on the available data high bioavailability of clomazone *via* the oral route was concluded and relevant pharmacokinetic parameters including t_{max}, C_{max} and AUC were established.	It is not possible to see if the absorption peaks at 8 h for the repeated dose, as the first data point thereafter is at 24h.	Chandrasekaran, A., 2016
In vitro metabolism of [^{14}C]clomazone in cryopreserved hepatocytes from	The *in vitro* metabolite profiles among rat, dog and human in liver microsomes and in	No metabolites are considered unique to humans.	Shen, L. 2015 R-2937

Method	Results	Remarks	Reference
rats and humans Batch/ Lot no.: CFQ40897 Active ingredient content: 98.4%	hepatocytes were qualitatively similar in all three species. Clomazone was more extensively metabolized by rat liver microsomes than dogs and humans. 5-Hydroxy clomazone was the major metabolite in liver microsomes of all species, and the glucuronide conjugate was also observed in all species. 5-keto clomazone hydrate appeared to be the major metabolite in the hepatocytes of all three species, and as seen in microsomes, glucuronide conjugates of 5-hydroxy clomazone were present in all species. The minor metabolites formed in human hepatocytes were also observed in either rat or dog. Hydroxymethyl clomazone was observed in small amounts in human hepatocytes only; however, in an *in vivo* study ([redacted] (1984), refer to CA 5.1.1/c) this metabolite was shown to be formed and excreted as a conjugate in rat urine following oral administration of radio-labelled clomazone. Thus, there was no unique human metabolite detected in liver microsomes or hepatocytes.		

2.6.1.1 Short summary and overall relevance of the provided toxicokinetic information on the proposed classification(s)

Absorption
Clomazone was rapidly and extensively absorbed after oral administration in rats. Peak blood concentrations were seen after 2.5-7.25 hours post dosing. Absorption rates of 87% after low dosing and up till 100% after high dosing were observed. The extent of absorption after oral administration may be considered as complete.

Distribution
Tissue residue distribution was detected 7 days post dosing. Residual tissue levels were generally very low (0-61 µg/kg) after oral low dose (5 mg/kg b.w.) and medium dose (50 mg/kg b.w.) in rats. The highest residues were found in liver, kidneys and blood, hair and carcass. The distribution was similar after single and repeated doses. In contrast, the residual tissue levels observed after administration of an oral high dose (900 mg/kg b.w.) were higher in the liver (up to 2336 µg/kg), kidney (up to 1728 µg/kg), lung (up to 354 µg/kg), blood (up to 2382 µg/kg), hair (up to 16446 µg/kg) and carcass (up to 6524 µg/kg).
Metabolism
Clomazone was almost completely metabolised indicated by the absence of non-metabolised parent compound and the presence of a total of 15 metabolites identified in urine or feces. Extensive first pass metabolism after oral administration seems to be the case. The six predominant metabolites were FMC 60217, FMC 83918, FMC 87010, FMC 87009, FMC 87008 and FMC 87011. The observed metabolites were similar, qualitatively, both in urine and feces in all four dosing groups in Report B.6.1.1/04, but

not quantitatively. After repeated dosing the amounts of three metabolites was significantly increased indicating development of an enzyme inducing activity on mixed function oxidase (MFO). The shorter half-life determined in study B.6.1.1/06 also indicate some enzyme induction after repeated exposure. The metabolites were hydroxylated derivatives of the parent compound, mono-, di- and trihydroxylated metabolites, and additional metabolites were formed by oxidation and opening of the 3-isoxazolidone (heterocyclic) ring.
The *in vitro* metabolism in human microsomes and hepatocytes was not as extensive as the equivalent in rats and dogs. No metabolites unique to humans were observed.

Elimination
The elimination of clomazone and its metabolites was fast and complete with a cumulative excretion value close to 100% after 7 days but the majority of the excretion occurred within the first two days. About 70% was excreted in urine and approximately 30% in feces. Elimination via expired air was negligible (0.01% of administered dose). The potential for accumulation of clomazone is low. The level of the parent compound found in urine and faeces was very low and metabolites were excreted as free (i.e. non-conjugated) and as conjugates.
The 14-day repeated dosing did not have significant influence on absorption, elimination, distribution of parent compound and metabolites in tissues. Cumulative excretion was complete within 7 days post administration, with a slight shift towards increased urinary excretion compared to the single dose group.

In general some minor variances in rate and extent of absorption, biotransformation and excretion may occur which could be attributed to sex and/or size of administered dose.

The data requirements are considered fulfilled.
See the RAR vol. 3, section B6.1 for details.

2.6.2 Summary of acute toxicity

2.6.2.1 Acute toxicity - oral route [equivalent to section 10.1 of the CLH report template]

Table 10: Summary table of animal studies on acute oral toxicity

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Value LD_{50}**	**Reference**
Acute oral toxicity study, OECD 401 (1981), No deviations, Acceptable	Male and female Sprague Dawley rats, 10/sex/dose group	Clomazone technical Purity: 88.8% Batch no.: E1756-146	381, 704, 864, 1060, 1174, 1300, 2400 mg/kg bw for females and 1300, 1595, 1766, 1956, 2167, 2400 mg/kg bw for males The endpoint is recalculated based on a purity of 88.8%	LD_{50} ($_{females}$): 1216 mg/kg bw	[redacted] 1982 A82-709
Acute oral toxicity study, OECD 401	Male and female Sprague Dawley rats,	Clomazone technical	1200, 1500, 2000, 2500 mg/kg bw for	LD_{50} ($_{females}$): 1461 mg/kg bw	[redacted] 1984 A84-1270

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Value LD_{50}	Reference
(1981), No deviations, Acceptable	10/sex/dose group	Purity: 93.4% Batch no.: E3376-112	females 1500, 2000, 2500, 3000 mg/kg bw for males The endpoint is recalculated based on a purity of 93.4%		
Acute oral toxicity up and down procedure, OECD 425 (2001), Water was withheld during fasting and fasting lasted up to five hours after test substance administration, Acceptable	Female Sprague-Dawley CD (Crl:CD® (SD) IGS BR), 3/dose group	Clomazone technical Purity: 98.2 % Batch no.: C1212	430 and 1370 mg/kg bw The endpoint is recalculated based on a batch purity of 98.2%	$LD_{50(females)}$ = 754 mg/kg bw	[redacted] 2007 0545/0573
Acute-Toxic-Class (ATC) test method, OECD 423 (2001), No deviations, Acceptable	Female Crl: CD(SD), 3/dose group	Clomazone technical Purity: 96.6% Batch no: D-20071015-4	300 and 2000 mg/kg bw The endpoint is recalculated based on the purity of 96.6%	290 < $LD_{50(females)}$ < 1932 mg/kg bw	[redacted] 2009 23497

2.6.2.1.1 Short summary and overall relevance of the provided information on acute oral toxicity

In the previous EU review two studies were available for evaluation of the oral LD_{50}-value in Sprague Dawley rats. Although the OECD TG 401 (1987) was rescinded in 2002 the studies are acceptable as they were conducted before 2002. The two LD_{50}-values were recalculated to be 1216 mg/kg bw ([redacted], 1982a) and 1461 mg/kg bw ([redacted] 1984). Female rats were more sensitive to clomazone than male rats. Further two studies were submitted in the supplementary dossier. The study ([redacted], 2007) is GLP compliant and performed according to OECD TG 425 (2001). The LD_{50} was estimated to be 754 mg/kg bw. The study ([redacted], 2009) is also GLP compliant, and the study is performed according to OECD TG 423/EU method B.1 tris (2004/73/EC). The LD_{50} is between 300 and 2000 mg/kg bw. The technical Clomazone with highest purity (98.2%) revealed the lowest LD_{50} value (754 mg/kg bw). However, all the tested technical Clomazone resulted in LD_{50} values of the same range resulting in CLP classification as category 4. The low purity (and theoretical effect from impurities) technical Clomazone does not seem to affect classification.
The lowest LD_{50} (754 mg/kg bw) is proposed as the ATE value for CLP classification of mixtures.
See the RAR vol. 3, section B6.2.1 for details.

2.6.2.1.2 Comparison with the CLP criteria regarding acute oral toxicity

All reported LD_{50} values for acute oral toxicity are within the range of 300<ATE≤2000 mg/kg bw corresponding to classification in Category 4.

2.6.2.1.3 Conclusion on classification and labelling for acute oral toxicity

Proposed classification and labelling: Acute tox 4, H302 harmful if swallowed, ATE=754 mg/kg bw

2.6.2.2 Acute toxicity - dermal route [equivalent to section 10.2 of the CLH report template]

Table 11: Summary table of animal studies on acute dermal toxicity

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Value LD_{50}**	**Reference**
Acute dermal toxicity limit test, OECD 402, Acceptable	New Zealand white rabbit, 10/sex/dose group	Clomazone technical Purity: 88.8 % Batch no.: E1756-146	2000 mg/kg bw for 24h	LD50 (combined) > 2000 mg/kg bw	[redacted] 1982 A82-710

2.6.2.2.1 Short summary and overall relevance of the provided information on acute dermal toxicity

One study was available for evaluation of the dermal toxicity at the last EU review. The acute dermal toxicity of clomazone is low with no systemic or local signs of toxicity being recorded after application of 2000 mg/kg bw to male or female New Zealand white rabbits. The conduct of the study is comparable to OECD TG 402 with the exception of the abrasion of the test site. However, the study is acceptable because of the negative result since an abrasion of the skin will only increase the dermal uptake. For the renewal three additional studies were submitted by CATF. The studies have previously been evaluated for data matching and they indicated no change of the EU agreed end-point. The studies are not to be assessed in this RAR (if necessary, see the RAR vol. 2. for the references).
See the RAR vol. 3, section B6.2.2 for details.

2.6.2.2.2 Comparison with the CLP criteria regarding acute dermal toxicity

The available LD_{50} exceeds the upper limit value for classification for acute dermal toxicity of 2000 mg/kg bw.
The substance does not meet the criteria for classification for acute dermal toxicity.

2.6.2.2.3 Conclusion on classification and labelling for acute dermal toxicity

No classification is proposed.

2.6.2.3 Acute toxicity - inhalation route [equivalent to section 10.3 of the CLH report template]

Table 12: Summary table of animal studies on acute inhalation toxicity

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, form and particle size (MMAD)**	**Dose levels, duration of exposure**	**Value LC_{50}**	**Reference**
Acute inhalation toxicity, OECD 403 (1981), No justification of the use of whole-body system, Acceptable	Albino rats (Crl:CD), 5/sex/dose group	Clomazone technical, aerosol, 2.20 µm ± 1.72 µm Purity:88.8% Batch no: E1756-	0, 1.74, 3.67, 5.15, and 6.15 mg/L air for 4 hours (whole-body exposure system)	$LC_{50\ (combined)}$ = 4.3 mg/L	[redacted] 1982 420-0939

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
		146	The result has been recalculated based on a purity of 88.8%		

2.6.2.3.1 Short summary and overall relevance of the provided information on acute inhalation toxicity

One study [redacted] 1982) submitted by the previous notifier was evaluated in the DAR (2005). The acute toxicity after inhalation exposure in albino rats is moderate. Numerous clinical signs were seen in treated animals: damp fur, irregular breathing, crusty muzzle, crusty eye, nasal discharge, prostration, salivation, crusty nose, red stained fur, ataxia, opacity of the eye, exophthalmus (abnormal protrusion of the eyeball), alopecia, yellow/brown stained fur, and poor coat quality. Untreated control animals showed crusty nose and crusty muzzle. No control animals died.
The LC_{50}-value was 4.3 mg/L (combined sexes, recalculated to account for purity of the active substance) and there were no sex-related responses. The study was performed in accordance with OECD-Guideline 403 (1981) and was acceptable although the study report did not state the purity; the test article came from the same batch, E1756-146 purity 88.8%, used in the acute oral and dermal toxicity study. For the renewal two additional studies were submitted by the CATF. The studies have previously been evaluated for data matching and they indicated no change of the EU agreed end-point. The studies are not to be assessed in this RAR (if necessary, see the RAR vol. 2. for the references).

See the RAR vol. 3, section B6.2.3 for details.

2.6.2.3.2 Comparison with the CLP criteria regarding acute inhalation toxicity

The reported LC_{50} for acute inhalation toxicity is within the range $1.0<ATE\leq5.0$ mg/L, corresponding to classification in category 4.

2.6.2.3.3 Conclusion on classification and labelling for acute inhalation toxicity

Proposed classification and labelling: Acute tox 4, H332 harmful if inhaled, ATE=4.3 mg/L

2.6.2.4 Skin corrosion/irritation [equivalent to section 10.4 of the CLH report template]

Table 13: Summary table of animal studies on skin corrosion/irritation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results - Observations and time point of onset[2] - Mean scores/animal - Reversibility	Reference
Acute skin irritation, OECD 404 (1992), No deviations, Acceptable	New Zealand white rabbits, 3 males/dose group	Clomazone technical Purity: 89.4% Batch no.: PL97-1113	0.5 ml undiluted clomazone, 4 hours under semi-occlusive dressing	In one animal very slight erythema persisted up to day 6 and in another animal the very slight erythema persisted up to day 8. Dryness of the skin was recorded in these two animals from day 7 to 8 and from day 7 to 11, respectively. The overall average Draize scores for erythema was 0.7 and for oedema 0, which indicates very low skin irritation potential.	[redacted] 1999 18094 TAL

Acute skin irritation, OECD 404 (1981), Deviations: Extended exposure period (24 h instead of 4 h), no observation performed at 48 hours, supportive	New Zealand white rabbits, 4 males and 2 females	Clomazone technical Purity: 88.8% Batch no.: E1756-146	0,5 ml undiluted clomazone, 24-hour exposure period	Very slight erythema occurred in both abraded (4/12) and intact skin (3/12) sites in the rabbits 24 hours after application. The erythema had disappeared at all test sites 72 hours after application. Differences between abraded and intact skin sites were very small. No oedema was observed at 24 hour or 72 hours after application.	[redacted] 1982 A82-712
Acute skin irritation OECD 404 (2002), No deviations	New Zealand white rabbits, 3 males/dose group	Clomazone technical Purity: 98.3% Batch no.: ALBEU/090511-3	0.5 g clomazone moistened in purified water, 4-hour semi-occlusive application	Very slight (barely perceptible) to well-defined erythema was observed on the treated skin of all animals at the 1-hour observation after removal of the dressing, and persisted as very slight up to the 24-hour reading (animal No. 62) or 48-hour reading (animal No. 61) after patch removal. No abnormal findings were observed on the treated skin of any animal 72 hours after treatment. The mean erythema/eschar score was 0.33 and the oedema score was 0.00 for all animals.	[redacted] 2010 C95077

2.6.2.4.1 Short summary and overall relevance of the provided information on skin corrosion/irritation

Two skin irritation studies submitted by the previous notifier were evaluated in the DAR (2005). Clomazone was found to be a non-irritant to the skin of rabbits following 4-hour exposure under semi-occlusion in a study performed in accordance with OECD TG 404 ([redacted] 1999). Application of undiluted clomazone for 24 hours led to minimal irritation to rabbit skin in the study by ([redacted] The study by [redacted] was not GLP and not according to the then and now current OECD TG 404 (1992 & 2002). A recent study ([redacted] 2010) was submitted for the renewal by a new notifier (OAS). The study is GLP compliant and according to the above mentioned OECD guideline. Clomazone technical is a mild skin irritant.
For the renewal three additional studies were submitted by the CATF. The studies have previously been evaluated for data matching and they indicated no change of the EU agreed end-point. The studies are not to be assessed in this RAR (if necessary, see the RAR vol. 2. for the references).

2.6.2.4.2 Comparison with the CLP criteria regarding skin corrosion/irritation

Clomazone is not considered a corrosive substance as it does not produce destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least 1 tested animal after exposure for 4 hours (Category 1). Neither is it considered a skin irritant as the mean value for erythema and oedema formation is lower than the 2.3 in at least 2 of 3 tested animals from gradings at 24, 48 and 72 hours after patch removal (Category 2). Likewise, no inflammation lasted for 14 days in at least 2 animals and no single animal had a very definite positive effect. The substance does not meet the criteria for classification for skin corrosion/irritation.
See RAR, vol. 3, section B6.2.4 for details.

2.6.2.4.3 Conclusion on classification and labelling for skin corrosion/irritation

No classification is proposed.

2.6.2.5 Serious eye damage/eye irritation [equivalent to section 10.5 of the CLH report template]

Table 14: Summary table of animal studies on serious eye damage/eye irritation

Method, guideline, deviations[1] if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Results** **- Observations and time point of onset[2]** **- Mean scores/animal** **- Reversibility**	**Reference**
Acute eye irritation, OECD 405 (1981), No deviations, Acceptable	New Zealand white rabbits, 9 animals (4 male and 5 female)	Clomazone technical Purity: 88.6 % Batch no.: E1756-146	0.1 ml of undiluted clomazone, The eyes of six rabbits remained unwashed, while the eyes of three rabbits were rinsed 20 to 30 seconds after instillation	In all animals, which eyes were not rinsed, redness of the conjunctiva was observed one hour after treatment. In one animal, with eyes rinsed after instillation, showed also redness of the conjunctiva one hour after treatment. The eyes of all animals appeared normal within 24 h. The overall mean scores for clomazone in rabbits which eyes were rinsed after instillation was 0 for all scoring parameters. In the 6 animals which eyes were not rinsed after instillation the overall mean scores (24h, 48h and 72 h) for all scoring parameters were also 0.	[redacted] 1982 A82-711

2.6.2.5.1 Short summary and overall relevance of the provided information on serious eye damage/eye irritation

One study submitted by the previous notifier was evaluated in the DAR (2005). Clomazone was a non-irritant to the ocular tissues of the New Zealand White rabbit eye according to the EEC Ocular Evaluation Criteria. The study performed in rabbits was performed according to OECD TG 405. See Table 14 for a summary of the results. See the RAR, vol. 3, section B.6.2.5 for details.

For the renewal three studies were submitted by CATF. The studies have previously been evaluated for data matching and they indicated no change of the EU agreed end-point. The studies are not to be assessed in this RAR (if necessary, see the RAR vol. 2. for the references).

2.6.2.5.2 Comparison with the CLP criteria regarding serious eye damage/eye irritation

Clomazone does not have the potential to seriously damage the eyes as it does not produce irreversible effects on the eye (Category 1). Neither does clomazone induce reversible eye irritation (Category 2) as scores were 0 in all parameters at 24, 48 and 72 hours..

2.6.2.5.3 Conclusion on classification and labelling for serious eye damage/eye irritation

The substance does not meet the criteria for classification for serious eye damage/eye irritation. No classification is proposed.

2.6.2.6 Respiratory sensitisation [equivalent to section 10.6 of the CLH report template]

No animal data are available.

Health investigations of workers at the manufacturing sites are performed routinely and reported (confidential information in the RAR vol 4.).

2.6.2.6.1 Short summary and overall relevance of the provided information on respiratory sensitisation

No repeated dose inhalation studies or other relevant animal data are available.

However, medical surveillance data are available. No respiratory sensitisation was observed in the workers at two different manufacturing sites. Each manufacturing plant employed 20-60 workers a year (see confidential RAR, vol. 4). Clomazone is not a skin sensitiser.

Data indicates that Clomazone is not a respiratory sensitiser.

2.6.2.6.2 Comparison with the CLP criteria regarding respiratory sensitisation

There are no animal data. The data from medical surveillance shows there is no evidence in humans that clomazone can lead to specific respiratory hypersensitivity.

2.6.2.6.3 Conclusion on classification and labelling for respiratory sensitisation

The substance does not meet the criteria for classification for respiratory sensitisation.

2.6.2.7 Skin sensitisation [equivalent to section 10.7 of the CLH report template]

Table 15: Summary table of animal studies on skin sensitisation

Method, guideline, deviations[1] if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Results**	**Reference**
Skin sensitisation – Buehler method, OECD 406 (1992), Deviations: no vehicle control group was investigated, only 10 instead of 20 animals were treated with the test substance, and the test should usually be conducted at the highest possible test concentration producing a mild but not excessive irritation, Supportive	Hartley guinea pigs, Two groups (test and control) of each 10 male animals	Clomazone technical Purity: 88.8% Batch no.: E1756-146	0.5 ml of undiluted clomazone technical	No skin reactions and no incidence of erythema or oedema were observed in test group animals neither after the induction applications nor upon challenge.	[redacted] 1982 A82-713

Method, guideline, deviations[1] if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
Skin sensitisation – Maximisation test, OECD guideline no. 406 (1992), No deviations	Hartley guinea pigs, 20 test animals and 10 in challenge control	Clomazone technical Purity: 96.5% Batch no.: G1149:118A	Intradermal induction: 5% w/v clomazone. Topical induction: 100 % test substance Topical challenge: 100 %. Topical rechallenge: 50 and 25%. Second topical rechallenge: 10 and 5% clomazone	Following challenge with 100% clomazone dermal scores of 1 (slight but confluent or moderate patchy erythema) were observed in 5/20 (25%) of test animals and 3/10 (30%) in challenge controls at 24 hours. At the 48 hours scoring interval 3/20 (15%) test animals and 1/10 (10%) challenge controls had dermal scores of 1. Following rechallenge with 50% clomazone in propylene glycol, dermal scores of 1 (slight, but confluent or moderate patchy erythema) were observed in 15/20 (75%) of test animals and 8/10 (80%) in rechallenge controls at 24 hours. At the 48 hours scoring interval 1/10 (10%) rechallenge controls had dermal scores of 1. Following rechallenge with 25% clomazone in propylene glycol, dermal scores of 1 (slight but confluent or moderate patchy erythema) were observed in 8/20 (40%) of test animals and 6/10 (60%) in rechallenge controls at 24 hours. At the 48 hours scoring interval 1/20 (5%) of the test animals had dermal scores of 1. Following both challenge and rechallenge a larger part of the control animals reacted with dermal scores of 1 as compared to the test animals both with and without the vehicle propylene glycol and therefore the results must be considered equivocal. At the second rechallenge with 10 % and 5% clomazone in propylene glycol no skin reaction indicative of skin sensitization were seen in test or control animals.	[redacted] 2006 KZH00137
Skin sensitisation – Magnusson & Kligman, OECD Guideline No. 406, No deviations, Acceptable	Albino Dunkin Hartley Guinea Pig, HsdPoc: DH, SPF, 10 male guinea pigs. 5 males in control group.	Clomazone technical Purity: 98.3% Batch no.: ALBEU/090511-3	0.1 mL/site of a 25% dilution of the test item for the intradermal induction, and 0.2 to 0.3 mL of a 50% dilution of the test item on a patch of filter paper for the epidermal induction.	There were no clinical signs of toxicity and body weights were within the normal range. <u>Intradermal induction</u> Expected common findings were observed in the test and control groups after the different injections using FCA intradermally. These findings consisted of erythema, oedema, necrotizing dermatitis, encrustation and exfoliation of encrustation. No detailed description of the skin reactions was given in the report as these FCA effects are well known. <u>Epidermal induction</u> Discrete/patchy to moderate/confluent erythema was observed in all test animals at the 24- and 48-hour readings after treatment with the test item prepared at 50% in PEG 300. No skin reactions were observed in the control animals treated	[redacted] 2010 C95088

Method, guideline, deviations[1] if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
				with PEG 300 alone. Epidermal challenge No skin reactions were observed in the control or test animals treated with PEG 300 alone or with the test item at 10% in	

2.6.2.7.1 Short summary and overall relevance of the provided information on skin sensitisation

Two skin sensitisation studies submitted by the previous notifier were evaluated in the DAR (2005) and final addendum (2007). Undiluted clomazone did not provoke skin sensitisation in a non-adjuvant Buehler test (10 inductions), since it failed to elicit any skin irritation either in induction or challenge ([redacted]. 1982e). The test had several experimental shortcomings such as lack of negative control (the substance was used undiluted), a non-irritating concentration used as induction (100% clomazone elicit no irritation) and a small number of animals tested. The study is considered supportive. In the Maximisation study ([redacted], 2006) irritation effects in control and test animals were seen at challenge and re-challenge, and the results were considered equivocal. At the second rechallenge with 10 % and 5% clomazone in propylene glycol (described as the maximum non-irritating concentration) no skin reaction indicative of skin sensitization were seen in test or control animals. A recent maximisation study ([redacted], 2010) was submitted for the renewal by the OAS. The study is GLP compliant and according to the above mentioned OECD/EC guideline. Clomazone technical did not produce any skin reaction at challenge with 10% clomazone. In conclusion, clomazone technical is not a skin sensitiser.
For the renewal three additional studies were submitted by the CATF. The studies have previously been evaluated for data matching and they indicated no change of the EU agreed end-point. The studies are not to be assessed in this RAR (if necessary, see the RAR vol. 2. for the references).

2.6.2.7.2 Comparison with the CLP criteria regarding skin sensitisation

There are no positive results in appropriate animal tests. Clomazone did not show a high (Sub-category 1 A) or low to moderate (Sub-category 1B) potency in animals, and cannot be presumed to have the potential to produce sensitisation in humans.

2.6.2.7.3 Conclusion on classification and labelling for skin sensitisation

The substance does not meet the criteria for classification for skin sensitisation.

2.6.2.8 Phototoxicity

The submission of such data are not required, since clomazone does not absorb electromagnetic radiation in relevant extent in the range of 290 – 700 nm as verified by the UV/VIS spectrum data for clomazone submitted in Section 2, CA 2.4 of the dossier. Therefore, clomazone is not considered to have photosensitive properties in combination with light.

2.6.2.9 Aspiration hazard [equivalent to section 10.13 of the CLH report template]

No studies available. Clomazone is not an organic solvent.

2.6.2.9.1 Short summary and overall relevance of the provided information on aspiration hazard

No studies available. Clomazone is not an organic solvent.

2.6.2.9.2 Comparison with the CLP criteria regarding aspiration hazard

Clomazone is not an organic solvent.

2.6.2.9.3 Conclusion on classification and labelling for aspiration hazard

No classification proposed.

2.6.2.10 Specific target organ toxicity-single exposure (STOT SE) [equivalent to section 10.11 of the CLH report template]

No studies specific for STOT SE are available. For more detailed data on toxicity after single exposure, please refer to Volume 3, section B.6.2 and B.6.7.

2.6.2.10.1 Short summary and overall relevance of the provided information on specific target organ toxicity – single exposure (STOT SE)

Clomazone is acute toxic by the oral route, with an LD_{50} of 754 mg/kg bw. Clinical signs of toxicity seen in surviving rats or up to death were e.g. decreased locomotion, ataxia, decumbency, chromodacryorrhea, haematuria, hunched posture, lethargy, pilo-erection, decreased respiratory rate, laboured respiration, splayed gait, prostration, dehydration, hypothermia, loss of righting reflex, pallor of the extremities, emaciation, increased lachrymation and ptosis. No consistent effects were seen at necropsy of the acute oral toxicity studies. Findings across studies were green fluid in the bladder and distended stomach, red fluid in the intestines, patchy pallor of the liver. One study did not find any macroscopic abnormalities. In general there were no gross abnormalities upon necropsy of surviving rats, most rats returned to normal and gained body weight.

Clinical signs observed in treated animals of the acute inhalation toxicity study were damp fur, irregular breathing, crusty muzzle, crusty eye, nasal discharge, prostration, salivation, crusty nose, red stained fur, ataxia, opacity of the eye, exophthalmus (abnormal protrusion of the eyeball), alopecia, yellow/brown stained fur, and poor coat quality. Necropsy revealed abnormalities of the lung, eye(s), stomach, liver, kidneys spleen, lymph node and testes in an irregular pattern across dose groups and test and control rats. 15/40 and 24/40 test and control rats, respectively, had no gross findings.

In the repeated dose studies the target organ was the liver and bodyweight. Only from the more recent developmental studies can information on the onset be found (see 2.6.6.2.1). In the rat developmental study [redacted] 2002) statistically significant reduced body weight gain were seen at 500 and 750 mg/kg bw/d with onset two days after dosing had started. Also in the rabbit developmental study ([redacted], 2002) statistically significant reduced body weight gain were seen at 700 mg/kg bw/d.

Health investigations of workers at the manufacturing sites are performed routinely and reported (confidential information in RAR vol 4.). There were no signs of toxicity.

The lack of consistent, severe and/or statistical significant toxicity, organ damage or functional changes does not warrant classification for STOT SE Cat.1 or Cat. 2.

2.6.2.10.2 Comparison with the CLP criteria regarding STOT SE (specific target organ toxicity-single exposure)

Category 1: There were no evidence from human cases or epidemiological studies that clomazone produces non lethal significant specific target organ toxicity following single exposure.
No consistent significant non-leathal toxic effects were observed after a single dose in animals.

Category 2: The effect on bodyweight gain was not considered to indicate significant toxicity. No other non-lethal consistent effects were observed after a single dose in animals.

Category 3:
Respiratory tract irritation: In the acute inhalation toxicity study the only clinical sign relating to the respiratory tract was irregular breathing. However, it is not considered sufficient to classify for respiratory tract irritation.

Narcotic effects: In the acute inhalation toxicity study ataxia was observed. In the acute oral toxicity studies no signs of toxicity observed at non-lethal doses of 300 and 430 mg/kg bw. Only at lethal doses of 1370 and 2000 mg/kg bw severe ataxia, lethargy and/or loss of righting reflex was observed.

Classification with STOT SE cat. 1, 2 or 3 is therefore not warranted.
On the basis of the weight of all evidence available clomazone is not presumed to have the potential to produce significant toxicity (Category 1) or to be harmful to human health following single exposure (Category 2). Neither does Clomazone have the potential to produce transient effects such as respiratory tract irritation or narcotic effects.

2.6.2.10.3 Conclusion on classification and labelling for STOT SE (specific target organ toxicity-single exposure)

No classification is proposed as the substance does not meet the criteria for classification for STOT SE cat 1, 2 or 3.

2.6.3 Summary of repeated dose toxicity (short-term and long-term toxicity) [section 10.12 of the CLH report]

2.6.3.1 Specific target organ toxicity-repeated exposure (STOT RE) [equivalent to section 10.12 of the CLH report template]

Table 16: Summary table of animal studies on repeated dose toxicity (short-term and long-term toxicity) STOT RE (specific target organ toxicity - repeated exposure)

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, route of exposure, dose levels, duration of exposure**	**Results** **- NOAEL/LOAEL** **- target tissue/organ** **- critical effects at the LOAEL**	**Reference**

28-days feeding study (via diet) in rats (CD rats) 10/sex/dose group Range finding Non-guideline but GLP compliant study. No histopathological examinations performed. Hence, only accepted as supportive.	Clomazone technical Purity 87.9% Batch no: E1382-95 0, 2000, 4000, 8000, 16000, 24000 and 50000 ppm corresponding to 0, 200, 400, 800, 1600, 2400, and 5000 mg/kg bw/d	Supporting study from DAR: No NOAELs and LOAELs could be set due to the nature as a range-finding study and since no histopathology is performed. The liver was the target organ indicated by increased absolute and relative weights in both sexes, gross pathology and elevated SGPT as sign of either leaky or damaged and dying liver cells. Mortality, reduced body weights, reduced food consumption and reduced body weight gain, gross pathology changes indicative of liver toxicity, organ weight changes (adrenal, brain, liver, kidney and gonads) and few changes in haematological (lower MVC and elevated blood urea nitrogen) and clinical parameters (increased SGPT). These effects were seen in the four high dose groups.	[redacted], 1982a 410-0743
28-days feeding study (via diet) in mice (CD mice) 10/sex/dose group. Range-finding Non-guideline but GLP compliant study. No histopathological examinations performed. Hence, only accepted as supportive.	Clomazone technical Purity 87.9% Batch no: E1382-95 0, 2000, 4000, 8000, 16000, 24000 and 50000 ppm corresponding to 0, 400, 800, 1600, 4800 and 10000 mg/kg bw/day	Supporting study from DAR: No NOAELs and LOAELs could be set due to the nature as a range-finding study and since no histopathology is performed. The liver was again the target organ as indicated by increased absolute and relative liver weight in both sexes and gross pathology observations. Mortality, reduced body weights, reduced food consumption, changes in organ weights (adrenal, brain, liver, kidney and ovary) and lower serum glucose were observed. Most of the organ weight changes, a change into lower absolute values only, are seen as an effect of reduced final body weight. All animals at 50000 ppm died or were sacrificed up till day 10.	[redacted], 1982b 410-0744

Oral 28-days range-finding study (Beagle dogs)	Clomazone technical Purity 88.8% Batch no.: E1756-146 0, 100, 1000, 5000 and 10000/2500 ppm corresponding to 0, 1.8, 18, 90 and 180 mg/kg bw/day	Supporting study from DAR: No NOAELs and LOAELs could be set due to the nature as a range-finding study and limited study design. Effects were seen predominantly in the two high dose groups: Increased a/r liver weight and hepatocellular swellings. Reductions in red blood cell counts, haemoglobin concentrations and haematocrit and reduced a/r testicular weights. Statistics evaluation is of no relevance due to the number of animals used. The liver was the target organ as indicated by increased absolute and relative liver weight in both sexes and gross pathology observations.	[redacted], 1983 6124-100
28-days oral range-finding study in Wistar rats 6 animals/sex/group OECD 407 (1995) Deviation: There are several parameters (histopathology, haematology, clinical chemistry) that were not investigated and the guideline has been updated in 2008 to include endocrine disrupting end-points. The study is considered supportive.	Clomazone technical Purity 92.9 % Batch: CLMZN(3)-536 0, 500, 1500, 4500 and 9000 ppm corresponding to 0, 47.7, 144.7, 421.8 and 842.8 mg/kg bw/d for males and 50.0, 144.7, 430.9 and 816.0 mg/kg bw/d for females. The endpoints are further recalculated to reflect the purity of 92.9%	NOAEL 134 mg/kg bw/d (1500 ppm) both sexes LOAEL 392 (m)/400 (f) (4500 ppm) Reduced body weight gain in males and increase in relative liver weight in males and females at 4500 ppm.	[redacted], 2000 2838/2000
28-days oral range-finding study in mice (Swiss albino) 6 animals/sex/group OECD TG 407 (1995). There are several parameters (histopathology, haematology, clinical chemistry) that were not investigated and the guideline has been updated in 2008 to include endocrine disrupting end-points. The study is considered supportive.	Clomazone technical Purity 95.0% Batch: D-10103 0, 200, 800, 3200 and 9000 ppm corresponding to 0, 52.4, 211.2, 816.7 and 2182.4 mg/kg bw/d in males and 55.8, 218.6, 887.7 and 2363.8 mg/kg bw/d in females. The endpoints are further recalculated to reflect the purity of 95.0%	NOAEL – (m) /53 (f) mg/kg bw/d (- /200 ppm) LOAEL 50 (m) / 208 (f) mg/kg bw/d (200 (m) / 800 (f) ppm) Effects on body weight gain are seen in all dose groups of the males. Hence the lowest dose group should be considered a LOAEL. The LOAEL is proposed at 200 ppm corresponding to 52.4 mg/kg bw/d in males based on reduced body weight gain at 200, 800, 3200 and 9000 ppm. In females a NOAEL is proposed at 55.8 mg/kg bw/d (200 ppm) based on increased relative and absolute liver weight at 800, 3200 and 9000 ppm.	[redacted]., 2004 3693/03

Oral 90-day study (combined with 24 month chronic study in rats), OECD 408, Deviations: No ophthalmological examinations were performed, serum sodium was not analysed and adrenals were not weighed. Spraque-Dawley rats, 120/sex/dose group Acceptable	Clomazone technical Purity: 88.8% Batch no.: E1756-146 0, 20, 100, 500, 1000, 2000, 4000 and 8000 ppm corresponding to 0, 1.4, 7, 35, 68, 138, 278 and 563 mg/kg bw/day The endpoints are further recalculated to reflect the purity of 88.8%.	NOAEL: 123/145 (2000 ppm) LOAEL: 247/288 The liver was the target organ. In the two high doses statistically significant effect such as increased a/r liver weight, consistently reduced body weight and increased cholesterol after 1, 2 and 3 month were observed. At the high dose statistically significant change in hepatocytes in forms of megalocytosis were observed. See the RAR vol 3 B6 for details: Liver weights at 3 month sacrifice Table B.6.5/01-4.	[redacted] 1984a 410-0816
Oral 90-day study (combined with 24 month chronic study in mice), OECD 408, Deviations: No ophthalmological examinations were performed, serum sodium was not analysed and adrenals were not weighed. CD mice, 120/sex/dose group Acceptable	Clomazone technical Purity: 88.8% Batch no.: E1756-146 0, 20, 100, 500, 1000, 2000, 4000 and 8000 ppm corresponding to 0, 3.8, 19.5, 98, 188, 371, 761 and 1766 mg/kg b.w./day The endpoints are further recalculated to reflect the purity of 88.8%.	NOAEL: 329/464 (2000 ppm) LOAEL: 676/932 In the two high dose groups statistically significant increase in a/r liver weight and in the high dose histopathologic changes in hepatocytes (mild megalocytosis) were observed. The liver was the target organ. See the RAR vol 3 B6 for details: Liver weights at 3 month sacrifice Table B.6.5/02-3	[redacted] 1984b 410-0817

90-days oral study, OECD 408 (1998), Deviations: None, Wistar rats, 10/sex/dose, Acceptable	Clomazone technical Purity: 94% Batch no: CLMZN (4)-536 0, 600, 1200 and 4800 ppm corresponding to 0, 47.7, 92.0, and 377.4 mg/kg bw/d in males and 50.4, 103.8, and 409.0 mg/kg bw/d in females The endpoints are further recalculated to reflect the purity of 94%	NOAEL: 45 / 98 mg/kg bw/d (600/1200 ppm) LOAEL: 88 / 370 mg/kg bw/d The liver and kidney were the target organs. In the mid and high dose groups, statistically significant effects of increased absolute/relative liver weights, consistently reduced body weights and increased cholesterol and creatinine levels were observed. Critical effects were reversible after recovery period. In addition, in the high dose group, statistically significant increased incidences of hyaline droplets in kidney tubular epitheliums in males, and hepatocellular hypertrophy in liver of high dosed females were observed. Both effects were reversible after recovery period. See in the RAR vol 3 B6 for details: Clinical chemistry values in Table B.6.3.2/04-10 and Table B.6.3.2/04-11 Liver weights males in Table B.6.3.2/04-12 Liver and spleen weights females in Table B.6.3.2/04-13 Histopathological findings in liver and kidneys in Table B.6.3.2/04-14	[redacted] 2001 2839/2000

Oral 1-year study, OECD 452, Deviation: None, Beagle dogs, 6/sex/dose group, Acceptable	Clomazone technical 0, 100, 500, 2500 and 7500 (reduced to 5000 ppm on day 8) ppm corresponding to 0, 3, 13, 67, and 147 (5000 ppm) mg/kg b.w./day The endpoints are further recalculated to reflect the purity of 88.8%.	NOAEL: 12 (500 ppm) LOAEL: 59/63 In the two high dose groups: Statistically significant elevated serum cholesterol in both sexes and some inconsistent organ weight changes (a/r liver weight, a/r ovary and relative brain). Sign of transient mild anaemia in the high dose group up till 6 month. The liver was the target organ.	[redacted] 1984 6124-101
2-year rat study	See section 2.6.5 for the details.	NOAEL male/female: 36/49 mg/kg bw/d (1000ppm) LOAEL male/female: 74/98 mg/kg bw/d Relative liver weights were statistically significant increased at the 2000 ppm dose group and with a trend of increasing through all dose groups After two years exposure a non-dose related increase in the number of animals with hepatocytomegaly.	2.6.5
2-year mice study	See section 2.6.5 for the details	NOAEL male/female: 126/79 mg/kg bw/d (1000/500 ppm) LOAEL male/female: 258/162 mg/kg bw/d Liver enlargement and hepatocytomegaly in males at 2000 ppm. Persistent thymic glands in females at 1000 and 2000 ppm	2.6.5
Other studies			
28-days dermal toxicity study (Sprague-Dawley rats) 10/sex/dose group OECD TG 410 (1981). The guideline has not been updated and there were no deviations.	Clomazone technical Purity 92.7% Batch no: PL01-0346 0 and 1000 mg/kg bw/day The endpoints are further recalculated to reflect the purity of 92.7%	NOAEL 927 mg/kg bw/d LOAEL > 927 mg/kg bw/d No adverse systemic toxicity was observed. Minimal skin irritation indicated by epidermal hyperplasia was observed in the dose group. Increased a/r heart weight, reduction in red blood cell counts and decreased phosphate levels, seen at 1000 mg/kg b.w. were only seen in one sex and with no corresponding microscopic findings and are therefore not regarded as adverse effects.	[redacted], 2002 A2001-5436

2.6.3.1.1 Short summary and overall relevance of the provided information on specific target organ toxicity – repeated exposure (short-term and long-term toxicity)

In the three eldest 28 day range finding studies in rats, dogs and mice, the liver was the target organ with increases in absolute and/or relative weights, gross pathological findings (hepatic discoloration, enlargement, hepatocellular hypertrophy) and changes in some of the clinical chemistry parameters being observed in the high-dose groups (increased serum glucose and SGPT). Effects on hematological parameters (slightly lower red blood cell counts, haemoglobin concentrations, haematocrit and neutrophils (males) at the two high doses) were seen in dogs only.

Furthermore, treatment related effects consisting of reduced body weight, body weight gain and food consumption were observed in high-dose rats and mice. Some other organ weight changes (ovary, brain, heart, adrenal, testis and kidney) were observed either in rats, mice or dogs but appearing without consistency, often only in one sex and with no corresponding histopathological findings or reconfirmation of the finding in the 90 days or 1 year studies. In the two eldest 28 days range finding studies all high dose group mice (50000 ppm) died or were sacrificed before day 10 due to severe intoxication and in rats at the same dose (50000 ppm) severe clinical signs including weakness, lethargy, emaciation and death were observed. In dogs the high dose of 10000 ppm was reduced to 2500 ppm because of low palatability, the 5000ppm dose remained unchanged.

Two new 28-day studies were submitted, one rat and one mice range finding study, both are performed according to guideline. In rats the NOAEL is proposed at 1500 ppm corresponding to 144.7 mg/kg bw/d in males and females based on reduced body weight gain in males and increase in relative liver weight in males and females. In mice a LOAEL is proposed at 200 ppm (50 mg/kg bw/d) in males based on reduced body weight gain at 200, 800, 3200 and 9000 ppm. Bodyweight was not affected in female mice. In females a NOAEL is proposed at 200 ppm (53 mg/kg bw/d) because of increased relative and absolute liver weight at the mid, high-intermediate and high dose. Hepatocellular hypertrophy was increased in a dose related manner in the mid, high-intermediate and high dose male and female mice. Reaching statistical significant at the two high doses.

In rats, a NOAEL of 123 mg/kg bw/day can be set in the 90-day feeding study based on statistically significant increased absolute and relative liver weight, consistently reduced body weight, increased cholesterol and alterations in hepatocytes (mild megalocytosis) observed in high-dose animals.

In mice, the NOAEL was found to be 329 mg/kg b.w./day in the 90-day feeding study based on a statistically significant increase in absolute and relative liver weight and alterations in hepatocytes (mild megalocytosis) observed at high doses.

In the 12 months dog study, a NOAEL of 12 mg/kg b.w./day is considered based on statistically significant elevated cholesterol levels in both sexes and some inconsistent organ weight changes (absolute and relative liver, absolute and relative ovary and relative brain) in high dose animals. Absolute and relative ovary weights were significantly increased in high dose females at interim sacrifice, but not at terminal sacrifice, and were thus not considered to be of biological relevance. Upon terminal sacrifice, a tendency for higher absolute and relative liver weights occurred in males. However, statistical significance in relative liver weights when compared to the control animals was only reached for high dose males. The statistical significance was in general hard to achieve due to the small number of animals at the interim sacrifice. Significantly increased relative brain weights were observed in high dose males but this was probably due to significant lower body weight found in males at the end of the study and therefore of no toxicological relevance. Although several absolute and relative liver weights were higher in the female upper dosage levels, an overall trend was not clearly present. Signs of mild but transient anaemia were observed in high-dose dogs up to 6 months of exposure but were not evident after 12 months.

One new 90-day feeding study in rats was submitted. Relative liver weight was statistically significant increased in females at the low, mid and high dose and in males at the mid and high dose. This increase was greater than 10% in the high dose only. Absolute liver weight was increased in both sexes at the high dose. At necropsy hepatocellular centrilobular hypertrophy was found in females at the high dose only. The increase in liver weight and hypertrophy was reversible in the high dose recovery group. In males creatinine levels were increased in the mid and high dose, this was reversible in the high dose

recovery group. At histopathology hyaline droplets in the tubular epithelium of males at mid and high dose was statistically significantly increased. In the high dose recovery the severity had decreased and the incidence was similar to the concurrent control although the incidence was only slightly reduced. The NOAEL is proposed at 600 ppm corresponding to 45 mg/kg bw/d in males based on increased creatinine levels and hyaline droplets of the tubular epithelium of the kidney in males at 1200 and 4800 ppm. And to 1200 ppm corresponding to 98 mg/kg bw/d in females based on increased absolute and relative liver weight and hepatocellular hypertrophy at 4800 ppm.

After two years exposure liver was still the target organ in both rats and mice. In rats relative liver weights increased through all dose groups but were only statistically significant increased at the highest dose (2000 ppm). The NOAEL is proposed at 1000 ppm corresponding to 36 and 49 mg/kg bw/d in males and females, respectively. The incidence of hepatocytomegaly was increased in a non-dose related manner and the biological significance is uncertain. In male mice liver enlargement and hepatocytomegaly was observed at 2000 ppm while in female mice the critical effect was persistent thymic glands. The NOAELs are proposed at 1000 ppm and 500 ppm corresponding to 126 and 79 mg/kg bw/d in males and females, respectively.

In a 28 day dermal toxicity study in rats, local effects (epidermal hyperplasia) indicative of skin irritation were observed in the dose group; no adverse systemic toxicity was noted resulting in a NOAEL of 927 mg/kg bw for systemic effects.

No repeated inhalation studies are available.

In general there were no significant sex-linked differences in the NOAEL values indicating a similar sensitivity to the substance.

2.6.3.1.2 Comparison with the CLP criteria regarding STOT RE (specific target organ toxicity-repeated exposure)

STOT-RE is assigned on the basis of a substance demonstrating evidence of significant (Category 1) or severe (Category 2) toxicity, generally at or below the oral guidance value of 100 mg/kg/d (for a classification in category 2) obtained in a 90-day rat study. The oral guidance value for a classification in category 1 is ≤ 10 mg/kg/d. The equivalent guidance values for a 28-day study are ≤ 300 mg/kg/d and ≤ 30 mg/kg/d, respectively; for a one-year study, they are ≤ 25 mg/kg/d and 2.5 mg/kg/d, respectively. 'Significant' toxicity is taken to mean changes that clearly indicate functional disturbance or morphological changes that are toxicologically relevant. 'Severe' toxicity is considered to be more profound or serious and indicates changes that are of a considerably adverse nature with a significant impact on health.

<u>Liver</u>
In general liver was the target organ in the repeated dose studies, with reduced absolute and relative liver weight and hypertrophy. In the older 90-day studies ([redacted], 1984a & b) in rats and mice the effects where seen at LOAELs greater than 100 mg/kg bw/day.

In a newer 90-day rat study ([redacted], 2001) relative liver weights were increased statistically significant at all dose levels in females and absolute liver weight increased in the high dose females. Histopathology revealed centrilobular hypertrophy in the high dose. The effects were reversible and although statistical significant the relative liver weight were increased less than 10% in the low and mid dose. The effects on liver of females were seen at a LOAEL of 369.6 mg/kg bw/day.

In two 28-day studies in rats and mice ([redacted] 2000 and [redacted], 2004) NOAEL and LOAEL were set. In the rat study the NOAEL was 134 mg/kg bw/day and the LOAEL was 392/400 mg/kg bw/day. In the male mice there was no NOAEL but the LOAEL was 50 mg/kg bw/day based on reduced body weight gain. Increased relative liver weight is only seen in males at the high dose of 9000ppm. In female mice the NOAEL was 53 mg/kg bw/day and the LOAEL was 208 mg/kg bw/day based on increased absolute and relative liver weight.

In the two year studies effects on the liver (increased liver weight and hepatocyomegaly) was observed at 2000 ppm. The male rat is the animal in the two studies corresponding to the lowest dose at 2000 ppm, namely, 74 mg/kg bw/d. If the Habers rule can be used then the guidance value would be around 12 mg/kg bw/d for category 2 which is not even close.

The liver effects are generally seen at doses greater than the guidance values to assist classification. Thus, on the weight of evidence classification is not considered justified for liver effects.

Kidney

In the 90-day rat study by [redacted] the kidney was a target organ for males. Creatinine levels and hyaline droplets were increased statistical significant in the mid and high dose of males. However, creatinine levels were reversible in the high dose recovery group and hyaline droplets were of lower severity and there were slightly fewer incidences of a comparable level with the concurrent control. The LOAEL of the effect is 88 mg/kg bw/day.

Few other studies report on effects on the kidney. In the 2-year rat study relative increased kidney were seen at 3 month sacrifice, but not at the later sacrifices. In the developmental study in rats ([redacted]) renal pelvis dilation (either normal variants or minor anomalies depending on the severity) were seen in foetuses across control and dose groups and reaching statistical significance at the high dose only. In the rabbit developmental study ([redacted], 2002) a single incident of the major malformation hydronephrosis was found at the mid dose. Also the less severe normal variant - renal pelvis dilation - was seen across control and test groups without reaching statistical significance. The renal pelvis dilation in foetuses is of low to moderate concern according to the ECETOC Guidance on Evaluation of Reproductive Toxicity Data, Monograph no. 31, 2002.

The kidney effects are rare, unspecific and not severe. Thus, on the weight of evidence classification is not considered justified for kidney effects.

2.6.3.1.3 Conclusion on classification and labelling for STOT RE (specific target organ toxicity-repeated exposure)

No classification is proposed.

2.6.4 Summary of genotoxicity / germ cell mutagenicity [equivalent to section 10.8 of the CLH report template]

Table 17: Summary table of genotoxicity/germ cell mutagenicity tests *in vitro*

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations /Results	Reference
Bacterial reverse mutation assay, OECD 471 (1997), only one plate incorporation assay, Supportive	Clomazone technical Purity: not stated Batch no: E249-1	0.04 to 4.0 µL/plate (with and without activation) (S. typhimurium TA98, TA100,TA1535, TA1537 and TA1538)	Negative	Haworth, S.R., 1980 013-679-407-1
Bacterial reverse	Clomazone technical Purity: not stated	6.0 to 600 µg/plate (with	Negative	Haworth, S.R., 1982 013-522-700-1

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations /Results	Reference
mutation assay, OECD 471 (1997), only one plate incorporation assay, Supportive	Batch no: E1382-95	and without activation) (S. typhimurium TA98, TA100, TA1535, TA1537 and TA1538)		
Bacterial reverse mutation assay, OECD 471 (1997), only one plate incorporation assay, Supportive	Clomazone technical Purity: 93.4 % Batch no: E3376-112	50 to 5000 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA1535, TA1537 and TA1538)	Negative	Haworth, S.R., 1984 T2467.501
Bacterial reverse mutation assay, OECD 471 (1997), No deviations. Acceptable	Clomazone technical Purity: 96.8% Batch no.: PL13-0237	1.5 to 5,000 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA1535, TA1537 and E. coli WP2 uvrA)	Negative	Wagner, V.O, 2014 AD86RT.503.BTL
Bacterial reverse mutation assay, OECD 471 (1997), Deviation: Growth phase no indicated, Acceptable	Clomazone technical Purity: 98.2 % Batch no.: C1212	1.6 to 5000 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA102, TA1535, TA1537)	Negative	Taylor, H., 2008 676/79
Bacterial reverse mutation assay, OECD 471 (1997), No deviations, Acceptable	Clomazone technical Purity: 96.45 % Batch no.: 726	10 to 3160 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA102, TA1535, TA1537)	Negative	Lauenstein, H.-D., 2013 30366
Bacterial reverse mutation assay, OECD 471 (1997), No deviations, Acceptable	Clomazone technical Purity: 96.6 % Batch no.: D-20071015-4	31.6 to 3160 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA102, TA1535, TA1537)	Negative	Flügge, C., 2009 23499

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations /Results	Reference
Bacterial reverse mutation assay, OECD 471 (1997), No deviations, Acceptable	Clomazone technical Purity: 96.6 % Batch no.: D-723	10.0 to 3160 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA102, TA1535, TA1537)	Negative	Flügge, C., 2013 29575
Bacterial reverse mutation assay, OECD 471 (1997), No deviations, Acceptable	Clomazone technical Purity: 92.9 % Batch no.: CLMZN(3) - 536	50 to 5000 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA1535, TA1537 and E. coli WP2 uvrA pKM 101)	Negative	Indrani, B.K., 2000 2842/2000
Bacterial reverse mutation assay, OECD 471 (1997), No deviations, Acceptable	Clomazone technical Purity: 96.5 % Batch no.: 126400004F	5.0 to 5000 µg/plate (with and without activation) (S. typhimurium TA98, TA100, TA102, TA1535, TA1537)	Negative	Schreib, G., 2013 135310
In vitro mammalian gene mutation test, HGPRT locus mutation assay using CHO-K1-BH4 cells , OECD 476 (1997), No deviations, Acceptable	Clomazone technical Purity: 88.8% Batch no: E1759-146	200 to 600 µg/mL (with and without activation)	Negative	Thilagar, A., 1984 T2198.332
In vitro mammalian gene mutation test, mouse lymphoma L5178Y cells, OECD 490 (2015), No deviations, Acceptable	Clomazone technical Purity: 96.8 % Batch no.: 14640C1016	2.5 to 500 µg/mL (with and without activation)	Negative	Gilby, B., 2016 BQ27PK
In vitro	Clomazone technical	78.13 to 625	Negative	Flügge, C., 2009

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations /Results	Reference
mammalian chromosome aberration test, cultured human peripheral lymphocytes, OECD 473 (1997), No deviations, Acceptable	Purity: 96.6 % Batch no.: D20071015-4	µg/mL (with and without activation)		23882
In vitro unscheduled DNA synthesis (primary rat hepatocytes), OECD 482 (1986), Deviations: A repeat assay was not performed, Supportive	Clomazone technical Purity: not stated Batch no.: E1756-146-20	0.001 to 0.10 µL/mL	Negative	Thilagar, A., 1983 T2107.380

Table 18: Summary table of genotoxicity/mutagenicity tests in mammalian somatic or germ cells *in vivo*

Method, guideline, deviations[1] if any	Test substance	Relevant information about the study (as applicable)	Observations/Results	Reference
In vivo mammalian chromosome aberration test, (Sprague-Dawley rat bone marrow cells), OECD 475, No deviations, Acceptable	Clomazone technical Purity: 88.8 % Batch no.: E1756-146-20	200 to 2000 mg/kg bw/day	Negative	[redacted]., 1982 T1839.102
Mammalian erythrocyte micronucleus test, Deviations: A minimum of 50 metaphase cells instead of 100 were analysed, the proportion of cells in mitosis was determined for a minimum of 500 cells instead of 1000 cells, sampling performed 6 hours after final dosing (instead of 1.5 cycle length of usually 18-27 hours), Supportive	Clomazone technical Purity: 96.6 % Batch no.: D-20071015-4	125-500 mg/kg bw	Negative	[redacted] 2009 23881
Unscheduled DNA synthesis test with mammalian liver cells in i*n vivo*, OECD 486 (1997), No deviations, Acceptable	Clomazone technical Purity: 96.6 % Batch no.: D-	500 and 1000 mg/kg bw	Negative	[redacted] 2009 23987

Method, guideline, deviations[1] if any	Test substance	Relevant information about the study (as applicable)	Observations/Results	Reference
	20071015-1			

2.6.4.1 Short summary and overall relevance of the provided information on genotoxicity / germ cell mutagenicity

In the original DAR three Ames tests were evaluated, these were conducted with one trial only. As seven new, guideline compliant Ames tests, have been provided, the old studies are considered supportive. The seven new tests conducted with and without metabolic activation were negative, and this shows that clomazone (of different technical specifications) does not induce point mutations in *S. typhimurium* or *E.coli*.

In the previously peer-reviewed study investigating gene mutations in Chinese hamster ovary (CHO) cells, clomazone did not induce a significant increase in the frequency of mutants. At the highest dose level the number of mutants was increased in the assay without metabolic activation. However, there was no indication of a positive dose response observed in any of the cultures exposed to the test substance. Clomazone is considered as non-mutagenic in the cultured mammalian cells.

In the previously peer-reviewed *in vitro* study investigating DNA damage and repair, clomazone did not induce an increase in DNA repair synthesis measured by the mean net nuclear counts and is therefore considered as non-mutagenic under the conditions of this test. However these negative results were not confirmed in an independent experiment as requested in Guideline 482 and hence, the study is not considered acceptable.

A new mammalian gene mutation study was submitted. Under the conditions of this test, clomazone did not induce an increase in mean mutation frequency at the *tk* locus in mouse lymphoma cells that exceeded the sum of the mean concurrent vehicle control mutant frequency and the global evaluation factor. Clomazone did not induce gene mutations.

A new *in vitro* chromosome aberration study was submitted. There was no increase in chromosomal aberrations in human peripheral lymphocytes in the presence and absence of an exogenous metabolic activation system. Clomazone was not clastogenic under the conditions of the test.

In a previously peer-reviewed *in vivo* chromosome aberration study clomazone did not induce chromosome aberrations in the bone marrow of rats and is therefore not clastogenic or aneugenic under the conditions of this *in vivo* test. The study was conducted prior to adoption of OECD 475 (1997) and several deviations from the Guideline were observed. Because of the deviations and the concern that the bone marrow might not be exposed the study is considered supportive.

The test substance was also examined in an *in vivo* bone marrow micronucleus test in mice. No test substance-related increase in micro-nucleated polychromatic erythrocytes was observed in the treated groups as compared to the corresponding vehicle control group after sampling at 24 and 48 h. Exposure of the bone marrow was demonstrated by the PCE/NCE ratio. The test substance showed no clastogenic or aneugenic properties under the conditions of the test.

Unscheduled DNA synthesis was tested in a new *in vivo*/*in vitro* rat USD assay. Clomazone did not produce an increase in NNG nor were cells found in repair. Under the conditions of this test clomazone did not induce unscheduled DNA synthesis.

Based on the overall weight of evidence clomazone is not considered genotoxic.

2.6.4.2 Comparison with the CLP criteria regarding genotoxicity / germ cell mutagenicity

There are no human data. Clomazone was negative *in vitro* and *in vivo* studies on mutagenicity, clastogenicity or aneugenity. It is therefore considered unlikely that clomazone may induce mutations (Cat 2) in the germ cells of humans on the basis of negative results in *in vitro* and *in vivo* studies.

2.6.4.3 Conclusion on classification and labelling for genotoxicity / germ cell mutagenicity

There is no evidence of genotoxic potential of clomazone, therefore, no classification is proposed. Clomazone does not meet the criteria for classification for germ cell mutagenicity.

2.6.5 Summary of long-term toxicity and carcinogenicity [equivalent to section 10.9 of the CLH report template]

Table 19: Summary table of animal studies on long-term toxicity and carcinogenicity

<table>
<tr><th>Method, guideline, deviations if any</th><th>Species, strain, sex, no/group</th><th>Test substance, dose levels duration of exposure</th><th>Results
- NOAEL/LOAEL
- target tissue/organ
- critical effects at the LOAEL</th><th>Reference</th></tr>
<tr>
<td>2-year feeding study, combined chronic toxicity and carcinogenicity study, OECD 453 (1981), Deviation: Serum sodium was not analysed and adrenals were not weighed, histopathology on male and female reproductive organs not included, no historical control data Acceptable</td>
<td>Sprague-Dawley CD rats, 120/sex/dose group</td>
<td>Clomazone technical
Purity: 88.8%
Batch no.: E1756-146

0, 20, 100, 500, 1000, 2000 ppm corresponding to 0, 0.8, 4, 20, 41 and 83 mg/kg b.w./day for males and 0, 1.1, 5, 27, 55 and 110 mg/kg b.w./day for females

The NOAELs and LOAELs have further been recalculated to 100% purity, based on a purity of 88.8%

Study design:
<table>
<tr><th>Study interval</th><th>Animals sacrificed* (number/sex /group)</th><th>Study segment affiliation</th><th>Animals remaining on study* (number/sex /group)</th></tr>
<tr><td>Day 0</td><td>0</td><td>90 day/chronic</td><td>120</td></tr>
<tr><td>Day 30</td><td>10</td><td>90 day</td><td>110</td></tr>
<tr><td>Day 60</td><td>10</td><td>90 day</td><td>100</td></tr>
<tr><td>Day 90</td><td>20</td><td>90 day</td><td>80</td></tr>
<tr><td>6 month</td><td>10</td><td>chronic</td><td>70</td></tr>
<tr><td>12 month</td><td>10</td><td>chronic</td><td>60</td></tr>
<tr><td>18 month</td><td>10</td><td>chronic</td><td>50</td></tr>
<tr><td>24 month</td><td>50</td><td>chronic</td><td>-</td></tr>
</table>
*animals dying intercurrently or sacrificed as moribund are not considered</td>
<td>NOAEL
male/female: 36/49 mg/kg bw/d (1000ppm)

LOAEL
male/female: 74/98 mg/kg bw/d

The liver was the target organ. No indication of a carcinogenic potential.

At the 24 month sacrifice the relative liver weights were statistically significant increased at the 2000 ppm dose group and with a trend of increasing through all dose groups (Table B.6.5/01-6 in the RAR vol 3 B6). In the 20 ppm group an increase in relative liver weight was attributed to malignant lymphoma. No other rats had this finding at study termination. Effects on liver weights were not observed at 12 and</td>
<td>[redacted] 1984 410-0816</td>
</tr>
</table>

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results - NOAEL/LOAEL - target tissue/organ - critical effects at the LOAEL	Reference
			18 month sacrifice. Megalocytosis of centrilobular hepatocytes observed after 3 months in the 2000 and 8000 ppm dose groups (4000 was not examined for this). The findings were significantly increased among females in the 8000 ppm dose group. Hepatocytomegaly observed at 18 months was slightly more frequent in treated animals compared to control animals. After two years exposure a non-dose related increase in the number of animals with this lesion (Table B.6.5/01-7 in the RAR vol 3 B6). The biological significance is uncertain. After 2 years exposure, hepatocellular adenomas were increased in the 20 and 500 ppm dose groups but not statistical significant (See Table B.6.5/01-7 in the RAR vol 3 B6). After 90 days the groups of 4000 and 8000 ppm were sacrificed. The groups showed decreased bw and food consumption.	

				[redacted]

Study interval	Animals sacrificed* (number/sex)	Study segment affiliation	Animals remaining on study* (number/sex)

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results - NOAEL/LOAEL - target tissue/organ - critical effects at the LOAEL	Reference
Acceptable		Day 0 | 0 | 90 day/chronic | 120 Day 30 | 10 | 90 day | 110 Day 60 | 10 | 90 day | 100 Day 90 | 20 | 90 day | 80 6 month | 10 | chronic | 70 12 month | 10 | chronic | 60 18 month | 10 | chronic | 50 24 month | 50 | chronic | - * animals dying intercurrently or sacrificed as moribund are not considered	trend towards liver enlargement in males (Table B.6.5/02-5 in the RAR vol 3 B6). Hepatocytomegaly and hepatomegalocytosis was observed in treated mice only, especially males. At 2000 ppm this lesion was observed in all time intervals in male mice (Table B.6.5/02-6 in the RAR vol 3 B6). The biological significance of this lesion is uncertain. Females exposed for 1000 and 2000 ppm clomazone had a larger portion of persistent thymic glands than control animals. After 90 days the groups of 4000 and 8000 ppm were sacrificed. In both groups absolute and relative liver weights were increased (Table B.6.5/02-3 in the RAR vol 3 B6). In the 8000 ppm group minimal or mild megalocytosis of centrilobular hepatocyes were observed in 9/20 male mice (Table B.6.5/02-6 in the RAR vol 3 B6).	

2.6.5.1 Short summary and overall relevance of the provided information on long-term toxicity and carcinogenicity

Two studies submitted by the previous notifier were evaluated in the DAR (2005). Both studies ([redacted], 1984a & b) were GLP compliant and performed according to OECD TG 453 (1981). Both

studies were deemed acceptable. No new studies on long-term toxicity and carcinogenicity were submitted.

OECD TG 453 was updated in 2009 to include parameters such as weight of reproductive organs. The two studies submitted in the original dossier are considered acceptable with some reservations.

Long-term toxicity and carcinogenicity was investigated in combined studies in rat and mice, which included a 90-day oral toxicity study with interim sacrifice, but also additional groups of test animals which were extended to a duration of 24 months in a combined chronic toxicity/carcinogenicity design.

For both species, rats and mice, the liver was the target organ. The effects seen were in the high dose group (2000 ppm) for rats and two high dose groups (1000 and 2000 ppm) for mice.

Body weight, body weight change and food consumption were not significantly affected by clomazone treatment in mice and rats.

Rat:
At 2000 ppm (high dose) a significant increase in the absolute liver weight was seen in male and female rats at 3 months and although the relative liver weight was not statistically elevated the effect is regarded as toxicological relevant, since the elevation in both the absolute and relative liver weight was increased in a dose related manner. After 24 month a statistically significant increase in the relative liver weight in females at 2000 ppm was observed. Hepatocytomegaly was observed at 18 months, which was found to be slightly more frequent in treated animals than in control animals. Following two years of testing, administration of the test article was associated with a non-dose related increase in the number of animals with hepatocytomegaly (see Table 19a below), the significance of this finding is uncertain.
A NOAEL for systemic effects was 1000 ppm corresponding to 36/49 mg/kg b.w./day based on the liver weight effect.

Table 19a: Incidences of hepatocellular adenomas in males and incidences of hepatocytomegaly in males and females (24 month)

	Dose group (ppm)					
Parameter	**0**	**20**	**100**	**500**	**1000**	**2000**
Hepatocellular adenomas in males						
No. of animals	37	45	44	43	42	40
No. of tumours	1	4	2[a]	6	0	2
Hepatocytomegaly						
No. of males	37	45	44	43	42	40
Hepatocytomegaly	9	23*	25*	20*	18	16
No. of females	36	43	42	43	42	42
Hepatocytomegaly	15	26	28*	24	27*	22

[a] = one tumour was a carcinoma
* = statistically significant increase when compared to the control (Fisher Exact test, $p < 0.05$)

Mice:

In the high dose group male mice had statistically significant increased relative liver weight and a dose-related trend towards liver enlargement among males was also apparent (see table 19b). In addition, histopathology of mice at 3, 6, 12, 18 and 24 months revealed cytomegaly and megalocytosis in livers of high dose male mice. In the two high doses, females had a larger portion of persistent thymic glands than control animals. There was no apparent pathophysiological explanation for the changes observed in the hepatocytes or thymus. A systemic NOAEL of 500 ppm (equivalent to 79 mg/kg b.w./day) can be set for females and 1000 ppm (equivalent to 126 mg/kg b.w./day) for males based on treatment-related effects observed on the liver and thymus changes (females only).

Table 19b: Incidences of hepatocytomegaly in males and females

Test interval	Dose group (ppm) 0	20	100	500	1000	2000	8000
Hepatocytomegaly in males							
Three month	0	1/20	-	0	-	2/20	**9/20***
Six month	0	0	0	0	2/10	5/10	-
Twelve month	0	0	0	1/10	0	3/10	-
Eighteen month	0	0	1/10	0	0	2/10	-
Twenty-four month	0	0	1/19	1/23	1/23	3/22	-
Hepatocytomegaly in females							
Three month	0	0	-	0	-	0	2/20
Six month	0	0	0	0	0	0	0
Twelve month	0	0	0	0	0	0	0
Eighteen month	0	0	0	0	0	1/10	0
Twenty-four month	0	0	0	0	1/25	0	0

- = tissues were not examined first number denotes the number of incidences/ second number denotes the number of animals analysed
* = statistically significant difference ($p < 0.01$)

Clomazone did not show any carcinogenic potential in any of the studies available for evaluation.

Refer to the RAR vol 3, section B6.5 for details.

2.6.5.2 Comparison with the CLP criteria regarding carcinogenicity

Clomazone is not known to have or presumed to have carcinogenic potential for humans (Cat 1A and 1B). No oncogenic effects were observed in studies conducted with clomazone, neither in the rat nor in the mouse carcinogenicity studies. Hence, clomazone is not a suspected human carcinogen (Cat 2).

2.6.5.3 Conclusion on classification and labelling for carcinogenicity

There is no evidence of oncogenic potential of clomazone, therefore, no classification is proposed.

Clomazone does not meet the criteria for classification for carcinogenicity.

2.6.6 Summary of reproductive toxicity [equivalent to section 10.10 of the CLH report template]

2.6.6.1 Adverse effects on sexual function and fertility – generational studies [equivalent to section 10.10.1 of the CLH report template]

Table 20: Summary table of animal studies on adverse effects on sexual function and fertility – generational studies

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results - NOAEL/LOAEL (for sexual function and fertility, offspring, parental) - target tissue/organ - critical effects at the LOAEL	Reference

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, dose levels duration of exposure**	**Results** **- NOAEL/LOAEL (for sexual function and fertility, offspring, parental)** **- target tissue/organ** **- critical effects at the LOAEL**	**Reference**
Dietary 2-generation study, OECD 416 (1983), GLP, Deviation: The pre-mating period was 8 weeks for the F0 parental generation instead of 10 weeks. Several reprocuctive parameters (included by opdates of the guideline) are not covered,Acceptable	Charles River CD strain of albino rats, 25/sex/dose group	Clomazone technical Purity: 88.8% Batch no.: E1756-146 0, 100*, 1000, 2000 and 4000 ppm Corresponding to 0, 84, 158, 354 mg/kg bw/day recalculated to 0, 75, 140, 314 mg/kg bw/day based on a purity of 88.8 % (*not recalculated to actual intake in the DAR)	NOAEL/LOAEL parental: 75 /140 mg/kg bw/d (1000/2000 ppm) NOAEL offspring: 314 mg/kg bw/d (4000 ppm) NOAEL fertility: 314 mg/kg bw/d (4000 ppm) Effects at 314 and 140 mg/kg bw/day: Decreased maternal body weights, maternal body weight gain and food consumption in parental animals. No significant effects on offspring. No significant effects on reproduction.	[redacted] 1984 450-1095

2.6.6.1.1 Short summary and overall relevance of the provided information on adverse effects on sexual function and fertility – generational studies

In the two-generation study in rats no toxicity was experienced to reproduction, but the two highest doses had some effects on adult rats in form of decreased body weights, body weight gain and food consumption. The increase in the relative liver weight in the high dose in both sexes was not accompanied with an increase in the absolute liver weight and there was no histopathological findings supporting this increase. The increase in the relative liver weight was therefore probably a reflection of the tendency towards lower final body weight in the high dose (however not statistically significant) and is not considered as toxicological relevant. There were no significant differences between control and treatment groups in number and viability of pups delivered, stillborn and cannibalised pups at birth as well as pup survival. The effects seen on the body weights of F_1/F_2 pups occurred inconsistently, with no relation to increasing dose, were never consistent during the whole lactation period and are therefore not considered related to dosing, but rather a result of strain variance. The reduced fertility index was only seen in the F1 'b' litter in the high dose and had no impact on population data. No other effects on fertility index, mating index and gestation index were observed. The parental NOAEL was 75 mg/kg b.w./day and the highest tested dose 314 mg/kg b.w./day was NOAEL for offspring and reproduction. The NOAELs are based on 100% purity.
See the RAR volume 3 B.6.6.1 for details.

2.6.6.1.2 Comparison with the CLP criteria regarding adverse effects on sexual function and fertility

No adverse effects on sexual function and fertility were observed in studies conducted with clomazone. Reduced fertility index was seen at the high dose only and limited to the F1 'b' litter, it was thus, not considered treatment related. No classification is proposed with respect to sexual function and fertility.

2.6.6.2 Adverse effects on development [equivalent to section 10.10.4 of the CLH report template]

Table 21: Summary table of animal studies on adverse effects on development

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, dose levels duration of exposure**	**Results** **- NOAEL/LOAEL (for maternal and for developmental effects)** **- target tissue/organ** **- critical effects at the LOAEL**	**Reference**
Teratogenicity study (oral by (gavage)), OECD 414 (1981), Deviations: Dosing only until day 15 (organogenesis) – not until sacrifice, Endpoints included in updates of the guideline are not covered. Acceptable	Sprague Dawley Rats, 25/dose group	Clomazone technical in corn oil Purity: 88.8% Batch no.: E1756-146 0, 100, 300 and 600 mg/kg b.w./day recalculated to 0, 89, 266 and 533 mg/kg/day based on a purity of 88.8 % Dosing day 6-15 of gestation. Animals sacrificed on GD 20.	NOAEL/LOAEL maternal: 89/266 mg/kg bw/d NOAEL/LOAEL developmental: 89/266 mg/kg bw/d Maternal toxicity: Decreased food consumption and clinical signs as abdominogenital staining and decreased locomotion in the two high dose groups. Developmental toxicity: Decreased female foetal body weight (in high dose only), while in males this was only seen as a non-significant downward trend. Significant increase in the incidence of foetal skeletal malformations (delayed ossifications) and in visceral anomalies (increased incidence of hydroureter) in the two high dose groups.	[redacted] 1984 A83-1142
Teratogenicity study (oral (by gavage)), OECD 414 (1981), GLP,Deviations: Dosing only until day 18 (organogenesis), end-points missing (no food consumption reported). Endpoints included in updates of the guideline are not covered. Acceptable	New Zealand white Rabbits, 18/dose group	Clomazone technical in aqueous methyl cellulose (1%) Purity: 88.8% Batch no.: E1756-146 0, 30, 240 and 1000 (day 6-12)/700 (day 13-18) mg/kg b.w./day recalculated to 0, 27, 213, 622 mg/kg/day based on a purity of 88.8 % Dosing day 6-18 of gestation. Animals sacrificed on GD 29.	NOAEL/LOAEL maternal: 213/622 mg/kg bw/d NOAEL developmental: 700 mg/kg bw/d Maternal toxicity: Decreased body weight, death of 3 animals, four females aborted, clinical signs and no or decreased defecation. Developmental toxicity: No treatment related developmental effects were observed.	[redacted] 1982 WIL-81157 (A81-655)
Teratogenicity study (oral via gavage), OECD 414 (1981), Deviations: No HCD,	Wistar rats, 28/dose group	Clomazone technical in carboxymethyl cellulose	NOAEL/LOAEL maternal: 232/465 mg/kg bw/d NOAEL/LOAEL developmental: 232/465	[redacted] 2002 2840/2000

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, dose levels duration of exposure**	**Results** **- NOAEL/LOAEL (for maternal and for developmental effects)** **- target tissue/organ** **- critical effects at the LOAEL**	**Reference**
Acceptable (HCD were supplied during the assessement)		Purity: 92.9%, 94 % Batch no.: 184, ZS/184/12 0, 250, 500 and 750 mg/kg/d recalculated to 0, 232, 465 and 697 mg/kg/day based on a purity of 92.9 % Dosing day 6-19 of gestation. Animals sacrificed on GD 20.	mg/kg bw/d Maternal toxicity: Clinical signs of toxicity and one dead animal in high dose animals. Significant reduction in body weight, weight gain and food intake at 465 and 697 mg/kg bw/d. Total resorptions in 4 dams at 695 mg/kg bw/d (statistically significant). Increase in early resorptions and post-implantation loss at the high dose (not statistically significant). Mean litter weight of male/female animals statistically significantly affected at 697 mg/kg bw/d Embryo-/foetotoxicity/teratogenicity: At 465 mg/kg bw/d arthrogryposis in 2 pups of 2 litters and one foetus with multiple skeletal malformations including malformed fore- and hindlimbs. At 697 mg/kg bw/d, tendency towards increased incidence of renal pelvis dilation, one foetus with multiple major malformation in visceral organs, and a significant increase in the incidence of arthrogryposis (7 pups of 4 litters), and foetuses with major malformations.	
Teratogenicity study (oral via gavage), OECD 414 (1981), Deviations: No HCD, randomization to treatment groups, Acceptable (HCD were supplied during the assessement)	New Zealand white, 25/dose group	Clomazone technical in carboxymethyl cellulose Purity: 95.0 % Batch no.: D-10096 150, 350, 700 mg/kg bw/d recalculated to 143, 333, 665 mg/kg/day based on a purity of 95.0 % Dosing day 6-28 of gestation. Animals sacrificed on GD 29.	NOAEL/LOAEL maternal: 333/665 mg/kg bw/d NOAEL developmental: 333/665 mg/kg bw/d Maternal toxicity: One death in the high and mid dose. At 333 mg/kg bw/d two dams aborted, they had clinical signs of weakness and dullness; Body weight gain and food intake statistically significantly reduced; Diarrhoea seen in a few dams of all treatment groups, wet perineum in one dam also having diarrhoea at the high dose. Embryo-/foetotoxicity/teratogenicity: One foetus of the high dose group had multiple external, visceral and skeletal malformations (e.g. doublesided flexed wrist, hind limbs turned inwards) and one foetus had forelimb flexed at wrist. Malformations related to arthrogryposis.	[redacted] 2002 2841/2000
Historical control data Prenatal Developmental Toxicity study in rats	Wistar rats		The data consist of control data from 1998 to 2003 and was compiled by the same test faccility as the 2002 rat and rabbit studies were performed at.	[redacted] 2007a KCA 5.6.2/05

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results - NOAEL/LOAEL (for maternal and for developmental effects) - target tissue/organ - critical effects at the LOAEL	Reference
			However, it is not specified if the data are from that laboratory.	
Historical control data Prenatal Developmental Toxicity study in rabbits	Rabbits		The data consist of control data from 1998 to 2003 and was compiled by the same test faccility as the 2002 rat and rabbit studies were performed at. However, it is not specified if the data are from that laboratory.	[redacted] 2007b KCA 5.6.2/06

2.6.6.2.1 Short summary and overall relevance of the provided information on adverse effects on development

In the developmental toxicity study from 1984 in rats with dose levels of 100, 300 or 600 mg/kg bw/day on days 6 through 15 of gestation, impairment of the maternal food consumption and clinical signs were seen at the two highest dose levels. Developmental toxicity was of minor character in form of decreased foetal body weight of high dose females, increased incidence of delayed ossifications in rat foetuses in the two high doses, and increased incidence of hydroureter in the high dose group only. The NOAEL was 89 mg/kg bw/day for both maternal and developmental toxicity. The NOAELs are based on 100% purity.

In a newly submitted developmental toxicity study rats were dosed with 250, 500 and 750 mg/kg/d on days 6-19. Reduced body weight gain was observed at the mid and high dose and reduced food intake was observed in all test groups. At the high dose one dam died after clinical signs of lethargy and slight salivation was observed. Symptoms that were seen in the high dose dams on single occasions (5 of 28 dams had lethargy, each on a single day; 22 dams had slight salivation with a duration of 1-5 days). There was no effect on number of corpora lutea, implantations, early or late resorptions, pre- or post-implantation loss or dams with any resorptions. Dams with total resorptions at the high dose were significantly higher than control (4 dams/17%). Mean foetal weights were statistically significant reduced in the high dose and litter size and total numbers of foetuses were lower than control. The findings at external examinations consisted of protruding tongue and anasarca in one foetus at the mid dose, and anasarca and forelimbs flexed at wrist in two foetuses, respectively, at the high dose. With a single incidence of anasarca in the mid and high dose there was no dose response. The foetus of the high dose group that exhibited anarsarca also had multiple visceral malformations. A single foetus in the high dose had malformed forelimbs (short humerus and bent ulna) after skeletal examination. Athrogryposis were observed at the mid (2) and high (7) dose of 500 and 750 mg/kg bw/d. Reaching statistical significance in the high dose and showing dose response relationship. The proposed NOAELs are 232 mg/kg bw/d for maternal and developmental toxicity. The NOAELs are based on 100% purity.

Incidences of major external, visceral and skeletal malformations

Parameters	Doses [mg/kg bw/d]				Historical control ranges (%)
	Control	250	500	750	
Major external malformations					
Number of foetus examined	265	254	260	204	-
Forelimbs flexed at wrist	0.0	0.0	0.0	0.5[c]	0.0-2.1
Anasarca	0.0	0.0	0.4[a]	0.5[b]	na.
Foetuses with major malformations (%)	0	0	1 (0.4)	2 (1.0)	0.0-4.0
Dams with major malformed fetuses (%)	0	0	1 (4)	2 (10)	0.0-11.0

Major visceral malformations					
Number of foetus examined	133	127	130	102	-
Multiple malformations	0.0	0.0	0.0	1.0[b]	na.
Foetuses with major malformations (%)	0	0	0	1 (1.0)	0.0-2.0
Dams with major malformed fetuses (%)	0	0	0	1 (5.0)	0.0-10.0
Major skeletal malformations					
Number of foetus examined	132	127	130	102	-
Multiple malformations	0.0	0.0	0.8[a]	0.0	0.0-0.9
Arthrogryposis	0.0	0.0	1.5	**6.9****	0.0-0.9[e]
Forelimbs malformed	0.0	0.0	0.0	1.0[d]	0.0-0.1
Foetuses with major malformations (%)	0	0	3 (2.3)	**8** **(7.8)**	0.0-0.9
Dams with major malformed fetuses (%)	0	0	3 (12)	**5** **(25)**	0.0-5.0

** p<0.01; *p<0.05, na = not available; [a]Same dam, possibly same foetus, malformations: delayed skeletal ossification of skull bones with partial ossified frontal, parietal, interparietal and squamous bones, radius and ulna malformed, absent femur and fibula, hypoplastic malformed tibia; [b]Same dam, possibly same foetus, malformations: brain 3rd and 4th ventricle dilated, lungs hypoplastic, right lobes fused, heart globular-inter ventricular septa absent, liver right lobe undivided, intestine short and stomach displaced towards right; [c]also indicated as arthrogryposis in study report, dam different from the dams with major malformed fetuses under skeletal malformations; [d]humerus short, ulna bent – the indicated HCD is for bent ulna; [e]F.limbs (Rt/Lt/B)(+/++) flexed at wrist, which is indicated in the HCD as a minor skeletal anomaly.

Historical control data (HCD) have been provided for the newer rat developmental study (see the RAR vol 3, B.6.6.2 for details). In the HCD arthrogryposis has not been used as term or was not a finding in the HCD. Of the *external* observations a single study defined the high range of 2.1% of forelimbs flexed at wrist. *Skeletal* observations of forelimbs flexed at wrist, although considered a minor skeletal anomaly, was reported up to 0.9% in other four of the 11 studies. In the high dose group there was one finding at the *external* observation of forelimbs flexed at wrist (0.5%). At the *skeletal* observation there was 7 findings of arthrogryposis (6.9%) in the high dose and 2 findings of arthrogryposis (1.5%) in the mid dose group. Except for the *external* finding of forelimbs flexed at wrist, the arthrogryposis found at *skeletal* observation were above HCD if compared with forelimbs flexed at wrist indicated as minor anomaly in the HCD for skeletal observations. The high dose *skeletal* finding of 6.9% arthrogryposis was outside HCD if compared even with forelimbs flexed at wrist at the *external* observation (2.1%). The one finding of malformed forelimbs (humerus short and ulna bent, 1.0%) was also greater than the HCD (0.1% for bent radius, ulna, tibia, fibula).

In the developmental toxicity study in rabbits dose levels were 30, 240 or 1000 (reduced to 700 from day 13) mg/kg b.w./day from day 6 through 18 of gestation. Maternal toxicity in the high dose group was manifested by effects on maternal body weight, death of 3 animals, four females aborted during the study, red vaginal discharge was most often seen in animals which aborted. Additional indicators of maternal toxicity was decreased or no defecation in the high dose group. There were no significant differences between control and treatment groups with respect to the number or percentage of foetuses with malformation or developmental variations. The increased incidence of anomalies observed at 30 and 240 mg/kg b.w./day was not seen at the highest dose and not considered of toxicological relevance. The developmental toxicity of the offspring was not affected.The maternal NOAEL was 213 mg/kg bw/day and the developmental NOAEL was 622 mg/bw/day. The NOAELs are based on 100% purity.

In a newly submitted developmental toxicity study rabbits were dosed at 150, 350 and 700 mg/kg bw/d on days 6-28. There was one death in the mid and high dose, the death in the mid group was attributed to gavage error. Two dams aborted, they had clinical signs of weakness and dullness. Diarrhoea was seen in all test groups. Body weight gain and food intake was significantly reduced compared to control in the high dose group. The significant increase in pre-implantation loss found in the low and mid dose

could not be established at the high dose. Sporadic and statistically non-significant malformations and anomalies were found in all treatment groups. One high dose foetus had forelimbs flexed at wrist and another foetus had multiple malformations associated with arthrogryposis (arthrogryposis of forelimbs, hindlims turned inwards). The proposed maternal NOAEL is 333 mg/kg bw/d based on mortality, abortions, clinical signs and statistically reduced body weight gain at the high dose. The proposed developmental NOAEL is 333 mg/kg bw/d based on multiple and skeletal malformations in high dose foetuses. The NOAELs are based on 100% purity.

Incidences of major external, visceral and skeletal malformations

Parameters	**Doses [mg/kg bw/d]**				**Historical control ranges (%)**
	Control	**150**	**350**	**700**	
Major external malformations					
Number of fetuses examined	157	158	138	137	-
Omphalocele	0.6	0.0	0.0	0.0	0.0-0.0
Forelimbs flexed at wrist	0.0	0.0	0.0	0.7	0-2.6[d]
Multiple	0.0	0.0	0.0	0.7[a, c]	0.0-0.9
Foetuses with major malformations (%)	1 (0.6)	0	0	2 (1.4) ~~1 (0.7)~~[b]	0.0-3.4
Dams with major malformed fetuses (%)	1 (4.5)	0	0	2 (9.6) ~~1 (4.8)~~[b]	0.0-18.8
Major visceral malformations					
Number of fetuses examined	157	157	137	135	-
Brain agenesis	0.0	0.0	0.0	0.7[c]	na.
Diaphragmatic hernia	0.0	0.0	0.7	0.0	na.
Hydronephrosis	0.0	0.0	0.7	0.0	na.
Foetuses with major malformations (%)	0	0	2 (1.5)	1 (0.7)	0.0-1.1
Dams with major malformed fetuses (%)	0	0	2 (8.7)	1 (4.8)	0.0-7.7
Major skeletal malformations					
Number of fetuses examined	157	157	137	135	-
Skull bones absent	0.0	0.0	0.0	0.74[c]	na.
Hind limbs turned inwards	0.0	0.0	0.0	0.74[c]	na.
Fused CdV centra 6/7	0.0	0.0	0.73	0.0	na.
Forelimbs flexed at wrist	0.0	0.0	0.0	0.74[c]	0-2.6
Foetuses with major malformations (%)	0	0	1 (0.7)	1 (0.7)	0.00-2.60
Dams with major malformed fetuses (%)	0	0	1 (4.3)	1 (4.8)	0.00-18.80

** p<0.01; *p<0.05; na. = not available; [a]malformations: acephalostomia, microtia of left ear, arthrogryposis of both fore limbs, ectrodactyly of 2 digits, small foetus, hindlimb bent inwards RB4174; [b]there are two foetuses with major malformations from different dams, therefore the indicated values were wrong; [c]same foetus; [d]value indicated for forelimbs flexed at wrist in the HCD, the value CATF indicated in their position paper was 0-3.2 for arthrogryposis.

Historical control data (HCD) have also been provided for the newer rabbit developmental study (see the RAR vol 3, B.6.6.2 for details) . For HCD *external* observations, left and right forelimb flexed at wrist, both of which had a prevalence of 0.72% and both forelimbs flexed at wrist occurred up to 2.6% in one HCD study (3 pups from 3 dams), 2 other HCD studies had this finding at 0.9 and 0.8%. One rabbit had forelimbs flexed at wrist (0.74%) and one had multiple malformations (0.74%). The effects are within HCD.

Discussion

In the recent rat developmental study arthrogryposis was seen in the mid and high dose in a dose related manner for litters (2 litters at the mid dose and 4 in the high dose) as well as for pups (2 pups at the mid dose and 7 in the high dose). The effect was statistically significant in pups in the high dose only (no statistics on litter incidence). Additional 2 foetuses, one of the mid and one of the high dose had multiple, skeletal and visceral malformations, respectively, malformations that could be associated with arthrogryposis. Two foetuses of the high dose had malformations that could be related to arthrogryposis (forelimbs flexed at wrist and forelimbs malformed), but possibly less severe/fewer joints to consider them arthrogryposis. Comparison with HCD showed that the effects were rare.

In the recent rabbit study two foetuses in the high dose have malformations related to arthrogryposis in one or several joints, one foetus in combination with multiple skeletal malformations. The effects were not statistically significant and were within HCD, but the findings suggest the effect in a possible second species.

In the older rat developmental study no major skeletal malformations were noted in any foetuses. All minor malformations were observed sporadically among groups without regard to type or incidence except for a significant increased incidence of abnormal thoracic vertebrae with split or dumbbell shaped centra in high dose animals. Delayed ossifications seen in the mid and high dose groups were most likely linked to maternal toxicity. There were no findings of statistical significance or relevant malformations in the older rabbit developmental study.

Arthrogryposis refers to the congenital development of nonprogressive multiple joint contractures affecting two or more areas of the body. A contracture occurs when a joint becomes permanently fixed in a bent (flexed) or straightened position[1], caused by a limitation of joint movements. Although arthrogryposis is the most common limb deformity in domestic animals, experimentally induced arthrogryposis in rodents is rare. It is not a primary failure of skeletal development, but can be caused by neurologic, muscular, connective tissue or skeletal defects or intrauterine crowding.[2] Maternal toxicity in humans leading to decreased *in utero* movement could be acute or chronic illness (e.g. myasthenia gravis and myotonic dystrophy), viral infections, fever, nausea, drugs, conditions related to the amniotic fluid, trauma, bleeding, threatened abortion etc[3].

Maternal toxicity was manifested in rats by reduced body weight gain and food intake, increased relative liver weight, slight salivation and few observations of lethargy. A single rat died in the high dose and four had total resorptions. One high dose rabbit died and 2 rabbits aborted. Reduced body weight gain and food intake was seen in addition to clinical signs of weakness and dullness in the two dams that died. In literature, fetal akinesia leading to arthrogryposis, is described as being the result of severe maternal illness for a longer period of time than the observed maternal toxicity would suggest. Hence, the statistically significant and relevant arthrogryposis is not considered secondary to maternal toxicity.
See the RAR volume 3 section B.6.6.2 for details.

2.6.6.2.2 Comparison with the CLP criteria regarding adverse effects on development

There is no human evidence to allocate clomazone to Category 1A. The effect is not considered secondary to maternal toxicity and with effects in one, possibly two, species the evidence is sufficiently convincing to place it in category 1B. Since, the effect is serious and there are no mechanistic information available raising doubt about the relevance of the effect for humans, classification in category 2 is not warranted.

[1] www.rarediseases.info.nih.gov, 20. October 2017. Last updated: 1/12/2015. National Institute of health, Genetic and Rare disease Information Center.
[2] Hood RD, Rousseaux CG, Blakley PM. Embryo and Fetus. Handbook of Toxicologic Pathology Vol. 2, Second Edition. Haschek WM, Rousseaux CG, Wallig MA eds. Academic Press 2002.
[3] Hall JG and Vincent A. Arthrogryposis. In Neuromuscular Disorders of Infancy, Childhood and Adolescence, Second edition. Darras BT, Jones HR, Ryan MM, De Vivo DC eds. Elsevier 2015

It is proposed to classify clomazone Repr. 1B, H360D May damage the unborn child.

2.6.6.3 Adverse effects on or via lactation [equivalent to section 10.10.7 of the CLH report template]

Reference is made to 2.6.6.1.

2.6.6.3.1 Short summary and overall relevance of the provided information on effects on or via lactation

The effects seen on the body weights of F_1/F_2 pups occurred inconsistently, with no relation to increasing dose, were never consistent during the whole lactation period and are therefore not considered related to dosing but rather a result of strain variance.

2.6.6.3.2 Comparison with the CLP criteria regarding effects on or via lactation

There are no results of the two generation study in rats indicating adverse effect in the offspring due to transfer in the milk or adverse effect on the quality of the milk.

2.6.6.4 Conclusion on classification and labelling for reproductive toxicity

It is proposed to classify clomazone Repr. 1B, H360D May damage the unborn child.

2.6.7 Summary of neurotoxicity

In the original dossier reaction to sensory stimuli of different type, grip strength and functional observations were not assessed in the 90-day studies. However, in the newly submitted 90-day study ([redacted], 2001) in rats motor activity, sensory reactivity to different stimuli, grip strength and landing footsplay was assessed. Although, there were some effects on grip strength and landing footsplay they were inconsistent and not considered treatment related.

2.6.8 Summary of other toxicological studies

2.6.8.1 Toxicity studies of metabolites and impurities

The toxicological significance of the five plant metabolites, FMC 59234, FMC 57096, FMC 57091, FMC 113728, and FMC 61569 was addressed in addition to the rat and plant metabolite Clomazone-3-OH propanamide (FMC 65317).

In the first EU assessment the plant metabolite 2-Chlorobenzyl alcohol was assumed to be of no toxicological significance. The metabolite 2-Chlorobenzyl-alcohol metabolite (FMC 61569) was found in all plant species studies, primarily in the green parts of the plant. Information from published literature indicates that 2-Chlorobenzyl-alcohol (the major metabolite of 2-chlorotoluene) is conjugated as glucuronide or as mercapturic acid, and is rapidly eliminated in rats. This metabolite is also presented as an impurity in technical clomazone and has therefore been assessed in the toxicology package, apart from being a likely intermediate in the rat metabolic pathway. Recent acute oral toxicity studies and AMES tests – a pair of them evaluated in the framework of the MRL review of clomazone – have been provided that support the toxicological non-relevance of this plant metabolite.

The plant metabolite 2-Benzoyl-Isoxazolidinone (FMC 59234) was only found in the conjugated form in forage samples of the cotton metabolism study and in very small quantities (0.062 ppm). The apparent dechlorination of the benzyl ring is considered very improbable, particularly without a corresponding substitution reaction. Furthermore the metabolite is only seen in the ^{14}C-Carbonyl labelled sample and not in the ^{14}Phenyl labelled sample which is unexpected if this is a true plant

metabolite. It was considered that this metabolite is an impurity associated with the ^{14}C-Carbonyl labelled Clomazone and therefore this compound is considered to have no toxicological significance.

The metabolite 3, N-Dihydroxy- propanamide (FMC 57096) is likely to occur in rats as well as plants and is an intermediate between FMC 60217 and FMC 87008 in the rat pathway. It is considered that that FMC 87008 is formed through oxidation from the primary alcohol i.e. FMC 57096. However, this metabolic step in the rat would be too rapid to allow observation of FMC 57096. The metabolite FMC 57096 is considered toxicologically insignificant.

The metabolite isoxazolidine (FMC 57091) occurs following hydroxylation of the methylene bridge carbon of clomazone to produce carbinolamide, which rapidly degrades to FMC 57091. The metabolite is a highly unstable compound and readily undergoes hydrolysis, oxidation and reduction to yield related products leading to glycoside and amino acid conjugates. It was not found in metabolism studies for sweet potato, cotton or corn probably due to its instability. It was found in the tobacco study but with the carbonyl label only. The absence of this metabolite in the rat metabolism studies does not mean that it is not produced. Both rats and plants metabolize clomazone by comparable hydrolysis and oxidative pathways (although rats favour hydrolysis whereas plants favour oxidative degradation). It is proposed as an intermediate, which cannot usually be detected. This metabolite is not deemed to be of toxicological significance due to its instability. Further studies on this metabolite indicate that the substance is minimal irritating to skin, does not possess any acute dermal toxicity (study not fully in accordance with current test Guideline) and is negative in an Ames test.

It is concluded that the toxicology of 3'OH Clomazone (FMC 113728) may have been considered in the mammalian studies with clomazone, since hydroxylation is a general pathway in mammals. Further to this, as the hydroxy metabolites of Clomazone are only found as conjugates, they are not believed to present a concern.

Studies on clomazone-3-OH propanamide (FMC 65317) have been provided to assess the toxicological relevance of this metabolite although it is not a plant metabolite only, but also a rat metabolite. The LD_{50} is greater than 5000 mg/kg bw and it was not mutagenic in a bacterial reverse mutation assay. Thus, it is considered a toxicological non-relevant metabolite.

2.6.8.2 Supplementary studies on the active substance

A waiver request was submitted that gives an overview of indicators of immune system endpoints in the different toxicology studies of the original dossier. For the following reasons immunotoxicity testing in not required:

- No toxic effects on organs of the immune system i.e. WBCs, spleen, thymus and lymph nodes were observed in sub-acute, sub-chronic and chronic studies in the rat, mouse and dog, a rat multi-generation reproduction study and sub-acute dermal studies in the rat.
- Liver is the target organ.
- Clomazone, an iso-oxazole herbicide, is not likely to cause immunotoxicity, because two oxazole herbicides have shown no evidence of immunotoxicity.
- Two retrospective analysis of the OPPTS 870.7800 immunotoxicity guideline concluded that the test did not provide the most sensitive endpoint for risk assessment for any pesticide under evaluation.
- Acute dietary exposure is negligible (less than the US limit of 0.1%).

No immunotoxic effect is foreseen.

2.6.8.3 Endocrine disrupting properties

A comprehensive report going through the repeat dose studies of the original dossier of clomazone have been submitted. It concludes that the overall weight of evidence points toward clomazone not having endocrine disrupting properties because of the following reasons:

- Slight changes seen on endocrine tissues only at toxic doses
- Repeat dosing and reproductive higher-tier studies did not detect significant effects on apical endpoints or perturbations at histopathological levels of endocrine organs or system
- Liver toxicity not associated with downstream effect on endocrine systems
- No effect on reproduction

In the 28- and 90-day in rats, dogs and mice studies there were few indications of change in weight of adrenals, gonads, ovary and testes. Reduced body weight gain and liver were target effect/organ and some weight changes were only seen in absolute weight. The following organs were not weighed in the two 90-day studies in the original dossier: adrenals, epididymis, uterus and thymus. However, they were weighed in the recent 90-day study in rats and no changes were found.

In the 2-year rat study findings in a few rats included changes in colour and/or texture of the adrenals, pituitary enlargement, cystic ovaries or uterus and small testes. No effects on pituitary are reported in other studies.

There are no effects of clomazone on reproduction. However, key reproductive end-points such as sexual development, estrous cycle and sperm motility haven't been investigated in this study. Taking the overall weight of evidence into consideration there is low concern that clomazone is affecting the endocrine system.

2.6.9 Summary of medical data and information

No clinically relevant health problems associated with clomazone production have been observed.

2.6.10 Toxicological end points for risk assessment (reference values)

Table 22: Overview of relevant studies for derivation of reference values for risk assessment

Species	Study (method/type, length, route of exposure)	Test substance	Critical effect	NOAEL	LOAEL	Cross reference
Spraque-Dawley rats	Oral 90-day study *0, 20, 100, 500, 1000, 2000, 4000 and 8000 ppm corresponding to 0, 1.4, 7, 35, 68, 138, 278 and 563 mg/kg bw/day*	Clomazone technical	In the two high doses statistically significant effect such as increased a/r liver weight, consistently reduced body weight and increased cholesterol after 1, 2 and 3 month were observed. At the high dose statistically significant change in hepatocytes in forms of megalocytosis were observed. The liver was the target organ.	138/163 (2000 ppm)	278/324	[redacted]., 1984 410-0816
CD mice	Oral 90-day study *0, 20, 100, 500, 1000, 2000, 4000 and 8000 ppm corresponding to 0, 3.8, 19.5, 98, 188, 371, 761 and 1766 mg/kg b.w./day*	Clomazone technical	In the two high dose groups statistically significant increase in a/r liver weight and in the high dose histopathologic changes in hepatocytes (mild megalocytosis) were observed. The liver was the target organ.	371/522 (2000 ppm)	761/1049	[redacted] 1984 410-0817
Wistar rats	90-days oral study *0, 600, 1200 and 4800 ppm corresponding to 0, 47.7, 92.0, and 377.4 mg/kg bw/d in males*	Clomazone technical	In the mid and high dose groups, statistically significant effects of increased absolute/relative liver weights, consistently reduced body weights and increased cholesterol and creatinine levels were observed. Critical effects were reversible after recovery period. In addition in the high dose group, statistically significant increased incidences of hyaline droplets in kidney tubular epitheliums in males, and hepatocellular hypertrophy in liver of high dosed females were observed. Both effects were reversible after recovery period.	47.7 / 50.4 (600 ppm)	92.0 / 103.8	[redacted] 2001 2839/2000
Beagle dogs	Oral 1-year study *0, 100, 500, 2500 and 7500 (reduced to 5000 ppm on day 8) ppm*	Clomazone technical	In the two high dose groups: Statistically significant elevated serum cholesterol in both sexes and some inconsistent organ weight changes (a/r liver weight, a/r ovary and relative brain). Sign of transient mild anaemia in the high dose group up till 6 month.	13.3/14 (500 ppm)	67/71	2.6.3 [redacted] 1984 6124-101

Species	Study (method/type, length, route of exposure)	Test substance	Critical effect	NOAEL	LOAEL	Cross reference
	corresponding to 0, 3, 13, 67, and 147 (5000 ppm) mg/kg b.w./day)		The liver was the target organ.			
Sprague-Dawley CD rats	2-year feeding study, diet *0, 20, 100, 500, 1000, 2000 ppm (4000, 8000 ppm terminated after 90 days)* *Corresponding to 0, 0.8, 4, 20, 41 and 83 mg/kg b.w./day for males and 0, 1.1, 5, 27, 55 and 110 mg/kg b.w./day for females*	Clomazone technical	At the high dose statistically significant increased absolute liver weight were observed in both sexes at 3 months, relative liver weight was not statistically elevated, but still regarded as toxicological relevant, since the elevation in the both the absolute and relative liver weight was increased in a dose related manner. Hepatocytomegaly was more frequent in treated animals than in controls; a non-dose related increase in the number of animals with this lesion. The biological significance is uncertain. The liver was the target organ. No indication of neoplastic or non-neoplastic changes.	36/49 (1000 pm)	74/98	[redacted]., 1984 410-0816
CD-1 mice	2-year feeding study, diet *0, 20, 100, 500, 1000, 2000 ppm (4000, 8000 ppm terminated after 90 days)* *corresponding to 0, 3, 15, 73, 142 and 290 mg/kg b.w./day for males and 0, 4, 18, 89, 182 and 359 mg/kg b.w./day for females*	Clomazone technical	Increased relative liver weight and a dose-related trend towards liver enlargement in males. Hepatocytomegaly and hepatomegalocytosis was observed in treated mice only, especially males. At 2000 ppm this lesion was observed in all time intervals in male mice. The biological significance of this lesion is uncertain. Females exposed for 1000 and 2000 ppm clomazone had a larger portion of persistent thymic glands than control animals. The liver was the target organ. No indication of neoplastic or non-neoplastic changes.	126/79 (1000/500 ppm)	258/162	[redacted] 1984 410-0817
CD rats	Dietary 2-generation study *0, 100, 1000, 2000 and 4000 ppm*	Clomazone technical	Decreased maternal body weights, maternal body weight gain and food consumption in parental animals. No significant effects on offspring.	84 corresp. to 1000 ppm	158 (parental)	[redacted], 1984 450-1095

Species	Study (method/type, length, route of exposure)	Test substance	Critical effect	NOAEL	LOAEL	Cross reference
			No significant effects on reproduction.	(parental)		
Sprague Dawley Rats	Teratogenicity study (oral by (gavage)) *0, 100, 300 and 600 mg/kg b.w./day*	Clomazone technical	Maternal toxicity: Decreased food consumption and clinical signs as abdominogenital staining and decreased locomotion in the two high dose groups. Developmental toxicity: Decreased female foetal body weight (in high dose only), while in males this was only seen as a non-significant downward trend. Significant increase in the incidence of foetal skeletal malformations (delayed ossifications) and in visceral anomalies (increased incidence of hydroureter) in the two high dose groups.	100[1)] (maternal) 100[1)] (foetal)	300 (maternal) 300 (developmental)	[redacted] 1984 A83-1142
New Zealand white Rabbits	Teratogenicity study (oral by (gavage)) *0, 30, 240 and 1000 (day 6-12)/700 (day 13-18) mg/kg b.w./day*	Clomazone technical	Maternal toxicity: Decreased body weight, death of 3 animals, four females aborted, clinical signs and no or decreased defecation. Developmental toxicity: No treatment related developmental effects were observed.	240[1)] (maternal) 700[1)] (foetal)	700 -	[redacted] 1982 WIL-81157 (A81-655)
Wistar rats	Teratogenicity study (oral via gavage) *250, 500 and 750 mg/kg/d*	Clomazone technical	Maternal toxicity: Clinical signs of toxicity and one dead animal in high dose animals. Significant reduction in body weight, weight gain and food intake at 500 and 750 mg/kg bw/d. Early resorption, implantation sites, mean litter weight of male/female animals statistically significantly affected at 750 mg/kg bw/d Embryo-/foetotoxicity/teratogenicity: Arthrogryposis and foetuses with multiple skeletal malformations at 500 mg/kg bw/d. At 750 mg/kg bw/d, tendency towards increased incidence of renal pelvis dilation, one foetus with multiple major malformation in visceral organs, and a significant increase in the incidence of arthrogryposis and foetuses with major malformations.	250 (maternal) 250 (embryo-/foetotoxicity) 250 (teratogenicity)	500 (maternal) 500 (embryo-/foetotoxicity) 500 (teratogenicity)	[redacted] 2002 2840/2000
New Zealand white	Teratogenicity study (oral via gavage)	Clomazone technical	Maternal toxicity: Mortality, clinical signs of weakness, dullness, wet perineum, diarrhoea and abortion; body weight gain and food intake	350 (maternal) 700	700 (maternal)	[redacted] 2002 2841/2000

Species	Study (method/type, length, route of exposure)	Test substance	Critical effect	NOAEL	LOAEL	Cross reference
rabbits	*150, 350, 700 mg/kg bw/d*		statistically significantly reduced Embryo-/foetotoxicity/teratogenicity: No treatment related findings	(embryo-/foetotoxicity) No teratogenicity effects were observed	> 700 (embryo-/foetotoxicity)	

2.6.10.1 Toxicological end point for assessment of risk following long-term dietary exposure – ADI (acceptable daily intake)

The critical effect identified based on the chronic toxicity studies is considered to be the effect observed on the liver in the three animal species tested (rat, mouse, dog). The NOAEL values are predominantly based on changes in liver weights, but in addition female and male dogs also had statistically significant dose-related elevation in cholesterol levels though out the study. In female mice changes in thymic glands (diagnosed as lymphoid hyperplasia) was also observed but at higher dose levels than the one eliciting the effect on the liver. The findings were discussed by the experts and summarised in the addendum (December 2006). They were considered to be delayed normal thymic involution, but treatment-related, and taken into account for the setting of the NOAEL.

The dog is the most sensitive species and therefore the ADI should be derived on the basis of the 1-year dog study. A safety factor of 100 will be applied.
The proposed ADI is:

ADI = 12 mg/kg bw/day / 100 = **0.12 mg/kg bw/day**.

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

At the last EU evaluation no acute reference dose was proposed. Although liver was the target organ in the short and long term studies, also body weight and -gain were affected. In the teratogenicity study in rats ([redacted]2) daily body weight data were reported. This show that already on day 8 (2 days after dosing had started) and onwards the maternal body weight was statistically significant reduced at 500 and 750 mg/kg bw/day. Also the body weight gain was statistically reduced in the treatment period in the mid and high dose groups. The maternal NOAEL of this particular study was 250 mg/kg bw/day. Body weight and body weight gain were not affected in the older teratogenicity study in rats ([redacted], 1984). In the rabbit teratogenicity study ([redacted], 2002) body weight was not statistically reduced, but body weight gain in the treatment period (day 6-29) was statistically significant reduced at the high dose of 700 mg/kg bw/day. Also in the older rabbit teratogenicity study ([redacted], 1982) statistically significant reduced body weight gain was seen in the beginning of the treatment period (day 6-18) in the high dose group. Bodyweight and body weight gain is therefore considered an adequate end-point to determine ARfD.

The proposed ARfD is:

ARfD = 250 mg/kg bw/day / 100 = **2.5 mg/kg bw/day**.

2.6.10.3 Toxicological end point for assessment of occupational, bystander and residents risks – AOEL (acceptable operator exposure level)

In the short-term studies, the target organ was the liver predominantly with liver weight changes, elevation of serum cholesterol and changes in hepatocytes. Some transient anemia was observed in dogs.

As clomazone is not carcinogenic, not toxic to reproduction or a developmental toxicant the most relevant study to be chosen as a basis for setting the AOEL seems to be the 1 year dog study which has the lowest relevant NOAEL (~12 mg/kg bw/day). No 90-day dog study was available.

A safety factor of 100 will be applied, as the substance has no serious short-term or long-term effects.

No correction for oral absorption of clomazone is necessary, since the value is greater than 80%.

The proposed AOEL is:

AOEL = 12 mg/kg bw/day / 100 = **0.12 mg/kg bw/day**.

2.6.10.4 Toxicological end point for assessment of occupational, bystander and residents risks – AAOEL (acute acceptable operator exposure level)

Clomazone is of moderate acute oral toxicity. Clinical signs of toxicity were many. Although liver was the target organ in the short and long term studies, also body weight and -gain were affected. In the teratogenicity study in rats [redacted], 2002) daily body weight data were reported. This show that already on day 8 (2 days after dosing had started) and onwards the maternal body weight was statistically significant reduced at 500 and 750 mg/kg bw/day. Also the body weight gain was statistically reduced in the treatment period in the mid and high dose groups. The maternal NOAEL of this particular study was 250 mg/kg bw/day. Body weight and body weight gain were not affected in the older teratogenicity study in rats [redacted], 1984). In the rabbit teratogenicity study ([redacted], 2002) body weight was not statistically reduced, but body weight gain in the treatment period (day 6-29) was statistically significant reduced at the high dose of 700 mg/kg bw/day. Also in the older rabbit teratogenicity study ([redacted], 1982) statistically significant reduced body weight gain was seen in the beginning of the treatment period (day 6-18) in the high dose group. Bodyweight and body weight gain is therefore considered an adequate end-point to determine AAOEL.

The proposed AAOEL is:

AAOEL = 250 mg/kg bw/day / 100 = **2.5 mg/kg bw/day**.

2.6.11 Summary of product exposure and risk assessment

FMC Clomazone 360 CS: With LD_{50} values greater than 5000 mg/kg bw/day and a LC_{50} value of 5.21mg/L, the product was of low oral, inhalation and dermal toxicity. It was not a skin or eye irritant in rabbits. Neither was it a skin sensitiser in a LLNA study.
No dermal absorption study was provided. Default dermal absorption values of the Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665) were proposed by the Applicant and used for exposure assessment.
In accordance with the risk envelope approach the use in oilseed rape has been used in the exposure assessment. The outdoor, downward spraying scenario has been chosen for the use in oilseed rape. The operator exposure amounts to 127% of the AOEL without the use of PPE and 78% of the AOEL with the use of PPE. The operator exposure amounts to 38% of the AAOEL without the use of PPE. Thus, the acute and non-acute exposure of operators is acceptable.
The exposure amounts to 32% of the AOEL (All pathways (mean)) for the child resident and 10% of the AOEL (All pathways (mean)) for the adult resident. The exposure of the child and adult bystander is below 1.5% of the AAOEL for all of the pathways. Thus, the resident and bystander exposure is acceptable.
The inspection and irrigation scenario has been chosen for the use in oilseed rape. The worker exposure amounts to 94% of the AOEL and 11% of the AOEL considering the use of workwear. Thus, the worker exposure is acceptable. No waiting periods required.

ALB 36 CL: The product was of low oral and dermal toxicity with LD_{50} values greater than 2000 mg/kg bw/day. It was not possible to generate a test atmosphere in the inhalation toxicity study. Therefore, the calculation method has been used to predict the inhalation toxicity. With an ATE_{mix} greater than 5 mg/L, ALB 36 CL was not considered an inhalation toxicant. The product was not a skin or eye irritant in rabbits. Neither was it a skin sensitizer. It should be indicated on the label that the product contains benzisothiazolinone.

No dermal absorption study was provided. Default dermal absorption values of the Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665) were proposed by the Applicant and used for exposure assessment.
In accordance with the risk envelope approach the use in oilseed rape has been used in the exposure assessment. The outdoor, downward spraying scenario has been chosen for the use in oilseed rape. The operator exposure amounts to 126% of the AOEL without the use of PPE and to 77% of the AOEL with the use of PPE. The operator exposure amounts to 38% of the AAOEL without the use of PPE. Thus, the acute and non-acute exposure of operators is acceptable.
The exposure of the child and adult bystander is below 1.1% of the AAOEL for all of the pathways. The exposure amounts to 30% of the AOEL (All pathways (mean)) for the child resident and 10% of the AOEL (All pathways (mean)) for the adult resident. Thus, the resident and bystander exposure is acceptable.
The inspection and irrigation scenario has been chosen for the use in oilseed rape. The worker exposure amounts to 93% of the AOEL and 9% of the AOEL considering the use of workwear. Thus, the worker exposure is acceptable. No waiting periods required.

2.7 RESIDUE

2.7.1 Summary of storage stability of residues

Plants
In the DAR (2005) storage stability was determined in several commodities and both task forces rely on the conclusion from the DAR. RMS has re-evalauted all the studies from the DAR. In addition, Task force FMC Chemical, sprl and ADAMA Agan Ltd have submitted new studies and all the studies are summarized below in table 2.7.1-1.

Table 2.7.1-1 Overview of storage stability data for clomazone

Matrix	Fortification level (mg/kg)	Storage stability period	Reference
Task force FMC Chemical, sprl and ADAMA Agan Ltd and Task force Oxon, Albaugh, Sapec			
Corn grain	0.5	24 months	Chen, A.W. & Wendt, H.R., 1992
Silage	0.5	24 months	
Stover	0.5	24 months	
Soybean	0.2	6 months	Witkonton, M. et al., 1984
Green tobacco	0.5	6 months	
Cured tobacco	0.5	6 months	
Soybean	0.2	40 months	Arabinick, J.R., 1987
Green tobacco	0.5	39 months	
Cured tobacco	0.5	39 months	
Cottonseed	0.2	15 months	
Cottonseed	0.2	25 months	Arabinick, J.R. , 1988
Task force FMC Chemical, sprl and ADAMA Agan Ltd			
Sugar cane	0.5	15 months	Arabinick, J.; Chen, A. 1999
Molasses	0.5	15 months	
Refined sugar	0.5	Not possible to determine	
Peas	0.05	9 months	Burgert, K., 2008
Potato tubers	0.1	6 months	Fiedler, E., 2007
Rape seeds	0.1	6 months	
Rape seeds (stability 1)	0.1	32 days	Lefresne, S., 2009a
Rape seeds (stability 2)	0.1	Not possible to determine	
Rape, whole plant	0.1	124 days	

Matrix	Fortification level (mg/kg)	Storage stability period	Reference
Potato tubers	0.1	197 days	Lefresne, S., 2009b

For rape seed the results are contradicting. The study by Lefresne (2009a) shows that the stability is very short, namely about 1 month while in the study by Fiedler (2007) the storage stability is shown to be at least 6 months. The analytical methods used in the two studies are not the same but both methods are validated according to SANCO 825/00 rev. 1. Since the storage stability of other oily commodities (soybean and cottonseed) are respectively 6 months and 25 months RMS think that it is most likely that the stability of clomazone in rape seed also is at least six months. RMS therefore is of the opinion that the evaluation of storage stability in rape seed should be based on the study conducted by Fiedler so the storage stability of rape seed is at least 6 months.

For soybean the storage stability is based on Witkonton et al, (1984) while it for cottonseed is based on Arabinick, 1988 (see the table above).

In potatoes the storage stability is at least 6

months. Animal products
No studies are submitted and no studies are necessary. Residues in feeding items are < 0.01 mg/kg and calculated dietary burden is < 0.004 mg/kg bw so no metabolism studies or feeding studies are necessary. Both task forces rely on this conclusion.

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

Plants
In the DAR (2005) metabolism in plants were studied in several commodities. In the EFSA opinion from 2011 it was concluded:
The metabolism was considered to be similar for the different crops and timings of application. The most abundant plant metabolite is 2-chlorobenzyl alcohol (10 – 48% TRR). The parent compound was almost completely degraded and, if present, only at low levels (0.3 – 4% TRR). In the framework of former evaluations (EFSA, 2007, 2009a), the relevant residue was defined by default as clomazone only since the representative uses and the proposed GAP for rice led to insignificant amounts of clomazone and 2-chlorobenzyl alcohol in food and feed items (i.e. below the trigger value of 10 % or 0.01 mg/kg).

Both task forces rely on this conclusion.

In addition Task force FMC Chemical, sprl and ADAMA Agan Ltd has submitted two new studies in respectively oil seed rape and potatoes.

Three days after sowing, OSR was treated with either [phenyl-U-^{14}C]-clomazone or [isoxazolidine-3-^{14}C]-clomazone at 0.12 kg as/ha. TTR was very low namely ≤ 0.0112 mg/kg for seeds and ≤ 0.060 mg/kg for forage. The metabolism of clomazone in OSR results in the separation of the isoxazolidine and phenyl rings. This probably occurs by hydroxylation of the methylene bridge to generate the unstable carbinolamide that decomposes to yield dimethyl isoxazolidinone (DMI) and 2-chlorobenzaldehyde. The aldehyde may be further reduced to the corresponding alcohol or oxidized to the carboxylic acid. The former seems to be major route in OSR. These compounds could be conjugated to glycosides or amino acids but the majority of conjugates were glycosidic. The principal metabolites of clomazone were 2-chlorobenzyl alcohol (mostly conjugated) and dimethyl isoxazolidinone (DMI) and minor metabolites included 5′-hydroxyclomazone, 2-chlorobenzoic acid and 2-chlorobenzaldehyde.

Potatoes were treated pre-emergence application [Ph-U-^{14}C]-clomazone or [isoxazolidine-3-^{14}C]-clomazone at a nominal rate of 0.09 kg a.i./ha. TRR was found to be very low (≤ 0.0020 mg/kg) in the tubers at harvest. Due to the very low levels it was not possible to analyse these samples and thus samples of haulm were analysed to provide some indication of the nature of the metabolism occurring

in the plants. It was concluded that the major components of the extractable residue were likely to be parent clomazone and polar material.

Task force FMC Chemical, sprl and ADAMA Agan Ltd has submitted a confined rotational metabolism study. Overall, it was concluded that all metabolites found in this confined rotational crop study were also detected in primary crop metabolism.

Animal products
Not necessary since no residues are expected in animal products. Residues in feeding items are < 0.01 mg/kg and the calculated dietary burden is < 0.004 mg/kg bw. Studies on the metabolism in poultry and ruminants were evaluated during the first EU review but considered as not acceptable by RMS Denmark and none of the studies were included in the list of references relied on in the DAR (2005). Both task forces rely on this conclusion.

2.7.3 Definition of the residue

Plants
In primary crop metabolism studies 2-chlorobenzyl-alcohol or OCB-alcohol (FMC 61569) is found to be the major metabolite in nearly all plant parts but it is not found in rats. In the 1st EU review, a question was raised concluding that insufficient toxicological data and information on OCB-alcohol was available. A few toxicological studies performed with 2-chlorobenzyl-alcohol were evaluated in an addendum from RMS Denmark. The conclusion from RMS Denmark was that 2-chlorobenzyl-alcohol was considered to be a toxicological non-relevant plant metabolite.

In the EFSA reasoned opinion (2011) it was concluded that overall, sufficient data are available to conclude that it is not necessary to include OCB alcohol in the risk assessment for clomazone. 2-chlorobenzyl-alcohol has a low acute oral toxicity and mutagenicity assays demonstrate the lack of a genotoxic potential.

Both task forces rely on this conclusion and both task forces have also further argued for the non-relevance (see B.7.8.1).

Also hydroxyl derivates are found in higher amounts than 0.01 mg/kg or 10% of the TRR but these are considered to be less toxic than clomazone due to that they are more polar in nature.

The residue definition for monitoring and risk assessment is therefore proposed to be: Clomazone.

The metabolism in rotational crops is similar to that in primary crops and the metabolites are not found in higher amounts. Therefore, the proposed residue definitions also cover rotational crops.

Animal products
Not necessary. No residues are expected in animals.

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

The critical GAPs are shown in table 2.7.4-1 below.

Table 2.7.4-1. Critical GAPs for the intended uses on potatoes and oilseed rape

Crop/Applicant	**Country / Region**	**Indoor / outdoor**	**Application**				**PHI days**
			Method (timing / BBCH stage)	Max. rate g a.s./ha a) per appl. b) per season	Water L/ha	Maximum number a) per use b) per season	
Potatoes Oxon, Albaugh, Sapec	CEU SEU	Outdoor	Pre-emergence (BBCH 01-08)	108	200 - 500	a) 1 b) 1	F

Crop/Applicant	Country / Region	Indoor / outdoor	Application				PHI days
			Method (timing / BBCH stage)	Max. rate g a.s./ha a) per appl. b) per season	Water L/ha	Maximum number a) per use b) per season	
Potatoes FMC,Adama	NEU SEU	Outdoor	Pre-emergence (BBCH 01-09)	90	150-400	a) 1 b) 1	F
OSR, Oxon, Albaugh, Sapec	CEU SEU	Outdoor	Pre-emergence (BBCH 01-08)	119	200-400	a) 1 b) 1	F
OSR FMC, Adama	NEU SEU	Outdoor	Pre-emergence (BBCH 00-09)	120	150-400	a) 1 b) 1	F

F = PHI determined by growth stage

All residues in the trials are < 0.01 mg/kg for both commodities. Trials have been evaluated in the DAR (2005) and both task forces rely on these studies. In addition task force FMC Chemical, sprl and ADAMA Agan Ltd has submitted new residue trials for both potatoes and oilseed rape while task force Oxon, Albaugh, Sapec has submitted new residue trials on oilseed rape. Due to that all residues are < 0.01 mg/kg results are not divided into NEU or SEU results.

The results are summarised in table 2.7.4-2 below.

Table 2.7.4-2. Summary of results for clomazone residue from trials in potatoes and oilseed rape

Crop	Residues (mg/kg)	STMR (mg/kg)	HR (mg/kg)
Potato	Both task forces: < 0.01 (17) FMC/Adama: <0.01 (20)	< 0.01	< 0.01
Oilseed rape	Both task forces: < 0.01 (25) FMC/Adama: <0.01 (20) Oxon, Albalugh, Sapec: < 0.01 (6)	< 0.01	< 0.01

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

Not necessary. It has been calculated that the expected dietary burden of animals is < 0.004 mg/kg bw.

2.7.6 Summary of effects of processing

No studies submitted and no studies are necessary since all residues are <0.01 mg/kg and because the exposure amounts to < 10% of the ADI (see 2.7.9).

2.7.7 Summary of residues in rotational crops

Task force FMC Chemical, sprl and ADAMA Agan Ltd

Radish, lettuce and barley were sown as rotational crops to tobacco treated with 360 g clomazone/ha. The studies were conducted both in NEU and SEU. The crops were sowed at different times (31-263 DAT) and harvested at maturity. All residues were < 0.01 mg/kg in leaves and roots of radish, leaves from lettuce and grain and straw from barley.

Task force Oxo, Albaugh, Sapec
This task force relies on the conclusion from the DAR and EFSA conclusion (2007). Due to that all residues < 0.01 mg/kg no studies are necessary.

2.7.8 Summary of other studies

As the supported representative uses of clomazone on potato or oilseed rape involve pre-emergence product application to bare soil, exposure to honey bees by any route will be negligible. This is

supported by the primary crop metabolism data. Besides, potato flowers do not produce nectar.

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

TMDI

TMDI has been calculated using EFSA PRIMo vers. 2. As input values were used the proposed MRLs for potatoes and rape seed of 0.01 mg/kg. For all other commodities the current MRLs are used as input values. The results are shown in table 2.7.9-1. As can be seen from the table the highest exposure is for UK infants and amounts to < 1% of the proposed ADI of 0.12 mg/kg bw/day. No refined calculation of the chronic exposure has been performed.

Table 2.7.9-1. Exposure assessment for clomazone with proposed and current MRLs as input values.

Prepar e workbook for refined calculations

Status of the active substance:	Code no.
LOQ (mg/kg bw):	proposed LOQ:

Toxicological end points

ADI (mg/kg bw/day):	**0,12**	ARfD (mg/kg bw):	**2,5**
Source of ADI:		Source of ARfD:	
Year of evaluation:		Year of evaluation:	

Undo refined calculations

Explain choice of toxicological reference values.

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 - 1

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)
0,6	UK Infant	0,3	PRODUCTS OF ANIMAL ORIGIN	0,1	SUGAR PLANTS	0,0	Root and tuber vegetables	
0,6	UK Toddler	0,2	PRODUCTS OF ANIMAL ORIGIN	0,2	SUGAR PLANTS	0,0	OILSEEDS AND OILFRUITS	
0,6	FR toddler	0,4	PRODUCTS OF ANIMAL ORIGIN	0,1	Root and tuber vegetables	0,0	CEREALS	
0,6	NL child	0,3	PRODUCTS OF ANIMAL ORIGIN	0,1	Pome fruit	0,1	Root and tuber vegetables	
0,5	DE child	0,2	PRODUCTS OF ANIMAL ORIGIN	0,1	Pome fruit	0,0	CEREALS	
0,4	WHO Cluster diet B	0,1	CEREALS	0,1	PRODUCTS OF ANIMAL ORIGIN	0,1	OILSEEDS AND OILFRUITS	
0,4	FR infant	0,2	PRODUCTS OF ANIMAL ORIGIN	0,1	Root and tuber vegetables	0,0	Pome fruit	
0,4	DK child	0,2	PRODUCTS OF ANIMAL ORIGIN	0,1	CEREALS	0,0	Root and tuber vegetables	
0,3	SE general population 90th percentile	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	Root and tuber vegetables	0,0	CEREALS	
0,3	ES child	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	CEREALS	0,0	TEA, COFFEE,	
0,3	IE adult	0,1	CEREALS	0,0	PRODUCTS OF ANIMAL ORIGIN	0,0	Root and tuber vegetables	
0,3	WHO cluster diet E	0,1	PRODUCTS OF ANIMAL ORIGIN	0,1	CEREALS	0,0	Root and tuber vegetables	
0,3	WHO cluster diet D	0,1	CEREALS	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	Root and tuber vegetables	
0,2	WHO regional European diet	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	Root and tuber vegetables	0,0	CEREALS	
0,2	WHO Cluster diet F	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	CEREALS	0,0	Root and tuber vegetables	
0,2	NL general	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	Root and tuber vegetables	0,0	CEREALS	
0,2	UK vegetarian	0,0	SUGAR PLANTS	0,0	PRODUCTS OF ANIMAL ORIGIN	0,0	OILSEEDS AND OILFRUITS	
0,2	ES adult	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	CEREALS	0,0	Citrus fruit	
0,2	UK Adult	0,0	PRODUCTS OF ANIMAL ORIGIN	0,0	SUGAR PLANTS	0,0	OILSEEDS AND OILFRUITS	
0,2	PT General population	0,0	CEREALS	0,0	Berries & small fruit	0,0	Brassica vegetables	
0,2	FR all population	0,0	PRODUCTS OF ANIMAL ORIGIN	0,0	Berries & small fruit	0,0	CEREALS	
0,1	DK adult	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	CEREALS	0,0	Root and tuber vegetables	
0,1	IT kids/toddler	0,1	CEREALS	0,0	Fruiting vegetables	0,0	Pome fruit	
0,1	LT adult	0,0	PRODUCTS OF ANIMAL ORIGIN	0,0	Root and tuber vegetables	0,0	CEREALS	
0,1	FI adult	0,1	PRODUCTS OF ANIMAL ORIGIN	0,0	CEREALS	0,0	Root and tuber vegetables	
0,1	IT adult	0,0	CEREALS	0,0	Fruiting vegetables	0,0	Pome fruit	
0,1	PL general population	0,0	Root and tuber vegetables	0,0	Pome fruit	0,0	Fruiting vegetables	

Conclusion:

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

IESTI

An ARfD of 2.5 mg/kg bw has been proposed. The acute exposure has been calculated with the proposed MRLs of 0.01 mg/kg for potatoes and rapeseed as input values. As can be seen from table 2.7.9-2 the acute exposure is below 0.062% of the ARfD for both commodities.

Table 2.7.9-2. Acute exposure assessment for clomazone for potatoes and rape seed

	Acute risk assessment /children - refined calculations						Acute risk assessment / adults / general population - refined calculations					
	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)
	0,062	Potatoes	0,01 / -	0,0	Potatoes	0,01 / -	0,0	Potatoes	0,01 / -	0,0	Potatoes	0,01 / -
	0,000	Rape seed	0,01 / -	0,0	Rape seed	0,01 / -						

2.7.10 Proposed MRLs and compliance with existing MRLs

Potatoes

All residues in the residue studies are < 0.01 mg/kg. Therefore it is proposed to set a MRL of 0.01* mg/kg for clomazone in potatoes

Oilseed rape

All residues in the residue studies are < 0.01 mg/kg. Therefore it is proposed to set a MRL of 0.01* mg/kg for clomazone in rape seed. The current MRL is 0.02* mg/kg but the LOQ of the methods used in the residue trials is 0.01 mg/kg so a MRL of 0.01* mg/kg can be enforced.

Animal products

No residues are expected in animal commodities and MRLs have therefore not been proposed . The MRL can be set to 0.01* mg/kg.

2.7.11 Proposed import tolerances and compliance with existing import tolerances

No import tolerances exist or are asked for in relation to this evaluation.

2.8 FATE AND BEHAVIOUR IN THE ENVIRONMENT

2.8.1 Summary of fate and behaviour in soil

2.8.1.1 Route of degradation in soil

Data on the route of degradation in soil is presented in Volume 3 – B.8 (AS) section B.8.1.1.1.

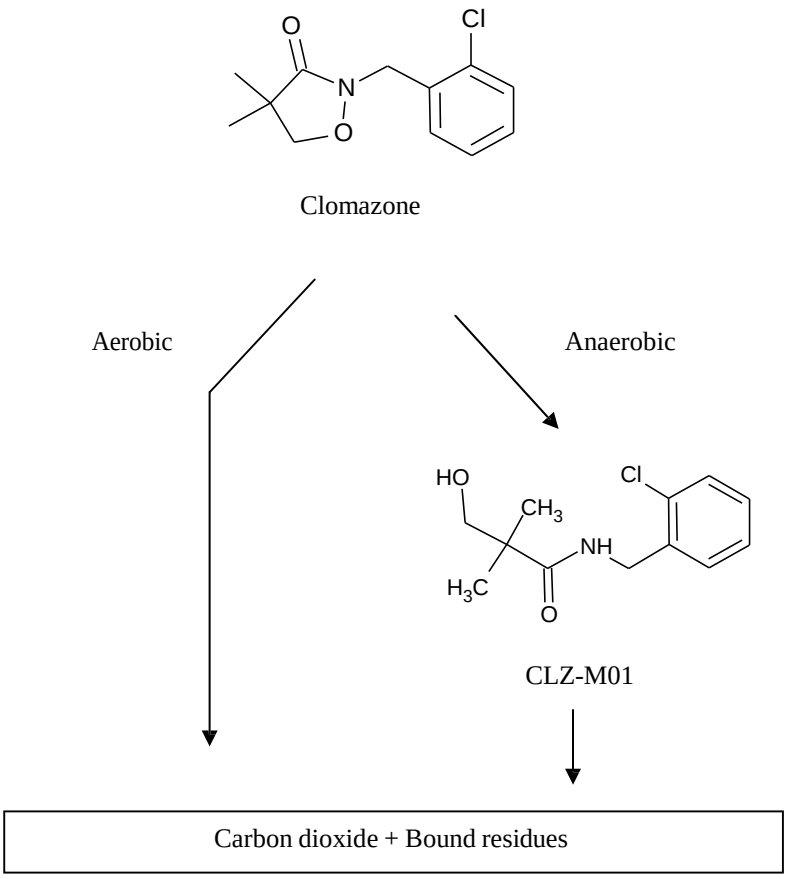
The route of degradation of clomazone has been described in the Draft Assessment Report (DAR, 2007) for the Annex I Inclusion. New studies have been submitted by the Notifiers in the dossiers for the renewal assessing the route of degradation of clomazone.

Under **aerobic soil** conditions, clomazone degrades in soil independent of soil pH without formation of any major metabolite. The data presented suggests that clomazone metabolism in aerobic soils involves cleavage of the isoxazolidinone ring and subsequent loss of the carbonyl carbon as CO_2. This results in the formation of relatively short-lived minor metabolites, none of them exceeding 5% AR.

Under **anaerobic soil** conditions, the major metabolite CLZ-M01 (N-[(2-chlorobenzyl)]-3-hydroxy-2,2-dimethyl propanamide) was detected with a maximum level of 37.9%AR (after 60 days) in one of the old studies, which is no longer considered acceptable. Each of the two notifiers has submitted a new anaerobic degradation study. In one of these studies no major metabolites were detected. In the other study CLZ-M01 was detected at a level of 24.99 % AR (n = 1) at day 120.

Soil photolysis experiments show, that sunlight irradiation did not result in any significant degradation of clomazone, without forming any metabolites exceeding 5% AR.

The proposed metabolic pathway for clomazone in aerobic and anaerobic soil is shown below:



2.8.1.2 Rate of degradation in soil

Data on the rate of degradation in soil is presented in Volume 3 – B.8 (AS) section B.8.1.1.2.

Data on the aerobic degradation rate of clomazone in soil were previously submitted by the original notifier FMC and evaluated in context of the first EU review of clomazone. The rates of degradation (DT_{50} and DT_{90} values) of clomazone in soil were calculated from one soil metabolism study and two additional laboratory experiments. All other submitted route studies (non-valid route studies from the last EU review), providing six DT_{50} values, were not accepted during the last EU review because of few sampling dates or low recoveries and/or too high experimental temperature. These studies are still considered unacceptable.

The original degradation rates presented in the study reports were re-calculated by the RMS of the last EU review at that time using SFO kinetics, following the recommendations of FOCUS kinetic guidance at that time. Non-normalised DT_{50} values at 20-25 °C ranged from 26.7 to 152.8 days and were cited in the EFSA Scientific Report (July 2007) 109, 1-73. Although reliable degradation rates from only 3 soils were available, despite the 4 required, the experts concluded that in this case the information was sufficient as a number of field studies were available to clarify the fate of clomazone in soil. Consequently, it was agreed that the longest DT_{50} value of 167.6 days (normalised to 20 ºC and soil moisture content of pF 2) was the recommended input value for PEC calculations.

New studies on the aerobic rate of degradation of clomazone in soil have been generated and submitted by both notifiers for the re-evaluation. A kinetic evaluation of all reliable studies, both old and new, has been performed by the notifiers. A total of 28 reliable half-lives were calculated showing that clomazone is non-persistent to persistent. Trigger-endpoints ranged from 9.7 – 138 d for DT_{50} and 32.3 – 617 d for DT_{90}. Normalised half-lives for modelling were in the range 6.3 – 145.7 d with a geometric mean of 22.6 d (n = 28)

One of the notifiers has submitted a study on the aerobic degradation of the anaerobic metabolite CLZ-M01. This study showed rapid degradation of CLZ-M01 under aerobic conditions with a geometric mean DT_{50} of 2.0 d (n = 3).

A number of field studies were available from the first evaluation of clomazone, and some of these are still considered acceptable. In addition to these studies both notifiers have submitted new field studies. The field degradation studies are presented in Volume 3 – B.8 (AS) section B.8.1.1.2.2.

A kinetic evaluation and normalisation of all field studies according to the newest FOCUS guidance has been performed. A total of 28 reliable trigger endpoints could be derived showing that clomazone is non-persistent to persistent. Trigger DT_{50} was 3 – 195 d and trigger DT_{90} was 65.4 – 645 d. With regard to reliable, normalised half-lives 19 could be derived. These ranged from 9.3 – 65.3 d with a geometric mean of 27.3 d.

No field data was generated for the metabolite CLZ-M01.

As the laboratory and field degradation endpoints are not from two different populations according to EFSA guidance the combined laboratory and field endpoints should be used for modelling. The geometric mean of all laboratory and field modelling endpoints is 24.4 d.

Each of the two notifiers provided a study with one soil on the rate of degradation of clomazone under anaerobic conditions. One study gave a DT_{50} of 39.1 d, the other >1000 d.

One of the notifiers provided a study with one soil on the rate of degradation of the metabolite CLZ-M01 under anaerobic conditions. This gave a DT_{50} of 600 d.

Both notifiers provided studies on photolytic degradation on soil. Half-lives between 337 d and 996 d were found. It was concluded that photolysis was not a major degradation process for clomazone in/on soils.

2.8.1.3 Adsorption and desorption in soil

Data on adsorption and desorption in soil is presented in Volume 3 – B.8 (AS) section B.8.1.2.

A soil adsorption/desorption study on clomazone using 4 different soil types was available from the last EU review. The results indicated that clomazone is moderately to slightly mobile in soil (K_{foc} = 139-608 mL/g, geomean = 241 mL/g). This study was not considered acceptable anymore as it overestimated the sorption. The same was the case with the open literature study submitted by one of the notifiers.

Three additional batch equilibrium studies, with a total of 20 soils, have been provided by one of the notifiers. These were all acceptable and demonstrated that clomazone is mobile to moderately mobile with K_{foc} from 33 mL/g to 317 mL/g. The geometric mean was 128.31 mL/g and the arithmetic mean was 151.33 mL/g. The Freundlich coefficient varied between 0.81 and 0.99 with a geometric mean of 0.89.

One of the notifiers provided a study on the sorption of the metabolite CLZ-M01 which showed it to be mobile in soil. The geometric mean K_{doc} was 29.3 mL/g with a range of 26.2 – 33.0 mL/g.

2.8.1.4 Mobility in soil

Data on mobility in soil is presented in Volume 3 – B.8 (AS) section B.8.1.3.

Column leaching studies are not required. However, studies are available from the first EU evaluation and one of the notifiers submitted an additional study. Some of the old studies are not acceptable anymore.

The new study is acceptable and shows that most of the Clomazone applied was extracted from the soil from the columns. Small amounts of Clomazone was detected in all leachate samples with an increase noted in the day 2 leachate sample, accounting for up to 7% of the total recovered. Metabolites were not detected in any leachate or soil sample from the columns.

The study on aged sorption is likely to be acceptable. The study shows that in total 2.0-2.9% AR, were detected in the leachates of the two test columns. Leachate analysis showed that none of the compounds were either clomazone or the primary metabolite. The radioactivity was found around the origin of the TLC plates, indicating that residues were unidentified polar compounds or natural, higher molecular-weight soil components. Another likely possibility is sorption to organic colloids, and perhaps clay mineral colloids.

It should be noted that the concentrations of ^{14}C in the leachate in the study are much higher than in the experiments without ageing prior to soil column leaching.

2.8.2 Summary of fate and behaviour in water and sediment [equivalent to section 11.1 of the CLH report template]

2.8.2.1 Rapid degradability of organic substances

Table 23: Summary of relevant information on rapid degradability

Method	Results*	Key or Supportive study	Remarks	Reference
OECD 301 D for testing of chemicals (adopted July 17, 1992)	The maximum degradation of Clomazone (purity 92.7 %) + inoculum was reached after 21 days, culminating in a biological oxygen demand of 1.06 mg/l (14% degradation). In the inoculum control vessels, the O_2-depletion increased to 1.89 mg/l at day 28. In the reference control vessels containing sodium acetate + inoculum, a maximum of 7.89 mg/l oxygen was depleted after 21 days. The minimum degradation rate in the toxicity control was reached at day 14, resulting in 0.49 mg/l oxygen demand (46% degradation). Clomazone must be regarded as not readily biodegradable. The biodegradation of the reference substance was not inhibited by the test substance.		**Acceptable**	Noack, M., 2002. Clomazone technical: Ready biodegradability closed bottle test.
OECD 301 D for testing of chemicals (adopted July 17, 1992)	The ready biodegradability of clomazone (purity 99.7 %) was assessed by measurement of dissolved oxygen (DO) concentration under standard conditions according to OECD guideline 301 D. The percentage biodegradation of clomazone at Day 28 was 0%. Clomazone cannot, therefore, be considered to be readily biodegradable. The mean specific biochemical oxygen demand (sBOD) for the blank controls was < 1 mg/L at Day 28, therefore meeting the criterion of not exceeding 1.5 mg/L in 28 days. The mean corrected sBOD for the test vessels containing clomazone remained at < 1 mg/L over the period of the study. The sBOD values for the reference and toxicity control vessels were comparable and increased to 6 mg/L at 28 days.		**Acceptable**	Graham, R., 2008. Clomazone: Assessment of ready biodegradability by measurement of oxygen uptake in the closed bottle test.
OECD 301 D for testing of chemicals (adopted July 17,	The ready biodegradability of clomazone (purity 96.6 %) was assessed by measurement of oxygen consumption in a manometric respirometry test according to OECD		**Acceptable**	Dickinson, R.A., 2008. Clomazone: Assessment of ready biodegradability by respirometry.

Method	Results*	Key or Supportive study	Remarks	Reference
1992)	guideline 301 F. The percentage biodegradation of clomazone at Day 13 was 2% of the theoretical value (25 mg O_2/500 mL). Therefore, clomazone should be considered as non-readily biodegradable.			
OECD 301 D for testing of chemicals (adopted July 17, 1992)	The biodegradability of clomazone (purity 98.3 %) was assessed using 2 mg/L solutions in a mineral medium, inoculated with secondary effluent from a sewage treatment plant. Degradation was assessed by measuring the dissolved oxygen concentration and the reduction in dissolved oxygen was compared to the theoretical oxygen demand to obtain percentage degradation. A positive control using sodium benzoate at the same concentration was used as a reference item under the same conditions, to demonstrate the microbial activity of the effluent. Degradation of the reference item was also determined with the addition of clomazone to check for inhibition effects. Degradation of clomazone was only 1.0% after 28 days. Degradation was far less than 60% in the 28 days and clomazone was found to be not readily biodegradable. The positive control showed 83.4% degradation after 14 days, demonstrating the validity of the system. The addition of clomazone to the positive control did not inhibit the degradation of the reference item.		**Acceptable**	D. Dengler (2010) Assessment of the ready biodegradability of clomazone TC with the closed bottle test.

** data on full mineralization should be reported*

2.8.2.1.1 Ready biodegradability

Data on the ready biodegradability is presented in Volume 3 – B.8 (AS) section B.8.2.2.1.

Data on the ready biodegradability of clomazone is available from the first EU Review. Clomazone was found to be not readily biodegradable in water.

In addition new ready biodegradability studies with clomazone have been generated and submitted by both notifiers. The studies confirm the non-readily biodegradability of clomazone.

2.8.2.1.2 BOD5/COD

In a study from the first evaluation a non-corrected BOD of 0.88 – 1.06 mg O_2/L was reported. From a new study a corrected BOD of 0.07 mg O_2/L was reported.

2.8.2.2 Other convincing scientific evidence

2.8.2.2.1 Aquatic simulation tests

No information.

2.8.2.2.2 Field investigations and monitoring data (if relevant for C&L)

No information.

2.8.2.2.3 Inherent and enhanced ready biodegradability tests

See 2.8.2.1.1.

2.8.2.2.4 Soil and sediment degradation data

Data on water-sediment studies is presented in Volume 3 – B.8 (AS) section B.8.2.2.3.

Data on the aerobic transformation of clomazone in aquatic sediment systems were submitted and evaluated in context of the first EU review of clomazone. A study to investigate the dissipation of clomazone in two water/sediment systems (sediment organic carbon content: 0.1% and 6.7%) is available from the first EU review, which was performed with radiolabelled clomazone. Clomazone degraded to concentrations of approximately 18% AR and 37% AR, with negligible amounts detected in sediment (< 3.0% AR). A maximum mineralisation of 7.2% AR was measured at the end of the study (100 days). One major metabolite was detected in the water phases, identified as CLZ-M01 (also referred to as FMC 65317 in the first EU review) and reaching maximum amounts of 24.9% AR and 28.1% AR at day 61. In the sediment phase CLZ-M01 was measured at levels < 4.5% AR. A second metabolite, CLZ-M02 (also referred to as FMC 55657 in the first EU review), was shown to occur at maximum concentrations of 11.6-11.8% AR (100d) in the water phase and < 4% AR in sediment. In view of the very low amounts of clomazone dissipated to sediment, 1st order DT_{50} were calculated only for the whole systems (40.4 days and 66.9 days). In line with the FOCUS kinetic guidance at that time, the experts agreed on the use of the mean value of 52.5 days for DT_{50} in water and a worst-case half-life of 1000 days for DT_{50} in sediment as input parameters in the modelling.

The validity and utility of the remaining study from the DAR for clomazone was questioned during the first EU review since the study was performed in paddy rice. Therefore, this study is not considered in this renewal assessment a summary of this study is given at the end of this section.

A new study has been submitted by one of the notifiers on the aerobic transformation of clomazone in water/sediment systems, and they have also performed a kinetic re-evaluation of the old study. The other notifier has not submitted any new studies, but they have performed a kinetic re-evaluation of the old study.

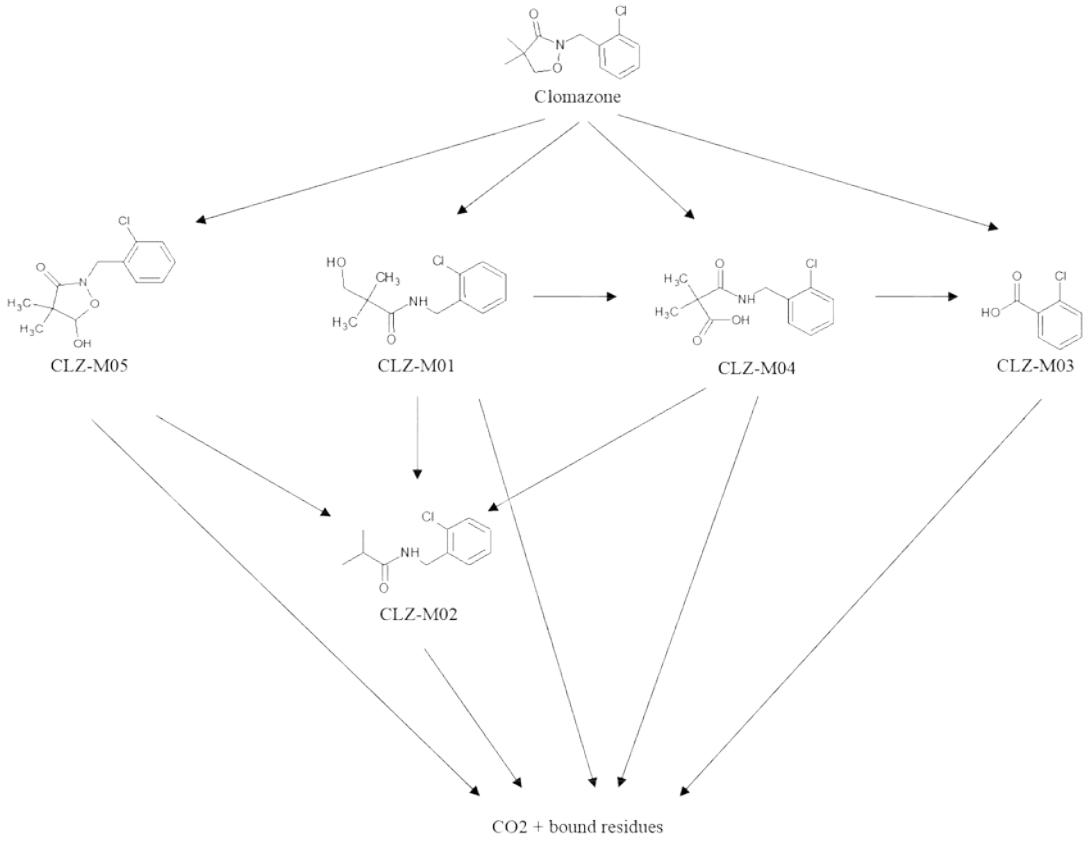
The results from the water sediment studies are summarised below.
The following metabolites were found in the water-sediment studies:

Compound	**Alternative codes**	**Compartment**	**Maximum occurrence (% AR) (time of maximum occurrence)**		
			Purser, 1996	**Roohi, 2011**	**Button, 2009**
Clomazone	FMC 57020	SW	96.75 (6 h)	**101.4 (day 0)**	94.3 (day 0)
		SED	2.7 (day 1)	9.58 (day 14) (> 5 % at day 14 till day 28)	**14.9 (day 7) (> 5 % at day 1 till day 30)**
CLZ-M01	FMC 65317* CHE65317, CHDMPA	SW	**28.1 (day 61) (> 5 % at day 61 till study end)**	5.9 (day 14)	6.5 (day 7) (> 5 % at day7 till day 14)
		SED	4.28 (day 30)	11 (day 91) (> 5 % at day 28 till day 120)	**16.4 (day 14) (> 5 % at day 7 till day 59)**

Compound	Alternative codes	Compartment	Maximum occurrence (% AR) (time of maximum occurrence)		
			Purser, 1996	**Roohi, 2011**	**Button, 2009**
CLZ-M02	FMC 55657*, CBMPA	SW	**11.78 (day 100) (> 5 % at day 61 till study end)**	Not detected(3	Not detected(3
CLZ-M03	FMC 14791*, OCB acid, 2-chlorobenzoic acid	SW	Not identified(2	**25.1 (day 150) (> 5 % at day 28 till study end)**	17.6 (day 30) (> 5 % at day 7 till day 59)
CLZ-M04	CADO	SW	Not identified(2	**31.7 (day 57) (> 5 % at day 14 till study end)**	Not identified(2
CLZ-M05	FMC 60217*, 5-hydroxy clomazone	SW	Not identified(2	Not identified(2	**14.7 (day 14) (> 5 % at day 7 till day 14)**

* FMC code used in the 1st EU review
(1 major metabolite: above 10 % or above 5 % on two sequential dates or above 5 % and still increasing at study end;
(2 might be detected in minor amounts, however, minor amounts were not characterised
(3 performance of co-chromatography with reference substance, however, not detected
bold values: maximum detected level throughout all studies

Proposed degradation pathway:



The following endpoints are found in the studies:

Location (study)	Compartment	Kinetic	Trigger DT_{50}	Trigger DT_{90}	Modelling DT_{50}
Mill Stream Pond (Purser, 1996, recalculated by CATF)	Total	SFO	43	143	43
	Water	SFO	42.2	140	42.2
Iron Hatch Pool (Purser, 1996, recalculated by CATF)	Total	SFO	61.8	205	61.8
	Water	SFO	61.6	205	61.6
Calwich Abbey Lake (Roohi, 2011)	Total	SFO	27.5	91.5	27.5
	Water	SFO	24.2	80.4	24.2

	Sediment	SFO	31.5	104.5	31.5
Swiss Lake (Roohi, 2011)	Total	SFO	27.2	90.3	27.2
	Water	SFO	24.7	81.9	24.7
	Sediment	HS	13.9	103	31.0
Calwich Abbey Lake (Button, 2009)	Total	SFO	11	36.7	11
	Water	SFO	7.6	25.4	7.6
	Sediment	SFO	28.6	94.6	28.6
Swiss Lake (Button, 2009)	Total	HS	12.9	79	23.8
	Water	DFOP	10.1	56.3	17
	Sediment	SFO	87.8	292	87.8

2.8.2.2.5 Hydrolysis

Data on hydrolytic degradation in water is presented in Volume 3 – B.8 (AS) section B.8.2.1.1.

Data on the aqueous hydrolysis of clomazone were previously evaluated in context of the first EU review of clomazone. In a hydrolytic degradation study performed in the dark clomazone was found to be stable under neutral, acidic and alkaline conditions. In addition, four new studies have been submitted by the two notifiers and these support the findings from the first evaluation that clomazone is hydrolytically stable.

2.8.2.2.6 Photochemical degradation

Data on photochemical degradation in water is presented in Volume 3 – B.8 (AS) section B.8.2.1.2.1.

Studies on the direct photochemical degradation in water of the active substance are only required if the compounds molar (decadic) absorption coefficient (ε) is > 10 L × mol^{-1} × cm^{-1} at a wavelength (λ) ≥ 295 nm.

Based on EU agreed UV/VIS absorption data on clomazone from the first EU review, the molar decadic absorption coefficient of clomazone for wavelengths at and above 295 nm is < 10. Therefore, no studies on the aqueous photolysis of clomazone were required during the last EU review. Additional new UV/VIS data on clomazone generated by the applicants confirm the results from the last EU review, that clomazone shows only slight (ε < 10) absorption for wavelengths ≥ 295 nm. Therefore, it was deemed that clomazone is not subject to direct photolysis.

2.8.2.2.7 Other / Weight of evidence

Data on aerobic mineralization in surface water is presented in Volume 3 – B.8 (AS) section B.8.2.2.2.

According to the data requirements set forth in the Annex to Reg. (EU) 283/2013, the aerobic mineralisation of clomazone in surface water has to be investigated following OECD guideline 309 (23 November 2004). Since this is a new data requirement, no data on the aerobic mineralisation of clomazone in surface water are available from the last EU review.

Therefore, new studies on the aerobic mineralisation of ^{14}C-clomazone according to current OECD guideline 309 have been submitted by both notifiers. Both studies demonstrated that clomazone is stable in aerobic surface water at the test conditions. Due to lack of degradation a DT_{50} could not be calculated.

2.8.3 Summary of fate and behaviour in air

Data on fate and behaviour in air is presented in Volume 3 – B.8 (AS) section B.8.3.

Volatilisation

Data on the vapour pressure of clomazone were previously submitted by the original notifier FMC and evaluated in context of the first EU review of clomazone. In the old study a vapour pressure of 1.92 × 10^{-2} Pa (extrapolated to 25 °C) was determined for clomazone which was accepted in the last EU review and included in the list of endpoints of the EFSA Scientific Report (2007) 109, 1-73, clomazone. From this, clomazone is very slightly volatile.

A new vapour pressure study was generated by CATF (FMC) after the first EU review which provided a vapour pressure of 4.72×10^{-3} Pa at 25 °C for clomazone. In addition, a new study is available from one of the notifiers. In this study, a vapour pressure of 5.04×10^{-2} Pa at 25 °C was determined.

The arithmetic mean of 2.76×10^{-2} Pa at 25 °C shows, that clomazone is very slightly volatile.

Photochemical oxidative degradation in air

Data on the photochemical oxidative degradation of clomazone in air is available from the last EU review. A DT_{50} of 0.567 d (1.5×10^6 OH-radicals/cm³ and a 12 hour day; Atmospheric Oxidation Programme V.3.1 (1994)) was calculated for the degradation of clomazone in air and the agreed endpoint cited in the EFSA Scientific Report (2007) 109, 1-73, clomazone.

A re-calculation with the latest AOPWIN model (ver. 1.92) was performed (Jackson, 2016) revealing a DT_{50} of clomazone in air of 0.487 d (12 hour day, 1.5×10^6 OH-radicals/cm³). The results confirmed the previous results from the last EU review.

Estimated atmospheric degradation rate for clomazone

AOPWIN version	1.92
Concentration of OH radicals	1.5×10^6 cm^{-3}
Time window	12 hours
k_{OH}	E^{-12} cm^3 $molecules^{-1}$ sec^{-1}
DT_{50}	0.487 days

2.8.3.1 Hazardous to the ozone layer

Due to the short half-life in air (<2 d) there are no concerns for long range transport in air and hence no concerns for the ozone layer.

Table 24: Summary table of studies on hazards to the ozone layer

Method	Results	Remarks	Reference

2.8.3.1.1 Short summary and overall relevance of the provided information on hazards to the ozone layer

See conclusion above.

2.8.3.1.2 Comparison with the CLP criteria

-

2.8.3.1.3 Conclusion on classification and labelling for hazardous to the ozone layer

Not hazardous to the ozone layer.

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

Data on monitoring is presented in Volume 3 – B.8 (AS) section B.8.5.

No monitoring data of clomazone is available from the last EU review.

Studies have been provided by the notifiers, which summarised findings from literature and subsequent public groundwater monitoring database searches as well as a follow-up field survey. Groundwater-monitoring data search efforts were focused on seven countries of interest (COIs): Belgium, Denmark, France, Germany, the Netherlands, Sweden, and the United Kingdom. Results suggested that clomazone has a low potential to be detected in groundwater when used on oil seed rape and potatoes. More than 83,000 analytical results for clomazone were identified, with just 205 (0.2%) results above the reported LOD (0.01 to 0.02 µg/L). The newly generated data supports the outcome of the groundwater risk assessment, that clomazone has a low potential for groundwater leaching for the intended GAP uses in oilseed rape and potato.

2.8.5 Definition of the residues in the environment requiring further assessment

Definition of the residue for risk assessment:

Compartment	Residue definition
Soil	Clomazone, CLZ-M01 (in anaerobic soil)
Groundwater	Clomazone, CLZ-M01 (in anaerobic soil)
Surface water	Clomazone, CLZ-M01, CLZ-M02, CLZ-M03, CLZ-M04, CLZ-M05
Sediment	Clomazone, CLZ-M01
Air	Clomazone

Definition of the residue for monitoring:

Compartment	Residue definition
Soil	Clomazone
Groundwater	
Surface water	
Sediment	
Air	

2.8.6 Summary of exposure calculations and product assessment

For the PEC calculations there are two representative products:

- FMC-Clomazone 360 CS to be used pre-emergence in potatoes at an application rate of 90 g a.s./ha and in oilseed rape at 120 g a.s./ha
- Clomazone 360 g/L to be used pre-emergence in potatoes at an application rate of 108 g a.s./ha and in oilseed rape at 119 g a.s./ha

PEC soil

Calculation for FMC-Clomazone 360 CS:

The PECsoil calculations were performed with the German model ESCAPE vers. 2 for the most critical GAP use of 'FMC-Clomazone 360 CS' represented by a single pre-emergence application of 120 g a.s./ha to oilseed rape or bare soil since no crop interception was considered. The calculations were conducted according to FOCUS (1997, 2006, 2014a).
Input values are given below:

Parameter	Compound	Value	Remarks
Model data			

Parameter	Compound	Value	Remarks
Soil depth for $PEC_{soil,1year}$ [d] (cm)		5	FOCUS recommendation
Soil depth for $PEC_{plateau}$		20	
Dry soil bulk density [bd] (g/cm^3)		1.5	
Separate consideration of residues from different applications		No	Not relevant for SFO kinetics
Compound data			
Molecular weight [MW_{par}, MW_{met}] (g/mol)	Clomazone	239.7	Phys.-chem. property
	CLZ-M01	241.7	
DT_{50} in soil (days)	Clomazone	145.7	pseudo-SFO (DFOP k_2), maximum from laboratory studies (normalised to 20 °C and pF 2)
	CLZ-M01	2.3	SFO kinetic, maximum from laboratory studies (normalised to 20 °C and pF 2)
Maximum observed fraction [f_{met}] (%)	CLZ-M01	100	conservative assumption
Application pattern			
Number of applications/year		1	according to risk envelope GAP use
Application rate (g a.s./ha)		120	
Crop interception (%)		0	pre-emergence (BBCH 00–09)

For the active substance clomazone the maximum initial $PEC_{soil,year1}$ and he maximum $PEC_{soil,accum}$ over 5 cm soil depth after many years of annually application was calculated.

For the metabolite CLZ-M01 the maximum initial $PEC_{soil,year1}$ was calculated. A calculation of the potential accumulation of CLZ-M01 in soil was not triggered.

Results were considered for the ecotoxicological risk assessment, and the PEC values are presented there.

Calculations for OAS taskforce Clomazone 360 g/L (ALB 360 CS)

Predicted environmental concentrations in soil (PEC_{SOIL}) for clomazone were calculated based on application of clomazone in accordance with the supported uses of the clomazone plant protection product (Clomazone 360 g/L CS). No major soil metabolites were observed so no PEC_{SOIL} calculations have been performed for metabolites. The calculations were performed using the equations provided in the FOCUS (1997[4]) guidance using Microsoft® Office Excel® 2013.

The clomazone soil degradation DT_{50} values from the field studies ranged from 10.3 - 195 days. The worst-case persistence/trigger DT_{50} value of 195 days (SFO kinetics) has been used in the soil PEC calculation to determine concentrations over 100 days.

Calculations were presented for the two supported uses of clomazone plant protection product (Clomazone 360 g/L CS). No crop interception was taken into account since the earliest growth stage at the time of application is BBCH 01-08.

$PEC_{plateau}$ was calculated.

Results were considered for the ecotoxicological risk assessment, and the PEC values are presented there.

PEC groundwater

Calculation for FMC-Clomazone 360 CS:
Tier 1 FOCUS PELMO 5.5.3, FOCUS PEARL 4.4.4 and FOCUS MACRO 5.5.4 PECgw were calculated for clomazone and its major anaerobic soil metabolite CLZ-M01 for the risk envelope GAP uses of 'FMC- Clomazone 360 CS' in potatoes and oilseed rape considering highest rate of application, i.e. 90 and

[4] FOCUS (1997) Soil persistence models and EU Registration - The Final Report of the Soil Modelling Workgroup of FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use) – 29 February 1997.

120 g a.s./ha, respectively. Treatments were set at the earliest possible dates of application in the year representing the time of the highest leaching potential. Since 'FMC-Clomazone 360 CS' is applied pre-emergence of the crop, no interception was taken into account.

Endpoints for sorption and degradation were based on endpoints from both notifiers. For degradation a combined geometric mean half-life for laboratory and field data was used.

The 80th percentile annual average PECgw of clomazone and CLZ-M01 at 1 m depth stayed clearly below the drinking water trigger of 0.1 µg/L for all models and all relevant FOCUS groundwater scenarios.

Thus, it can be concluded that clomazone and CLZ-M01 will not leach to groundwater to any environmentally hazardous extent under environmentally relevant conditions.

Calculations for OAS taskforce Clomazone 360 g/L (ALB 360 CS)

Simulations of the leaching behaviour of clomazone were conducted with the FOCUS groundwater scenarios in FOCUS PEARL (version 4.4.4), FOCUS PELMO (version 5.5.3) and FOCUS MACRO (version 5.5.4). The simulations were based on application of Clomazone 360 g/L CS to potatoes and oil seed rape.

A maximum of one application to potatoes (at a rate of 108 g a.s./ha) and oil seed rape (at a rate of 119 g a.s/ha) at BBCH 00-08 were simulated in accordance with the supported uses of the Clomazone 360 g/L CS formulation.

Endpoints for sorption and degradation were based on endpoints from both notifiers. For degradation a combined geometric mean half-life for laboratory and field data was used.

The predicted 80th percentile average annual concentrations for clomazone were lower than the 0.1 µg/L regulatory threshold at 1 m depth for all scenarios.

These results therefore demonstrate that Clomazone 360 g/L CS can be safely used as proposed in the EU without risk of clomazone exceeding acceptable levels in groundwater.

PEC surface water and sediment

Calculation for FMC-Clomazone 360 CS:
PECsw and PECsed calculations of clomazone and its metabolites of concern in surface water and sediment were performed in a tiered assessment with Steps 1–2 in FOCUS, FOCUS SWASH 5.3 and the SWAN tool for the risk envelope GAP uses of 'FMC-Clomazone 360 CS' in potatoes and oilseed rape. At step 3 & 4 spray-drift or drainage for the D scenarios and run-off for the R scenarios are the entry routes leading to the maximum PECsw values. Step 4 calculations were necessary for clomazone for the R3 stream scenario for the risk envelope GAP use in potatoes considering non-spraying buffer zones of 10 m width and vegetated filter strips of the same width in order to mitigate the run-off entry.

Calculations for OAS taskforce Clomazone 360 g/L (ALB 360 CS)

Predicted environmental concentrations of clomazone and its metabolites, in surface water and sediment have been generated in accordance with FOCUS guidelines, for the use of clomazone on potatoes and oil seed rape.

Concentrations of the metabolites in surface water and sediment have been generated up to Step 2. PEC_{SW} and PEC_{SED} values have been calculated up to Step 3 for clomazone.

The maximum Step 2 PEC_{SW} and PEC_{SED} values for metabolite CADO after application to potatoes were 4.6768 µg/L and 0.0467 µg/kg respectively, after application to oil seed rape (spring) were 5.1532 µg/L and 0.0515 µg/kg respectively and after application to oil seed rape (winter) 3.9571 µg/L and 0.0395 µg/kg respectively.

The maximum Step 2 PEC_{SW} values for the metabolites and Step 3 PEC_{SW} values for clomazone were less than the corresponding regulatory acceptable concentration (RAC) values, with the exception of the D2 (ditch and stream) scenarios following application to oil seed rape (winter) and the R3 (stream) scenario following application to potatoes. The D2 ditch scenario results from entry via drainage and as such is not influenced by the addition of mitigation at FOCUS Step 4. The D2 scenario is typically associated with the northern zone only, and is based on heavy clay soils (>45% clay), representing a small percentage of soil type and so would not be applicable for the majority of countries.

The R3 (stream) scenario following application to potatoes shows that runoff is the main route of aquatic exposure to clomazone, therefore further simulations at Step 4 were performed using a 10 metre spray drift and runoff buffer zone. Refinement at Step 4 reduced the maximum PEC_{SW} value.

PEC air

Calculation for FMC-Clomazone 360 CS:

Short-range transport:

The EU agreed vapour pressure of clomazone is 1.92×10^{-2} Pa at 25 °C (9.99×10^{-3} Pa at 20 °C). From this, clomazone is classified as volatile substance and its short-range transport potential has to be considered from plant and soil surfaces. Since for the envisaged GAP use of 'FMC-Clomazone 360 CS' clomazone is applied only pre-emergence, volatilisation from plant surfaces is not of relevance.

Laboratory volatility experiments have shown that the sum of evaporated radiolabelled clomazone was 6.9 %. A comparison of clomazone volatility over time using two formulated products in an environmental chamber showed that the encapsulated formulation is less volatile than the emulsifiable concentrate formulation and therefore is more effective at restricting volatility, and EFSA concluded that affection of non-target vegetation is less likely.

Due to the formation type of FMC-CLOMAZONE 360 CS, i.e. encapsulated formulation, dry deposition *via* volatilisation is considered negligible compared to spray drift entry. From this, an assessment for the aquatic and terrestrial deposition of clomazone is not considered necessary. Nonetheless, the aquatic deposition of clomazone was addressed in PECsw model calculations above where volatilisation and subsequent dry deposition was included in the simulations.

Long-range transport:

The EU agreed degradation of clomazone in air was calculated at 0.567 d (1.5×10^6 OH-radicals/cm³ and a 12 hour day; Atmospheric Oxidation Programme V.3.1 (1994)). Updated calculations with the current AOPWIN model (ver. 1.92) estimated a slightly lower DT_{50} of clomazone in air of 0.487 d (12-hour day, 1.5×10^6 OH-radicals/cm³). Both estimated DT_{50} values are clearly below the trigger of 2 days, thus, clomazone does not need to be assessed for long-range transport.

Calculations for OAS taskforce Clomazone 360 g/L (ALB 360 CS)

Exposure resulting from other routes of exposure such as dust deposition, amenity use or indirect exposure of surface water via a sewage treatment plant (STP) after application of the plant protection product in storage rooms, is not anticipated in accordance with the uses of the clomazone plant protection product (Clomazone 360 g/L CS) in agricultural crops as proposed. Therefore, further information is not required or provided.

Other routes of exposure

This point has not been addressed by the applicants.

2.9 EFFECTS ON NON-TARGET SPECIES

All endpoint used in the environmental risk assessment was either derived from measured exposure values or normalised to 100% purity of the active substance.

2.9.1 Summary of effects on birds and other terrestrial vertebrates

Data on effects on birds and other terrestrial vertebrates are presented in Volume 3 – CA B.9 section B.9.1

Data on toxicity of clomazone to birds and mammals were previously submitted by the original notifier FMC and evaluated in the context of the first EU review of clomazone, resulting in the approval of the active substance. Data were considered acceptable and resulting endpoints were cited in the EFSA Scientific Report (July 2007) 109, 1-73.

Birds

Additionally, new acute oral, short-term dietary and reproductive toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection.

Acute toxicity

Overall, three acute oral toxicity tests conducted with clomazone technical are available. The mallard ducks acute toxicity study was not included in the assessment, as only acute data for one bird species is required. All LD_{50} values determined in the acute toxicity studies are unbound values, indicating that clomazone does not cause acute toxicity. Under the conditions of these studies, no clinical signs and treatment-related deaths were observed even at the highest test doses. The acute toxicity endpoint of 2224 mg a.s./kg bw for Bobwhite quail was used in the risk assessment.

Short-term toxicity

Overall, three short-term dietary toxicity tests conducted with clomazone technical are available. The mallard ducks acute toxicity study was not included in the assessment as it is formally not require and the study with Japanese quail was not considered valid due to exposure issues. The available endpoint (>1480 mg a.s./kg bw/day) was used to underpin the acute risk assessment.

Reproductive toxicity

Overall, two reproductive toxicity tests conducted with clomazone technical are available for the Bobwhite quail. NOEC values derived from the two available reproductive toxicity studies are based on the highest test doses, indicating that clomazone does not cause reproductive toxicity. Since in these studies no clinical signs and treatment-related deaths were observed at doses up to and including 94 mg a.s./kg bw/d (1000 ppm), it is deemed acceptable still to consider the EU agreed NOEC in the long-term risk assessment for birds. No EC10/EC20 values were derived due to lack of effects. A $NOEC_{reproduction}$ = 76.5 mg a.s./kg bw/day was used in the risk assessment.

Mammals

Additionally, new acute oral toxicity tests and reproductive toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection.

Acute toxicity

Overall, four acute oral toxicity tests conducted with clomazone technical are available. The results of the two studies previously evaluated during the first EU review of clomazone are considered to be most robust with respect to the risk assessment for mammals, since the tests allow the estimation of a precise LD_{50} on the basis of sound data (dose response-tests with 10 individuals per treatment group). By contrast, the two new acute oral toxicity studies were performed with a limited number of animals (three female rats per dose level) and only two dose levels. The tests were merely performed for classification and labelling purposes. None of the three rats exposed to the lower doses died within the test period, whereas mortality was observed for all individuals receiving the higher doses. Based on these results, a new overall lowest LD_{50} value of 754 mg a.s./kg bw is indicated that is nominally lower than the EU agreed LD_{50} of 1216 mg a.s./kg bw (normalised to 100% purity rom 1369 mg a.s./kg bw). However, it should be noted that this new LD_{50} value can be considered as quit conservative.

Nevertheless, for precautionary reasons, the lowest acute LD_{50} value for mammals (i.e. 754 mg a.s./kg bw) is proposed to be used in the acute risk assessments for mammals and as new endpoint as a result of the renewal approval evaluation.

Reproductive toxicity

The two-generation reproduction study with mammals was previously submitted by the original notifier FMC and evaluated as part of the first EU review of clomazone. The data were considered acceptable.

In addition to the two developmental toxicity studies evaluated in the first EU review, two further developmental toxicity studies in rat and rabbit were newly generated. However, no critical change of the EU agreed endpoints set in the first EU review is indicated by the results of the newly submitted studies.

Overall, it is deemed acceptable still to consider the EU agreed NOAEL of 88.8 mg a.s./kg bw/d (normalised) derived from the developmental toxicity to rats in the long-term risk assessment for mammals.

Terrestrial vertebrate wildlife (birds, mammals, reptiles and amphibians)

According to the new data requirements set forth in the Annex to Reg. (EU) No 283/2013, toxicity tests are requested for birds and mammals but not for amphibians and reptiles. No official risk assessment guideline has been developed yet that could be used to estimate the extent of different exposure routes for amphibians and reptiles under natural conditions. In addition, almost no validated standard protocols are currently available for amphibian and reptile testing. Nevertheless, it is stated that relevant data, including data from the open literature for the active substance of concern, regarding the potential effects to amphibians and reptiles should be presented and taken into account in the risk assessment, if available. Thus, data from open literature were taken into account, indicating that the risk is covered by the conservative risk assessments for birds and mammals (*Reptiles and terrestrial life stages of amphibians*) and fish (*Aquatic life stages of amphibians*).

Endocrine disrupting properties

The potential of clomazone and its major metabolites to interact with endocrine systems in mammals and wildlife has been reviewed. This includes an assessment of whether clomazone may be judged as an endocrine disrupter (ED) within the framework of European legislation. Based on the information from currently available toxicological and ecotoxicity studies, clomazone does not appear to have any endocrine activity in wildlife either. The metabolites of clomazone were also analysed for their potential to interact with the endocrine systems and here too there is no evidence that they interact with endocrine systems, although data are limited.

In addition, a comprehensive search of scientific peer reviewed open literature on side effects of the active substance clomazone, its metabolites or plant protection products containing clomazone on non-target organisms (including terrestrial vertebrates) was conducted in accordance with Article (8) of Regulation 1107/2009 (for details please refer to CA, Section B.9). Again, no data relevant to the potential endocrine disrupting effects of clomazone or it metabolites to wildlife birds, mammals or other terrestrial vertebrates were found in the open literature.

Overall, based on the mode of action as well as available information from toxicology and ecotoxicology studies and open literature, it can reasonably be concluded that clomazone does not interfere with endocrine pathways. Therefore, clomazone and its metabolites should not be considered as endocrine disruptors.

2.9.2 Summary of effects on aquatic organisms [section 11.5 of the CLH report]

Data on effects on aquatic organisms are presented in Volume 3 – CA B.9 section B.9.2

Accepted data on acute and long-term toxicity of the active substance clomazone to aquatic organisms are cited in the EFSA Scientific Report (July 2007) 109, 1-73.

Acute toxicity data on clomazone technical and the representative product 'FMC-Clomazone 360 CS' to fish, aquatic invertebrates, algae and aquatic macrophytes indicate no significant higher toxicity of the formulated product 'FMC-Clomazone 360 CS' in comparison to the active substances clomazone. Since clomazone is more toxic to aquatic organisms when applied as technical grade, endpoints derived from the toxicity tests with clomazone technical were considered most relevant for the TER calculation.

2.9.2.1 Bioaccumulation [equivalent to section 11.4 of the CLH report template]

Table 25: Summary of relevant information on bioaccumulation

Method	Species	Results	Key or Supportive study*	Remarks	Reference
Uptake, deputation and bioconcentration in fish	*Lepomis macrochirus*	BCF for whole fish, day 28 = 40	Supportive study	As logPow = 2.17 (CATF)/2.58 (OAS) a BCF study is not required.	CA B.9.2.2.3/01

2.9.2.1.1 Estimated bioaccumulation

Results indicate a rapid uptake and excretion of Clomazone. Clomazone has no potential to accumulate in fish (BCF for whole fish, day 28 = 40). Depuration in uncontaminated water is rapid, leading to residue loss of 50% within 1 day.

Based on the experimental determination of the n-octanol/water partition coefficient of clomazone, no potential for bioaccumulation is expected. This conclusion is confirmed by the results of a fish bioconcentration study. It is noted that the fish bioconcentration study is noty assessed due to logPow < 3.

2.9.2.1.2 Measured partition coefficient and bioaccumulation test data

Clomazone should not be considered very lipophilic with a logPow around 2.5and a Kfoc of 128. This is also evident form the supporting BCF study where whole fish BCF = 40.

2.9.2.2 Acute aquatic hazard [equivalent to section 11.5 of the CLH report template]

Table 26: Summary of relevant information on acute aquatic toxicity. Endpoints in bold are used for the aquatic risk assessment. It is noted that all endpoint are normalised to 100% a.s.

Test item/purity/Test guideline	Species (exposure conditions)	Effect and duration	Result	Origin	Study number
Acute toxicity endpoints for fish					
Clomazone/92.7%/OECD 203 (1992)	*Oncorhynchus mykiss* (static)	LC_{50} (96 h)	**14.4** mg a.s./L (nominal)	LoE	CA B.9.2.1/01
CLZ-M01	*Oncorhynchus mykiss (static)*	LC50 (96 h)	**> 19.8 mg/L (nominal)**	LoE	CA B.9.2.1/03
CLZ-M01	*Oncorhynchus mykiss* (static)	LC_{50} (96 h)	**> 103.6** mg/L (mean measured)	CATF	CA B.9.2.1/09
CLZ-M02	*Oncorhynchus mykiss (static)*	LC50 (96 h)	> 19.8 mg/L (nominal)	LoE	CA B.9.2.1/04
CLZ-M02	*Oncorhynchus mykiss* (static)	LC_{50} (96 h)	**> 102.2** mg/L (mean measured)	CATF	CA B.9.2.1/10
LZ-M03	*Oncorhynchus mykiss* (semi-static)	LC_{50} (96 h)	**> 99.6** mg/L (nominal)	CATF	CA B.9.2.1/11
CLZ-M04	*Oncorhynchus mykiss* (semi-static)	LC_{50} (96 h)	**> 99.8** mg/L (nominal)	CATF	CA B.9.2.1/13
CLZ-M05	*Oncorhynchus mykiss* (static)	LC_{50} (96 h)	**> 99.4** mg/L (nominal)	CATF	CA B.9.2.1/14
Acute toxicity endpoints for to aquatic invertebrates					
Clomazone /92.7%/OECD 203 (1992)	*Daphnia magna* (static)	EC_{50} (48 h)	12.7 mg a.s./L (nominal)	LoE	CA B.9.2.4.1/01
Clomazone/92.94 %/ Adaptation of ASTM Standard Practice No. E729 (1980) and amendment 1 (3-18-86)	*Americamysis bahia (flow-through)*	EC50 (96 h)	**0.53** mg a.s./L (nominal)	LoE	CA B.9.2.4.2/01
CLZ-M01	*Daphnia magna (static)*	EC50 (48 h)	> 4.95 mg/L (nominal)	LoE	CA B.9.2.4.1/02
CLZ-M01	*Daphnia magna (static)*	EC50 (48 h)	**> 111** mg/L (mean measured)	CATF	CA B.9.2.4.1/06
CLZ-M02	*Daphnia magna (static)*	EC50 (48 h)	> 4.95 mg/L (nominal)	LoE	CA B.9.2.4.1/03
CLZ-M02	*Daphnia magna (static)*	EC50 (48 h)	**77.5** mg/L (mean measured)	CATF	CA B.9.2.4.1/09
CLZ-M03	*Daphnia magna (static)*	EC50 (48 h)	**> 99.6** mg/L (nominal)	CATF	CA B.9.2.4.1/10
CLZ-M04	*Daphnia magna (static)*	EC50 (48 h)	**> 118.3** mg/L (mean measured)	CATF	CA B.9.2.4.1/12
CLZ-M05	*Daphnia magna (static)*	EC50 (48 h)	> 99.4 mg/L (nominal)	CATF	CA B.9.2.4.1/13
CLZ-M05	*Americamysis bahia* (static)	EC_{50} (96 h)	**52** mg a.s./L (mean measured)	CATF	CA B.9.2.4.2/05
Acute toxicity endpoints for algae (mg a.s./L)					

Clomazone/98.2 % (w/w)/OECD 201 (2006)	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	> 245.5 / 90.9	CATF	CA B.9.2.6.1/06
Clomazone/96.6% w/w/ OECD 201 (2006)	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	104.3 / 36.2	CATF	CA B.9.2.6.1/07
Clomazone/96.6% w/w OECD 201 (2006)	*Navicula pelliculosa*	ErC50 (72 h) / EyC50 (72 h)	**102.4** / 61.2	CATF	CA B.9.2.6.2/03
CLZ-M01	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	> 3 / > 3	LoE	CA B.9.2.6.1/04
CLZ-M01	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	**76.01** / 50.85	CATF	CA B.9.2.6.1/08
CLZ-M01	*Navicula pelliculosa*	ErC50 (72 h) / EyC50 (72 h)	>98.6 / 46.5	CATF	CA B.9.2.6.2/04
CLZ-M01	*Navicula pelliculosa*	ErC50 (72 h) / EyC50 (72 h)	> 99.7 / > 99.7	CATF	CA B.9.2.6.2/05
CLZ-M02	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	> 3 / > 3	LoE	CA B.9.2.6.1/05
CLZ-M02	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	152.37 / 67.23	CATF	CA B.9.2.6.1/09
CLZ-M02	*Navicula pelliculosa*	ErC50 (72 h) / EyC50 (72 h)	93.0 / 24.1	CATF	CA B.9.2.6.2/06
CLZ-M02	*Navicula pelliculosa*	ErC50 (72 h) / EyC50 (72 h)	**46.5** / 23.2	CATF	CA B.9.2.6.2/07
CLZ-M03	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	96.6 / 96.6	CATF	CA B.9.2.6.1/10
CLZ-M03	*Navicula pelliculosa*	ErC50 (48 h) § / EyC50 (48 h)	**46.5** / 23.2	CATF	CA B.9.2.6.2/08
CLZ-M04	*Navicula pelliculosa*	ErC50 (48 h)§ / EyC50 (48 h)	> **99.8** / > 99.8	CATF	CA B.9.2.6.2/09
CLZ-M05	*Pseudokirchneriella subcapitata*#	ErC50 (72 h) / EyC50 (72 h)	**99.4** / 24.7	CATF	CA B.9.2.6.1/11
CLZ-M05	*Navicula pelliculosa*	ErC50 (72 h) / EyC50 (72 h)	>99.8 / 60.5	CATF	CA B.9.2.6.2/10

***** Command 360 G/L CS and Centium 360 CS are identical to FMC-Clomazone 360 CS
# *Pseudokirchneriella subcapitata* is also called *Selenastrum capricornutum*. The new name is *Raphidocelis subcapitata*
§ Shorter duration in order to respect validity criteria

2.9.2.2.1 Acute (short-term) toxicity to fish

In addition to existing data, new acute toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original

notifier FMC had claimed data protection. No critical change of the EU agreed endpoints set in the first EU review is indicated by the results of the newly submitted studies (*supportive information*).

Finally, new and already submitted toxicity data on fish are available for all clomazone metabolites (CLZ-M01 - CLZ-M05) that are formed from degradation of the parent compound in surface water as well as for metabolites in soil that may reach surface water *via* groundwater, drain flow or run-off from fields that have been treated with the plant protection product. Overall, available toxicity data indicate that clomazone metabolites are less toxic to fish than the parent compound clomazone.). The existing *O. mykiss* endpoint (LC50=14.4 mg a.s./L from DAR, 2005), which is the most critical acute fish endpoint is considered for CLP classification.

The acute toxicity data for fish exposed to clomazone and its metabolites is considered appropriate and sufficient for classification purposes..

2.9.2.2.2 Acute (short-term) toxicity to aquatic invertebrates

In addition to existing data, new acute toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection.

As indicated by the acute toxicity data, *Americamysis bahia* (also referred to as *Mysidopsis bahia*) is more sensitive than other aquatic invertebrate species, such as the standard test species *Daphnia magna*. The fact that it is a saltwater species is considered of less importance compared to the higher sensitivity of *A. bahai* as a surrogate species for aquatic invertebrates. Therefor this existing *A. bahai* endpoint (EC50=0.53 mg a.s./L from DAR, 2005), which is the most critical acute invertebrate endpoint is considered for CLP classification.

Finally, new as well as already submitted toxicity data on aquatic invertebrates are available for all clomazone metabolites (CLZ-M01 - CLZ-M05) potentially of concern in aquatic systems. Overall, available toxicity data indicate that clomazone metabolites are less toxic to aquatic invertebrates than the parent compound clomazone.

The acute toxicity data for invertebrates exposed to clomazone and its metabolites is considered appropriate and sufficient for classification purposes.

2.9.2.2.3 Acute (short-term) toxicity to algae or aquatic plants

In addition to existing data, new algae toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection. The new *N. pelliculosa* endpoint (ErC50=102.4 mg a.s./L), which is the most critical acute algae endpoint is considered for CLP classification.

Finally, new as well as already submitted toxicity data on algae are available for all clomazone metabolites (CLZ-M01 - CLZ-M05) potentially of concern in aquatic systems. Overall, available toxicity data indicate that clomazone metabolites are less toxic to algae than the parent compound clomazone.

It is noted that the OAS did not address the data requirements regarding algae studies for clomazone and metabolites with the exception of the CLZ-M01 and CLZ-M02 green algae studies.

The acute toxicity data for invertebrates exposed to clomazone and its metabolites is considered appropriate and sufficient for classification purposes.

2.9.2.3 Long-term aquatic hazard [equivalent to section 11.6 of the CLH report template]

Summary of relevant information on chronic aquatic toxicity. It is noted that all endpoint are normalised to 100% a.s.

Table 27:

Test item/purity/test guideline	Species (exposure conditions)	Effect and duration	Result	Origin	Study number
Chronic toxicity endpoints for to fish					
Clomazone Technical/95.6 %/Not stated (but test conditions were comparable to OECD 210)	*Oncorhynchus mykiss* (ELS study, flow-through)	$NOEC_{reproduction}$ (57 d)	**2.3** mg a.s./L (nominal)	LoE	CA B.9.2.2.1/01
Chronic toxicity endpoints for to aquatic invertebrates					
Clomazone95.6% Guidelines: Internal Springborn Bionomics protocol on chronic toxicity testing with Daphnia, 1983.	*Daphnia magna (semi-static)*	NOECreproduction (21 d)	2.2 mg a.s./L (nominal)	LoE	CA B.9.2.5.1/01
Clomazone/: 99.7 %/ OECD 211 (1998)	*Daphnia magna (semi-static)*	NOECreproduction (21 d)	4.6 mg a.s./L (nominal)	CATF	CA B.9.2.5.1/02
		EC10 reproduction (21 d)	**2.19** mg a.s./L (nominal)		
Clomazone/96.6% w/w /OECD 211 (1998)	*Daphnia magna (semi-static)*	NOECreproduction (21 d)	4.6 mg a.s./L (nominal)	CATF	CA B.9.2.5.1/03
Clomazone/96.8 % OCSPP Draft Guideline 850.1350	*Americamysis bahia (flow through)*	NOECreproduction (28 d)	**0.032** mg a.s./L (mean measured)	CATF	CA B.9.2.5.2/01
Chronic toxicity endpoints for to aquatic *Chironomus riparius*					
Clomazone/95.6% Internal Springborn Bionomics protocol on chronic toxicity testing with Daphnia, 1983.	*Chironomus riparius* (spiked sediment)	$NOEC_{development}$ (28 d) $EC_{10\ development}$ (28 d)	60.5 mg a.s./kg dw (nominal) **198.4** mg a.s./kg dw (nominal)	CATF	CA B.9.2.5.1/01
CLZ-M01	*Chironomus riparius* (spiked sediment)	$NOEC_{emergence}$ (28 d) $EC_{10\ emerge}$ (28 dage)	123 mg a.s./kg dw (nominal) **160.7** mg a.s./kg dw (nominal)	CATF	CA B.9.2.5.1/02
Acute toxicity endpoints for macrophytes					
Clomazone/90.4% EPA 122-2/123-2	*Lemna gibba*	E_rC_{50} *Frond number* (7d)	34 (mm)	LoE	CA B.9.2.7/02
Clomazone/98.2 % w/w OECD 221 (2006)	*Lemna gibba*	E_rC_{50} *Frond number* E_rC_{50} *Biomass increase* (7 d)	41.7 (mm) >98.2 (mm)	CATF	CA B.9.2.7/03
Clomazone/96.6% w/w Guidelines: OECD 221 (Draft 2002)	*Lemna minor*	E_rC_{5} *Frond number* * (7 d)	49.2 (mm)	CATF	CA B.9.2.7/04

Clomazone/96.8 % OECD Draft (2013)	*Myriophyllum spicatum*	E_rC_{50} *shoot length* / E_yC_{50} *shoot length* E_rC_{50} *wet weight* / E_yC_{50} *wet weight* E_rC_{50} *dry weight* / E_yC_{50} *dry weight,* (14 d)	>32/ 18.4 8.3/ 1.39 27.5/ 5.23	CATF	CA B.9.2.7/05
CLZ-M01	*Myriophyllum spicatum*	E_rC_{50} *shoot length* / E_yC_{50} *shoot length* E_rC_{50} *wet weight* / E_yC_{50} *wet weight* E_rC_{50} *dry weight* / E_yC_{50} *dry weight,* (14 d)	**>96 / >96 >96 / >96 >96 / >96**	CATF	CA B.9.2.7/06
CLZ-M02	*Myriophyllum spicatum*	E_rC_{50} *shoot length* / E_yC_{50} *shoot length* E_rC_{50} *wet weight* / E_yC_{50} *wet weight* E_rC_{50} *dry weight* / E_yC_{50} *dry weight,* (14 d)	69.0 51.8 **52.6** 39.5 >69 >69	CATF	CA B.9.2.7/07
Clomazone/ Purity: 96.92 % OECD 238	*Myriophyllum spicatum*	E_rC_{50} main *shoot length* /E_yC_{50} main *shoot length* E_rC_{50} *wet weight* / E_yC_{50} *wet weight* E_rC_{50} *dry weight* / E_yC_{50} *dry weight* E_rC_{50} total *shoot length* /E_yC_{50} total *shoot length* E_rC_{50} number of whorls /E_yC_{50} number of whorls E_rC_{50} total root length /E_yC_{50} total root length (14 d)	86.08/ 56.49 59.74/ 12.98 62.03/ 24.32 93.81/ 72.94 45.36/ 31.59 **4.70**/ -	OAS	CA B.9.2.7/08

2.9.2.3.1 Chronic toxicity to fish

In addition to existing data, new long-term toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection. No critical change of the EU agreed endpoints set in the first EU review is indicated by the results of the newly submitted studies (*supportive information*). The existing *O. mykiss* chronic endpoint ($NOEC_{reproduction}$ =2.3 mg a.s./L from DAR, 2005), which is the most critical chronic fish endpoint is considered for CLP classification.

The long-term toxicity data for fish exposed to clomazone is considered appropriate and sufficient for classification purposes.

2.9.2.3.2 Chronic toxicity to aquatic invertebrates

In addition to existing data, new long-term toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection. The overall lowest endpoint (i.e. NOEC = 1.25 mg a.s./L) derived from one of the new reproductive toxicity tests with *Daphnia magna* is slightly lower than the EU agreed endpoint cited in the EFSA conclusion (i.e. NOEC = 2.2 mg a.s./L

As indicated by the acute toxicity data, *Americamysis bahia* (also referred to as *Mysidopsis bahia*) is more sensitive than other aquatic invertebrate species, such as the standard test species *Daphnia magna*.

For this reason, also a long-term toxicity study (i.e. life cycle toxicity test) with this most sensitive invertebrate species was generated, as recommended in the new data requirements set forth in the Annex to Reg. (EU) No 283/2013. As a result, a new endpoint for long-term effects of clomazone on aquatic invertebrates was established at NOEC = 0.032 mg a.s./L. This chronic endpoint (based on data for *A. bahia*) is lower than the previously EU agreed endpoint for aquatic invertebrates (based on data for *D. magna*), i.e. NOEC = 2.2 mg a.s./L and will be used for the long-term aquatic invertebrate classification.

Finally, new as well as already submitted toxicity data on aquatic invertebrates are available for all clomazone metabolites (CLZ-M01 - CLZ-M05) potentially of concern in aquatic systems. Overall, available toxicity data indicate that clomazone metabolites are less toxic to aquatic invertebrates than the parent compound clomazone.

The long-term toxicity data for invertebrates exposed to clomazone and its metabolites is considered appropriate and sufficient for classification purposes.

2.9.2.3.3 Chronic toxicity to sediment dwelling organisms

No studies on sediment dwellers were submitted as part of the first EU review of clomazone However, based on the results of the newly submitted water-sediment studies (for details, please refer to the document CA, Section B.8), the active substance clomazone and its metabolite CLZ-M01 were identified as substances potentially of concern in sediment (i.e. formed at or more than 10 %). Thus, new studies investigating the effects on the development of *Chironomus riparius* in a sediment-water system (exposed *via* spiked sediment) were submitted, demonstrating that the substances of concern are of low toxicity to sediment dweller. EC10 values indicated that toxicity of clomazone and CLZ-M01 is in the same range for sediment dwellers. $EC_{10\ development}$ = 198.4 mg a.s./kg dw for clomazone will be used in a risk assessment.

2.9.2.3.4 Chronic toxicity to algae or aquatic plants

In addition to existing data, new *Lemna* toxicity tests with clomazone technical were generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection. According to the new EFSA guidance document for aquatic organisms, growth rate (r) is the preferred endpoint for algae and aquatic macrophytes that should be considered in the risk assessment for primary producers.

A general concern was raised in the PRAPeR meeting with regard to the appropriateness of *Lemna* as test organisms for selective herbicides (EFSA Scientific Report (2007) 109, 1-73). For this reason, toxicity tests with an additional aquatic macrophyte species, i.e. *Myriophyllum spicatum*, was conducted to generate data for a dicotyledonous plant species. The results of these studies indicate that clomazone is more toxic to *M. spicatum* than to *Lemna* sp. The most sensitive endpoint from these *Myriophyllum spicatum* studies is from the study by OAS where thr $E_rC_{50\ total\ root\ length}$ of 4.7 mg a.s./L was derived. In conclusion, the use of this new overall lowest endpoints derived from the study with *M. spicatum* is deemed relevant for the risk assessment on aquatic macrophytes.

Finally, new toxicity data on aquatic macrophytes are available for the clomazone metabolites CLZ-M01 and CLZ-M02. Available toxicity data indicate that clomazone metabolites are less toxic to aquatic macrophytes than the parent compound clomazone.

The toxicity data for macrophytes exposed to clomazone and its metabolites is considered appropriate and sufficient for classification purposes.

2.9.2.3.5 Chronic toxicity to other aquatic organisms

No studies on sediment dwellers were submitted as part of the first EU review of clomazone. However, based on the results of the newly submitted water-sediment studies (for details, please refer to the Annex document Clomazone_dRAR_10_VOL_3_CA_B-8_2018_01_29), the active substance clomazone and its metabolite CLZ-M01 were identified as substances potentially of concern in sediment (i.e. formed at or more than 10 %). Thus, new studies investigating the effects on the development of *Chironomus riparius* in a sediment-water system (exposed *via* spiked sediment) were submitted, demonstrating that the substances of concern are of low toxicity to

sediment dweller. EC10 values indicated that toxicity of clomazone and CLZ-M01 is in the same range for sediment dwellers. $EC_{10\ development}$ = 198.4 mg a.s./kg dw for clomazone will be used in a risk assessment.

2.9.2.4 Comparison with the CLP criteria

2.9.2.4.1 Acute aquatic hazard

Table 28: Summary of information on acute aquatic toxicity relevant for classification. . It ist noted that all endpoint are normalised to 100% a.s.

Method	Species	Test material/purity	Results[1]	Remarks	Reference
OECD 203	*Oncorhynchus mykiss*	Clomazone	LC50 = 14.4 mg a.s./L (nom)		CA B.9.2.1/01
Adaptation of ASTM Standard Practice No. E729 (1980) and amendment 1 (3-18-86)	*Americamysis bahia*	Clomazone/ 92.94 %	EC50 = 0.53 mg a.s./L (nom)	Considered relevant	CA B.9.2.4.2/01
OECD 201	*Navicula pelliculosa*	Clomazone/96.6% w/w	ErC50 = 102.4 mg a.s./L	-	CA B.9.2.6.2/03

The acute aquatic hazard shall be classified as 'Category Acute 1' (H400) with M-factor = 1, according to CLP classification criteria.

2.9.2.4.2 Long-term aquatic hazard (including bioaccumulation potential and degradation)

Table 29: Summary of information on long-term aquatic toxicity relevant for classification

Method	Species	Test material/purity	Results[1]	Remarks	Reference
Comparable to OECD 210	*Oncorhynchus mykiss*	Clomazone/95.6 %.	$NOEC_{mortality}$ = 2.3 mg a.s./L (nom)	-	CA B.9.2.2.1/01
OCSPP Draft Guideline 850.1350	*Americamysis bahia*	Clomazone/92.94 %	$NOEC_{development}$ = 0.032 mg a.s./L (mm)	Considered relevant	CA B.9.2.4.2/01
OECD 238	*Myriophyllum spicatum*	Clomazone/96.92 % w/w	$ErC50_{total\ root\ length}$ = 4.7 mg a.s./L (nom)	-	CA B.9.2.7/08

CATS: Toxicity endpoints for to aquatic organisms exposed to FMC-Command 360 CS.

Test item	Species (exposure conditions)	Effect and duration	Result (mg a.s./L)	Origin	Study number
Command 360 G/L CS*	*Oncorhynchus mykiss* (semi-static)	EC_{50} NOEC (96 h)	187.9 142.8 (Mean measured)	LoE	B.9.3.1-1
Command 360 G/L CS*	*Daphnia magna* (static)	EC_{50} NOEC (48 h)	155.7 79.3 (Mean measured)	LoE	B.9.3.1-2
Centium 360 CS	*Navicula pelliculosa* (static)	E_rC_{50} E_rC_{20} E_rC_{10} NOEC (72 h)	>15.3 11.6 4.49 1.38 (Mean measured)	CATF	B.9.3.1-4

***** Command 360 G/L CS and Centium 360 CS are identical to FMC-Clomazone 360 CS

OAS: Toxicity endpoints for to aquatic organisms exposed to ALB 36 CL

Test item	Species (exposure conditions)	Effect and duration	Result (mg a.s./L)	Origin	Study number
ALB 36 CL (Clomazone 360 g/L)	*Oncorhynchus mykiss* (static)	EC_{50} NOEC (96 h)	**88.0** **16.2** (Mean measured)	OAS	CP B.9.3.1-1
ALB 36 CL (Clomazone 360 g/L)	*Lepomis macrochirus* (static)	LC_{50} NOEC (96 h)	**71.0** **16.22** (Mean measured)	OAS	CP B.9.3.1-2
ALB 36 CL (Clomazone 360 g/L)	*Daphnia magna* (static)	EC_{50} NOEC (48 h)	**41.9** **13.1** (Mean measured)	OAS	CP B.9.3.1-3
Clomazone 360 g/L (ALB 36 CL)	*Pseudokirchneriella subcapitata*	E_rC_{50} E_rC_{10} NOEC (48 h)	**149.02** **67.50** **32** **12.07** (nominal)	OAS	CP B.9.3.1-4

The long-term aquatic hazard shall be classified as 'Category Chronic 1' (H410) with a M-factor = 1, according to CLP classification criteria. BCF = 40 (whole fish) indicate that clomazone shall not be classified due to potential for bioaccumulation.

Acute toxicity data on clomazone technical and the representative products 'FMC-Clomazone 360 CS' and OAS-Clomazone 360 CS to fish, aquatic invertebrates, algae and aquatic macrophytes indicate no significant higher toxicity of the formulated products 'FMC-Clomazone 360 CS' and OAS-Clomazone 360 CS in comparison to the active substances clomazone.

2.9.2.5 Conclusion on classification and labelling for environmental hazards

Acute: Category Acute 1' (H400) with M-factor = 1
Long-term: Category Chronic 1' (H410) with a M-factor = 1

2.9.3 Summary of effects on arthropods

Data on effects on arthropods are presented in Volume 3 – CA B.9 section B.9.3

Bees

A new acute honeybee toxicity test with clomazone technical was generated after the first EU review, matching essential Annex II (now CA) data of clomazone for which the original notifier FMC had claimed data protection. No critical change of the EU agreed endpoints set in the first EU review is indicated by the results of the new study (oral LD_{50} > 87.9 µg/bee /contact LD_{50} > 96.6 µg/bee).

Additionally, data on chronic toxicity of clomazone to adult honeybees (oral LD_{50} > 1728 µg/bee /contact LD_{50} > 28.1 µg/bee), honeybee larvae (NOEDD120 h 193.8 ug a.s./larva / LDD50 > 193.8 ug a.s./larva) and bumble bees (oral /contact LD_{50} > 968 µg/bee) were generated in accordance to the new data requirements set forth in the Annex to Reg. (EU) no. 283/2013, since bees may be exposed with respect to the intended uses of 'FMC-Clomazone 360 CS' and OAS ALB 360 CS in potato and oilseed rape.

For solitary bees, no acute toxicity study is provided within this renewal dossier, since up to now no validated testing methods have been developed for this species. This waiver is in line with recommendations of the guidance document SANCO/10181/2013.

Non-target arthropods other than bees

In these worst-case toxicity studies using artificial substrate, effects of 'FMC-Clomazone 360 CS' on the standard test species *Aphidius rhopalosiphi* and *Typhlodromus pyri* were evaluated at limit test rates of 360 g a.s./ha. Further results derived from standard tests with ground-dwelling arthropods, i.e. *Poecilus cupreus* and *Aleochara bilineata* (see also Final Addendum to DAR, 2007), are available.

Additionally, extended laboratory tests with *A. rhopalosiphi* and *T. pyri* (and two other arthropod species, i.e. *Aleochara bilineata* and *Pardosa* spp.) were generated that are considered to be more relevant for the risk assessment due to the more realistic exposure conditions (e.g. by using natural substrate). Tests were not evaluated as part of the first EU review of clomazone. Results of the extended laboratory tests indicate that 'FMC-Clomazone 360 CS' is of low toxicity to non-target arthropods even at higher test rates (up to and including 480 g a.s./ha) than those considered in the first EU review of clomazone. First tier laboratory toxicity test with *A. rhopalosiphi* and *T. pyri* exposed to 'ALB 36 CL' indicated LR_{50} > 120 g a.s/ha.

The toxicity data for arthropods exposed to clomazone and PPP's is considered appropriate and sufficient for an aquatic risk assessment.

2.9.4 Summary of effects on non-target soil meso- and macro-fauna

Data on effects on non-target soil meso- and macro-fauna are presented in Volume 3 – CA B.9 section B.9.4.

All clomazone endpoints have been corrected by the factor of 2, as logPow for clomazone is above 2.

Earthworms

Data on reproduction toxicity (56-days exposure) of clomazone (applied as 'FMC-Clomazone 360 CS') to earthworms were previously submitted by the original notifier FMC and evaluated in the context of the first EU review of this active substance, resulting in the approval of clomazone. Data were considered acceptable and resulting endpoints were cited in the EFSA Scientific Report (July 2007) 109, 1-73.

In addition, a new reproductive toxicity test with clomazone technical was generated that was not evaluated as part of the first EU review of clomazone. In this study, clomazone was incorporated into the soil to obtain a homogenous soil concentration and containing a reduced peat content of 5 %, which is considered more environmentally relevant. Rates up to and including 1000 mg a.s./kg $soil_{dw}$ were tested within the framework of the newly submitted study, indicating than clomazone is of low toxicity to earthworms even at much higher test rates than those considered in the EU review (i.e. 600 g a.s./ha, equivalent to 0.8 mg a.s./kg $soil_{dw}$).

An earthworm reproduction study with the anaerobic soil metabolite CLZ-M01 was generated that was not previously evaluated as part of the first EU review of clomazone. However, it should be noted that with respect to the intended uses of 'FMC-Clomazone 360 CS' in potato and oilseed rape, it is unlikely that anaerobic conditions in soil will occur for a relevant period of time and to a relevant spatial extent. Available data indicate that the soil metabolite (NOEC = 308.7 mg/kg $soil_{dw}$) is not more toxic than the parent compound (NOEC = 171.5 mg/kg $soil_{dw}$).

A earthworm reproduction study with the product ALB 36 CL was submitted by OAS giving a corrected NOEC of 35.1 mg a.s./kg soil dw.

For details, please refer to data point CA 8.4.1 of the document M-CA, Section 8 as well as CP 10.4.1 of the document M-CP, Section 10.

Soil meso- and macro-fauna (other than earthworms)

With respect to the new data requirements set forth in the Annex to Reg. (EU) No 283/2013, testing on *Folsomia candida* and *Hypoaspis aculeifer* was required, since the representative product 'FMC-Clomazone 360 CS' and ALB 36 CL is applied to bare soil (pre-emergence, BBCH 00-09).

Reproductive toxicity tests on *F. candida* and *H. aculeifer* were conducted with both 'FMC-Clomazone 360 CS', the representative product and clomazone. Tests were not evaluated as part of the first EU review of clomazone. Results from the reproductive toxicity studies with the FMC-Clomazone 360 CS indicate that the collembolan *F. candida* (NOEC = 11.3 mg a.s./kg $soil_{dw}$) is more sensitive to clomazone than the predatory mite *Hypoaspis aculeifer* (NOEC = 180 mg a.s./kg $soil_{dw}$). For this reason, the study with the metabolite CLZ-M01 that is potentially of concern in anaerobic soils was conducted with *F. candida*. Endpoints from the tests derived with clomazone were expressed as EC10 values (*Folsomia candida* $EC_{10\ reproduction}$ = 10.3 mg a.s./kg $soil_{dw}$, *Hypoaspis aculeifer* $EC_{10\ reproduction}$ = 32.2 mg a.s./kg $soil_{dw}$).

The toxicity data for soil meso- and macro-fauna exposed to clomazone and PPP's is considered appropriate and sufficient for an aquatic risk assessment.

2.9.5 Summary of effects on soil nitrogen transformation

Data on effects on soil nitrogen transformation are presented in Volume 3 – CA B.9 section B.9.5

To comply with the data requirements set in the Annex to Reg. (EU) No 283/2013, new data on the effects of clomazone technical on nitrogen transformation in soil were generated according to the most recent test guideline. In addition, in the newly submitted study, rates up to and including 4.08 mg a.s./kg $soil_{dw}$ have been tested (old study: 720 g a.s./ha, equivalent to 0.96 mg a.s./kg $soil_{dw}$) to demonstrate that clomazone is of low toxicity even at much higher test rates than those considered in the EU review. In conclusion, endpoints derived from the newly submitted nitrogen transformation study with clomazone technical are considered more relevant with respect to the renewal of approval of clomazone than the EU agreed endpoints and thus should be used instead in the risk assessment for soil microorganisms.

Additionally, a nitrogen transformation study with the anaerobic soil metabolite CLZ-M01 was generated that was not previously evaluated as part of the first EU review of clomazone.

A nitrogen transformations study was provided with 'Clomazone 360 g/L CS' (ALB 36 CL). No significant impact on soil micro-organisms was identified at 0.830.97 mg a.s/kg soil.

The toxicity data for soil nitrogen transformation exposed to clomazone and PPP's is considered appropriate and sufficient for an aquatic risk assessment.

2.9.6 Summary of effects on terrestrial non-target higher plants

Data on effects on terrestrial non-target higher plants are presented in Volume 3 – CA B.9 section B.9.6.

Effects of 'FMC-Clomazone 360 CS' on non-target plants were evaluated within the framework of two seedling emergence tests and two vegetative vigour tests. In the vegetative vigour tests, the overall lowest ER_{50} was established at 4.5 g a.s./ha based on effects on fresh weight of the common chickweed (*Stellaria media*). In the seedling emergence tests, the overall lowest ER_{50} was established at 43.7 g a.s./ha based on phytotoxcity effects on lettuce (*Lactuca sativa*). A comparison of the results derived from the four laboratory tests indicates that the vegetative vigour test is the more sensitive test system with respect to clomazone.

The number of plant species tested are sufficiently high for conducting a probabilistic risk assessment based on a HC_5 derived from the species sensitivity distribution (SSD). Thus, a SSD approach was implemented as refinement step in the non-target plant risk assessment for 'FMC-Clomazone 360 CS' by use of the median HC_5 of 6.6 g a.s./ha based on the vegetative vigour data (most relevant) for this product.

Effects of ALB 36 CL non-target terrestrial plants was evaluated by seedling emergence and vegetative vigour studies with 6 species. The most sensitive endpoints were ER50 (biomass, seedling emergence, *Helianthus annuus*) = 12.8 g a.s./ha and ER50 (biomass, vegetative vigour, *Allium cepa*)= 35.3 g a.s./ha.

The toxicity data for terrestrial non-target higher plants exposed to clomazone and PPP's is considered appropriate and sufficient for an aquatic risk assessment.

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

No data are provided as adequate risk assessments were performed for all indicator species relevant in the natural environment, including terrestrial vertebrates, bees and other terrestrial non-target arthropods, soil meso- and macro-fauna and terrestrial non-target plants in consideration of all GAP uses intended for the representative products.

2.9.8 Summary of effects on biological methods for sewage treatment

Data on effects on biological methods for sewage treatment are presented in Volume 3 – CA B.9 section B.9.8

Disturbances in the bio-degradation process of activated sludge are not expected if the test item is correctly introduced into adapted wastewater treatment plants at low concentrations. Nevertheless, for maximum protection, several studies were provided investigating the effects of clomazone on the activity of activated sludge, indicating that no adverse effects need to be expected on biological methods for sewage treatment following application of 'FMC-Clomazone 360 CS'. Under the conditions of the study considered most relevant with respect to the renewal of approval of clomazone, the 3-hour EC_{50} for total respiration was calculated to be 962.8 mg/L, for heterotrophic respiration the 3-hour EC_{50} was 709.5 mg/L and for the oxygen uptake due to nitrification the 3-hour EC_{50} was 1229.4 mg/L.

It is noted that OAS did not address the data requirements regarding effect studies on biological methods for sewage treatment.

The toxicity data for biological methods for sewage treatment exposed to clomazone and PPP's is considered appropriate and sufficient for an aquatic risk assessment.

2.9.9 Summary of product exposure and risk assessment

In the following environmental risk assessment, the conclusions are made for the oilseed rape use (120 g a.s./ha), unless explicit mentioned. The use in potatoes (90 g a.s./ha) is considered to be covered by the risk assessment for the oil seed rape use, as both uses are pre-emergence.

Birds and mammals risk assessment (see CATF and OAS CP B.9.2 for details)
At tier 1 there was no acute or long-term risk identified for birds or mammals in any of the evaluated risk assessments provided by the applicants. The risk was also addressed for drinking water, bioaccumulation and possible endocrine effects.

Applicant	Indicator species	Assessment step	Exposure	Rate [kg a.s./ha]	DDD [mg/kg bw/d]	Endpoint [mg/kg bw/d]		Mitigation	TER	TER trigger
OAS	Small granivorous bird	Screening	acute	0.119	2.67	LD50	>2224	-	833	10
			long-term		0.72	NOAEL	76.5	-	34	5
	Small granivorous mammal		acute		1.71	LD50	754	-	441	10
			long-term		0.41	NOAEL	88.8	-	211	5
CATF	Small granivorous bird	Screening	acute	0.12	3.0	LD50	>2000	-	667	10
			long-term		0.7	NOAEL	94	-	350	5
	Small granivorous mammal		acute		1.7	LD50	754	-	436	10
			long-term		0.4	NOAEL	88.8	-	222	5

Risk assessment to aquatic organisms (see CATF and OAS CP B.9.4 for details)
Clomazone is both very acute and chronic toxic to aquatic organisms. Classification and risk assessment is based on the most sensitive acute and chronic endpoints, which in this case is from the saltwater species *Americamysis bahai*. The fact that it is a saltwater species used for a freshwater risk assessment is not important as *A. bahai* is considered a surrogate species also representative for freshwater conditions. The toxicity and exposure of all metabolites was always lower than for clomazone. I.e. the risk assessment for clomazone addresses the risk for metabolites.
Exposure is estimated using FOCUSsw Step 1-3.
It is noted that CATF has derived RAC values in order to address the risk for aquatic organisms. OAS has used the convention TER approach. The latter approach is not in accordance with the EFSA Aquatic GD, 2013. As both CATF and OAS aquatic risk assessment builds on the same endpoints, and the dosing is virtually the same (CATF: 120 g a.s./ha in oilseed rape, OAS: 119 g a.s./ha in oilseed rape) only CATF results will be presented.

FOCUS$_{sw}$ step 1-3 - TERs for Clomazone used in winter and spring oilseed rape at 120 g a.s./ha (one application)

Scenario	PEC global max (µg L)	fish acute	fish chronic	Aquatic invertebrates	Aquatic invertebrates prolonged	Algae	Higher plant	Sed. dweller prolonged
		Oncorhynchus mykiss	*Oncorhynchus mykiss*	*Americamysis bahia*	*Americamysis bahia*	*Navicula pelliculosa*	*Myriophyllum spicatum*	*Chironomus riparius*
		LC_{50}	NOEC	EC_{50}	NOEC	EC_{50}	EC_{50}	EC10
		14400 µg/L	2300 µg/L	530 µg/L	32 µg/L	102400 µg/L	4700 µg/L	198400 µg/L
FOCUS Step 1								
	25.8	558	89	**21**	**1.2**	3969	18	7690
FOCUS Step 2								
North Europe	15.86	908	145	**33**	**2.0**	6456	30	12509
South Europe	12.86	1120	179	**41**	**2.5**	7963	37	15428
FOCUS Step 3								
D2 / ditch	7.8870			**67**	**4.1**			
D2 / stream	4.9380			107	**6.5**			
D3 / ditch	0.7688			689	42			
D4 / pond	0.4107			1290	78			
D4 / stream	0.6577			806	49			
D5 / pond	0.2720			1949	118			
D5 / stream	0.7095			747	45			
R1 / pond	0.0262			20229	1221			
R1 / stream	0.5028			1054	64			
R3 / stream	2.2100			240	14			
Trigger		100	10	100	10	10	10	10

The risk to aquatic organisms is addressed and all trigger values except D2 scenarios are respected without any mitigation. Furthermore, there are no indication of clomazone being an endocrine disrupter, based on both data following the data requirements and open literature data.

Risk assessment for arthropods

The risk assessment for bees followed the draft EFSA guidance document including acute assessment of adult honey bees and honey bee larva, long-term honey bee risk and risk to bumble bees. The risk to solitary bees was not addressed due to lack of data.

Assessment for – oilseed rape at 120 g a.s./ha (one application).

Species	Test substance	Risk quotient	HQ/ETR	Trigger
Honey bee *(Apis mellifera)*	Clomazone	HQcontact	< 0.12	42
Honey bee *(Apis mellifera)*	Clomazone	ETRacute adult oral	< 0.011	0.2
Honey bee *(Apis mellifera)*	Clomazone	ETRchronic adult oral	0.064	0.03
Honey bee *(Apis mellifera)*	Clomazone	ETRlarvae	0.009	0.2
	Clomazone	ETRhpg	No data	

The risk to NTA was addressed base on both standard tests with (*Typhlodromus pyri, Aphidius rhopalosiphi, Poecilus cupreus* and *Aleochara bilineata*) and extended laboratory test (*Aphidius rhopalosiphi, Typhlodromus pyri, Aleochara bilineata* and *Pardosa monticola*), i.e. HQ was clearly below 2 both in-field and off-field and effects in higher tier tests indicate very small effects (less than 10% at 4x the expected in-field dose). The latter test systems included more realistic exposure conditions.

Risk assessment for soil living organisms

The risk is assessed for earthworm and for *Folsomia candida* and *Hypoaspis aculeifer* (the latter due to the bare soil application of clomazone. The risk assessment for earthworms gave TER values above trigger for both clomazone, FMC-Clomazone 360 CS and CLZ-M01. The same conclusion can be drawn for the other soil macro-organisms (*Folsomia candida* and *Hypoaspis aculeifer*).

Test organism	Test substance	Time scale	Soil PEC[1] (mg a.s./kg soil dw)	TER	Trigger
Earthworms					
Eisenia fetida	Clomazone	Chronic	0.1686	492	5
Eisenia fetida	FMC-Clomazone 360 CS	Chronic	0.1686	9.5	5
Eisenia fetida	CLZ-M01	Chronic	0.0028	103214	
Other soil macro-organisms					
Folsomia candida	FMC-Clomazone 360 CS'	Chronic	0.1686	67	5
	CLZ-M01	Chronic	0.0028	43214	5
Hypoaspis aculeifer	FMC-Clomazone 360 CS'	Chronic	0.1686	1067	5

[1]indicate which PEC soil was used (e.g. plateau PEC)

Effects of clomazone and its metabolites CLZ-M01 and CLZ-M02 on nitrogen transformation was less than 25% at soil concentrations from 0.9 mg a.s./kg soil dw. I.e. concentrations significantly over the soil concentrations expected from the intended uses (0.1686 mg a.s./kg soil dw).

Risk assessment for non-target terrestrial plants

The vegetative vigour EC50 endpoint for Common chickweed of 4.5 g a.s./ha was the most sensitive endpoint of all plant species tested and this endpoint was driving the NTTP risk assessment. The predicted environmental concentration at 1 m is 3.32 g a.s./ha. I.e. a TER of 1.4 indicated need for risk mitigation. Introduction of a 5 meter no-spray buffer zone gave a TER of 6.6. I.e. the risk is addressed.

Enough valid plant toxicity data was however available to derive a step 2 SSD median HC5 endpoint of 6.6 g a.s./ha. With a trigger of 1 (according to EU terrestrial GD (2002)) the risk is addressed for non-target plants

without use of a no-spray buffer zone of 5 meter (6.6/3.2>1).

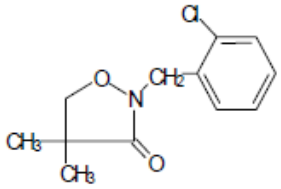
Field studies support the step 2 risk assessment and there was only indication of subtle and transient effects on plants in a few cases in the nearby vicinity of the treated field (distance of 1 m) when exposed to applications up to and including 120 g a.s./ha.

2.10 PROPOSED HARMONISED CLASSIFICATION AND LABELLING ACCORDING TO THE CLP CRITERIA *[SECTIONS 1-6 OF THE CLH REPORT]*

2.10.1 Identity of the substance [section 1 of the CLH report]

2.10.1.1 Name and other identifiers of the substance

Table 30: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one
Other names (usual name, trade name, abbreviation)	Clomazone 3-Isoxazolidinone, 2-[(2-chlorophenyl)methyl]-4,4-dimethyl-
ISO common name (if available and appropriate)	Clomazone (ISO); 2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one
EC number (if available and appropriate)	-
EC name (if available and appropriate)	-
CAS number (if available)	81777-89-1
Other identity code (if available)	509 (CIPAC)
Molecular formula	$C_{12}H_{14}ClNO_2$
Structural formula	
SMILES notation (if available)	-
Molecular weight or molecular weight range	239.7 g/mol
Degree of purity (%) (if relevant for the entry in Annex VI)	Min. 960 g/kg

2.10.1.2 Composition of the substance

Table 31: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
None			

Table 32: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	**Concentration range (% w/w minimum and maximum)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**	**The impurity contributes to the classification and labelling**
None				

Table 33: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	**Function**	**Concentration range (% w/w minimum and maximum)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**	**The additive contributes to the classification and labelling**
none					

Table 34: Test substances (non-confidential information)

The purity of the material tested is stated in the relevant sections of the dossier.

Identification of test substance	**Purity**	**Impurities and additives (identity, %, classification if available)**	**Other information**	**The study(ies) in which the test substance is used**

2.10.2 Proposed harmonized classification and labelling

2.10.2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 35: Proposed harmonised classification and labelling according to the CLP criteria

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	clomazone (ISO); 2- (2-chlorobenzyl)- 4,4-dimethyl-1,2-oxazolidin-3-one	-	81777-89-1	Repr. 1B Acute Tox. 4 Acute Tox. 4 Aquatic Acute 1 Aquatic Chronic 1	H360D H332 H302 H400 H410	GHS07 GHS08 GHS09 Dgr	H360D H332 H302 H410	inhalation: ATE = 4.3 mg/L oral: ATE = 754 mg/kg bw M = 1 (acute) M = 1 (chronic)		
Resulting entry in Annex VI if adopted by RAC and agreed by Commission	TBD	clomazone (ISO); 2- (2-chlorobenzyl)- 4,4-dimethyl-1,2-oxazolidin-3-one	-	81777-89-1	Repr. 1B Acute Tox. 4 Acute Tox. 4 Aquatic Acute 1 Aquatic Chronic 1	H360D H332 H302 H400 H410	GHS07 GHS08 GHS09 Dgr	H360D H332 H302 H410	inhalation: ATE = 4.3 mg/L oral: ATE = 754 mg/kg bw M = 1 (acute) M = 1 (chronic)		

2.10.2.2 Additional hazard statements / labelling

None

Table 36: Reason for not proposing harmonised classification and status under CLH public consultation

Hazard class	Reason for no classification	Within the scope of CLH public consultation
Explosives	data conclusive but not sufficient for classification	Yes
Flammable gases (including chemically unstable gases)	hazard class not applicable	No
Oxidising gases	hazard class not applicable	No
Gases under pressure	hazard class not applicable	No
Flammable liquids	data conclusive but not sufficient for classification	Yes
Flammable solids	data conclusive but not sufficient for classification	Yes
Self-reactive substances	hazard class not assessed in this dossier;	No
Pyrophoric liquids	hazard class not assessed in this dossier;	No
Pyrophoric solids	hazard class not assessed in this dossier;	No
Self-heating substances	data conclusive but not sufficient for classification	Yes
Substances which in contact with water emit flammable gases	hazard class not assessed in this dossier;	No
Oxidising liquids	data conclusive but not sufficient for classification	Yes
Oxidising solids	data inconclusive	Yes
Organic peroxides	hazard class not applicable	No
Corrosive to metals	hazard class not assessed in this dossier;	No
Acute toxicity via oral route	**harmonised classification proposed**	Yes
Acute toxicity via dermal route	data conclusive but not sufficient for classification	Yes
Acute toxicity via inhalation route	**harmonised classification proposed**	Yes
Skin corrosion/irritation	data conclusive but not sufficient for classification	Yes
Serious eye damage/eye irritation	data conclusive but not sufficient for classification	Yes
Respiratory sensitisation	data conclusive but not sufficient for classification	Yes
Skin sensitisation	data conclusive but not sufficient for classification	Yes
Germ cell mutagenicity	data conclusive but not sufficient for classification	Yes
Carcinogenicity	data conclusive but not sufficient for classification	Yes
Reproductive toxicity	**harmonised classification proposed**	Yes
Specific target organ toxicity-single exposure	data conclusive but not sufficient for classification	Yes
Specific target organ toxicity-repeated exposure	data conclusive but not sufficient for classification	Yes
Aspiration hazard	hazard class not applicable	Yes

Hazard class	Reason for no classification	Within the scope of CLH public consultation
Hazardous to the aquatic environment	**harmonised classification proposed**	Yes
Hazardous to the ozone layer	Hazard class not applicable	No

2.10.3 History of the previous classification and labelling

Clomazone has not previously been hazard classified according to Dangerous Substance Directive 67/548/EEC. As a result of the peer review process EFSA proposed in their EFSA conclusion of July 2007 that clomazone should be classified Xn, R20 Harmful by inhalation, R22 Harmful if swallowed and R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. A new evaluation has been conducted in this report according to the CLP classification criteria.

At the time of submission the substance has not been registered under REACH.

2.10.4 Identified uses

Clomazone is an herbicide for agriculture. On uses please see section 2.3.

2.10.5 Data sources

The data submitted in the context of renewal of pesticide active substances under Regulation no. 1107/2009 concerning the placing of plant protection products on the market. The data was evaluated in the Renewal Assessment Report (RAR) Vol. 1-4.

2.11 RELEVANCE OF METABOLITES IN GROUNDWATER

OAS:

An assessment has been conducted into the relevance of metabolites of clomazone in groundwater in accordance with the guidance document on the relevance of metabolites in groundwater (SANCO/221/2000-rev.10 final 25 February 2003[5]).

Clomazone degraded in soil under aerobic, anaerobic and photolytic conditions. Clomazone degraded to bound residue, carbon dioxide and minor metabolites (<5% AR) in each study type.

No soil metabolites of clomazone satisfied the following criteria:

- metabolites which account for more than 10 % of the amount of active substance added in soil at any time during the studies
- metabolites which account for more than 5 % of the amount of active substance added in soil in at least two sequential measurements during the studies
- metabolites for which at the end of soil degradation studies, the maximum of formation is not yet reached
- metabolites found in lysimeter studies at annual average concentrations exceeding 0.1 µg/L

No major soil metabolites were observed for clomazone, therefore a relevance assessment of soil metabolites in groundwater is not required.

[5] Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev.10-final 25 February 2003).

CATE:

A sequential assessment of the relevance of metabolites in groundwater according to SANCO/221/2000, rev. 10-final[4] was performed with respect to the intended uses of the representative product 'FMC-Clomazone 360 CS' considered for the renewal approval of clomazone.

According to the residue definition for exposure and risk assessment, CLZ-M01 (FMC 65317), a major anaerobic soil metabolite, is the only clomazone metabolite potentially of concern in groundwater.

2.11.1 STEP 1: Exclusion of degradation products of no concern

The above mentioned metabolite/degradation product potentially of concern does not meet the criteria for products of no concern defined in Step 1 of the guideline, since it is not an organic compound with an aliphatic structure with a chain length of less than four, an inorganic salt without heavy metals, CO_2 and are not naturally occurring at much higher concentrations in soil. In conclusion, exposure of groundwater with this compound was estimated in Step 2.

2.11.2 STEP 2: Quantification of potential groundwater contamination

Tier 1 FOCUS PELMO 5.5.3, FOCUS PEARL 4.4.4 and FOCUS MACRO 5.5.4 PEC_{gw} values were calculated for the anaerobic soil metabolite CLZ-M01 with respect to the representative GAP uses of 'FMC-Clomazone 360 CS' in potato and oilseed rape (spring, winter) considering the highest rate of application, i.e. 90 and 120 g a.s./ha, respectively.

The 80th percentile annual average PECgw of clomazone and CLZ-M01 at 1 m depth stayed clearly below the drinking water trigger of 0.1 µg/L for all models and all relevant FOCUS groundwater scenarios (see subchapter 8.6 - groundwater). Thus, no further non-relevance assessment at Step 3 (Hazard Assessment), 4 (Exposure assessment – threshold of concern approach) and 5 (Refined risk assessment) is required according to the principles of SANCO/221/2000, rev. 10-final.

2.11.3 STEP 3: Hazard assessment – identification of relevant metabolites

Not required.

2.11.4 STEP 4: Exposure assessment – threshold of concern approach

Not required.

2.11.5 STEP 5: Refined risk assessment

Not required.

2.11.6 Overall conclusion

CLZ-M01 (FMC 65317), which is the sole clomazone metabolite potentially of concern in groundwater, does not pose an unacceptable risk to groundwater.

2.12 CONSIDERATION OF ISOMERIC COMPOSITION IN THE RISK ASSESSMENT

The active substance clomazone is not a mixture of isomers. Therefore no information is presented or required.

2.13 RESIDUE DEFINITIONS

2.13.1 Definition of residues for exposure/risk assessment

Food of plant origin: Clomazone

Food of animal origin: Not necessary since no residues in animal products are expected. Clomazone if it is decided to set a residue definition.

Soil: Clomazone, CLZ-M01 (anaerobic soil)

Groundwater: Clomazone, CLZ-M01 (anaerobic soil)

Surface water: Clomazone, CLZ-M01, CLZ-M02, CLZ-M03, CLZ-M04, CLZ-M05

Sediment: Clomazone, CLZ-M01

Air: Clomazone

Body fluids and tissues: Clomazone

2.13.2 Definition of residues for monitoring

Food of plant origin: Clomazone

Food of animal origin: Not necessary since no residues in animal products are expected. Clomazone if it is decided to set a residue definition.

Soil: Clomazone

Groundwater: Clomazone

Surface water: Clomazone

Sediment: Clomazone

Air: Clomazone

Body fluids and tissues: Clomazone

Level 3

CLOMAZONE

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.	X		Clomazone in the products FMC Clomazone 360 CS and ALB Clomazone 360 CL have been assessed for uses in potatoes and oil seed rape.
3.1.1.2 Submission of further information				
		Yes	No	
i)	It is considered that a complete dossier has been submitted	X		Considering the two dossiers submitted by the two task forces all together a complete dossier has been submitted. However, there are data gaps in the dossiers individually. See 3.1.4.
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.	-		
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.		X	
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		Metabolism studies for pre-emergence treatment have been performed in at least three different kinds of commodities and the metabolism is similar in all the studies. The metabolism is similar to the metabolism in rats. The metabolism in succeeding crops is similar to that in the primary crops. Since all residues are < 0.01 and the dietary burden is < 0.004 mg/kg bw in animals no metabolism studies or feeding studies have been submitted and the studies are also not necessary. Processing studies are also not necessary. For plants only clomazone is considered to be the only substance of relevance and the residue definitions for monitoring and risk assessment is proposed to be "clomazone". All residues are < 0.01 mg/kg in both potatoes and oil seed. MRLs of 0.01* mg/kg can therefore be proposed. Clomazone can be determined with an independent validated multimethod.
	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.			The data submitted are considered sufficient for the environmental risk assessment. There are however data requirement to the applicant task forces in order to fulfil data requirements that were missing or where the submitted studies were assessed as not valid.
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 practice and having regard to realistic conditions of use is sufficiently effective.	X		Clomazone can be applied pre-emergence in a wide range of crops and is active on a wide range of broadleaved and grass weeds. See level 2 (section 2.3).
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		
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		X	The minimum degree of purity as defined in the specification is 96.0%. Clomazone does not contain isomers or additives. Possibly the current and proposed reference specification is not representative of the batches used for (eco)toxicology testing when it comes to impurities 3, 14 and 23.

	within acceptable limits.			
	It is considered that the specification is in compliance with the relevant Food and Agriculture Organisation specification, where such specification exists.	-		No FAO specification
	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	-		No FAO specification
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 specific, correctly calibrated, accurate and precise.	X		Technical material and formulations: Methods to analyse clomazone in the technical material and formulations are validated according to SANCO/3030/99 rev. 4.
	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		Residues: Methods for enforcement are validated according to SANCO 825/00 rev. 8.1. Soil and Water: Methods for enforcement are validated according to SANCO 825/00 rev. 8.1. Air: Methods were validated according to SANCO/825/00 rev. 8.1 Body fluids and tissue: The method was validated according to SANCO/825/00 rev. 8.1. Task force Oxon, Albaugh, Sapec did not submit any method for body fluids or tissue.
	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 and AOEL are proposed on the basis of the one year study in dogs as dogs are the more sensitive species. The NOAEL is 12 mg/kg bw/day and the AF 100. ADI and AOEL = 0.12 mg/kg bw/day ARfD and AAOEL are proposed on the basis of the maternal NOAEL of the developmental study in rats. The NOAEL is 250 mg/kg bw/day and the AF 100. ARfD and AAOEL = 2.5 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	Clomazone is not known to induce heritable mutations (Cat 1A) or to be regarded as if it induces heritable mutations (Cat 1B) in the germ cells of humans. Neither is it considered possible that clomazone may induce heritable mutations (Cat 2) in the germ cells of humans on the basis of negative results in in vitro and in vivo studies.
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 1272/2008, **as carcinogen category 1A or 1B.**		X	Clomazone is not known to have or presumed to have carcinogenic potential for humans (Cat 1A and 1B). No oncogenic effects were observed in studies conducted with clomazone, neither in the rat nor in the mouse carcinogenicity studies. Hence, clomazone is not a suspected human carcinogen (Cat 2).
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.	-		It is not necessary to evaluate on negligible exposure of clomazone as it is not proposed classified carcinogen category 1A or 1B.
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		There is no human evidence to allocate clomazone to Category 1A. The effect is not considered secondary to maternal toxicity and with effects in two species the evidence is sufficiently convincing to place it in category 1. It is proposed to classify clomazone Repr. 1B, H360d May damage the unborn child. See 2.6.3.
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance,		X	Clomazone is not used in closed systems, but is a PPP for spray application. Residues levels are less than 0.01 mg/kg.

	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.			
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 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**		X	Clomazone is not proposed to be classified for carcinogenicity.
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**		X	The overall weight of evidence points toward clomazone not having endocrine disrupting properties because of the following reasons: - Slight changes seen on endocrine tissues only at toxic doses - Repeat dosing and reproductive higher-tier studies did not detect significant effects on apical endpoints or perturbations at histopathological levels of endocrine organs or system - Liver toxicity not associated with downstream effect on endocrine systems - No effect on reproduction
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.	-		It is not necessary to evaluate on negligible exposure of clomazone as it is not considered to have endocrine disrupting properties.
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		X	As stated in level 2 the DT_{50} in surface water is 24.2 d (geometric mean, normalised), in sediment it is 39.6 d (geometric mean, normalised) and in

	Annex II Section 3.7.1.			soil it is 26.8 d in laboratory studies and 34.5 d in field studies (geometric mean, non-normalised). Clomazone does not bioaccumulate and there is no potential for long-range transport.
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	As stated in level 2 the DT_{50} in surface water is 24.2 d (geometric mean, normalised), in sediment it is 39.6 d (geometric mean, normalised) and in soil it is 26.8 d in laboratory studies and 34.5 d in field studies (geometric mean, non-normalised). Clomazone does not bioaccumulate but does fulfil the toxicity criteria for aquatic organisms. However, clomazone is proposed classified Repr. 1B.
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	As stated in level 2 the DT_{50} in surface water is 24.2 d (geometric mean, normalised), in sediment it is 39.6 d (geometric mean, normalised) and in soil it is 26.8 d in laboratory studies and 34.5 d in field studies (geometric mean, non-normalised). Clomazone does not bioaccumulate
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		The environmental risk from all intended uses is addressed and no unacceptable risk to non-target organisms is expected.
	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.		x	None of the ecotox data available indicates that clomazone should have any endocrine disrupting properties.
	Linked to the consideration of the endocrine properties immediately above.		x	There will be exposure of non-target organisms but clomazone is not considered an endocrine disrupter.

	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.			
	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		No unacceptable risk to bees is expected from use of clomazone according to the GAP. The evaluation of the risk for bees was performed in accordance with the recommendations of the "EFSA Guidance Document on the risk of plant protection products on bees (*Apis mellifera*, *Bombus* spp. And solitary bees)", as provided by EFSA (EFSA Journal 2013; 11(7): 3295; updated version published on 4 July 2014). For honeybees and bumblebees the risk assessment indicated no unacceptable risk from acute contact toxicity. The oral route for honey bees indicate no unacceptable risk for potatoes use. The oral route for honey bees indicate no unacceptable risk for oil seed rape use. The ETRoral value for the crop scenario is still slightly exceeded. Given the conservativeness of the SV value for preemergens use in oilseed rape, the exceedance is accepted. The oral route for bumblebees indicate no unacceptable risk for potatoes or oil seed rape use. No unacceptable risk to bees is expected from metabolites generated in pollen and nectar after use of clomazone according to the GAP. No unacceptable risk to bees is expected from contaminated water (guttation, surface water and water in puddles) after use of clomazone according to the GAP. The risk to solitary bees has not been assessed due to lack of experimental data.
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		For plants clomazone is considered to be the only substance of relevance and the residue definitions for monitoring and risk assessment is proposed to be "clomazone". See also 2.7.3. No residue definitions are proposed for animal products. All residues are < 0.01 mg/kg and the dietary burden is < 0.004 mg/kg bw.
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	X		For all representative uses the groundwater modelling demonstrates a low risk of leaching for all FOCUS scenarios. For further details refer to level 2.

	authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.			

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	Clomazone do not fulfil the criteria for Candidates for substitution.

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	Clomazone do not fulfil the criteria for low risk substances.

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				
-				
3.1.4.2 Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation				
CATF – active substance: • B.2.2/02 – volatility calculation • B.2.4/02 – a table in the dRAR with signal characteristics from IR spectra should be provided • B.2.4/03 – a table in the dRAR with signal characteristics from NMR spectra should be provided • B.2.4/04 – a table in the dRAR with signal characteristics from MS spectra should be provided • B.2.13/01 – oxidising properties for the active substances as manufactured (solid). The preliminary test did not exclude oxidising properties	Relevant for all representative uses			
CATF – formulation:	Relevant for all representative uses	X	B.2.7/03 – study report	

• B.2.2/01 – a clear case of explosive properties should be provided. • B.2.7/03 - Storage at ambient temperature for 2 years			on Storage at ambient temperature for 2 years is expected submitted in 2017	
OAS – active substance: • B.2.1/02 – test on boiling point not accepted • B.2.4/02 – IR with purified a.s. • B.2.4/03 – NMR spectra with purified a.s • B.2.7/02 – partition coefficient n-octanol/water of metabolites M03, M04 and M05. • B.2.9/01 – flammability of active substances as manufactured as two of the three technical materials are solids • B.2.11/01 – explosive test for the solid active substances as manufactured. • B.2.13/01 – oxidising properties for the active substances as manufactured. The statement was not accepted.	Relevant for all representative uses	X		
OAS – formulation: • B.2.2/01 – explosive properties. The statement was not accepted. • B.2.2/02 – oxidizing properties. The statement was not accepted. • B.2.5/01 – awaiting method specification for viscosity • B.2.5/02 – awaiting test concentration specification for surface tension • B.2.6/01 – awaiting method and	Relevant for all representative uses	X		

temperature specification for relative density				
3.1.4.3 Data on uses and efficacy				
-				
3.1.4.4 Data on handling, storage, transport, packaging and labelling				
-				
3.1.4.5 Methods of analysis				
A data gap was identified for an analytical method for body fluids and tissues for OAS.	A validated method was supplied by CATF.	X		
3.1.4.6 Toxicology and metabolism				
Data gaps was identified for OAS for: - a study on *in vitro* metabolism - an *in vivo* micronucleus test	Studies were supplied by CATF.	X		
3.1.4.7 Residue data				
-				

3.1.4.8 Environmental fate and behaviour				
OAS does not have a valid sorption study, but this is ongoing and should be submitted.	Relevant for all representative uses		OAS please indicated	
Both notifiers needs to address transport through air and exposure of off-field non-target plants in more detail.	Relevant for all representative uses	X		
3.1.4.9 Ecotoxicology				
OAS does not have valid algae ecotox studies for clomazone and the metabolites, CLZ-M03, CLZ-M04 and CLZ-M05.	The aquatic risk assessment is based on valid CATF data		April 2018	
OAS does not have valid fish ecotox studies for clomazone and the metabolites, CLZ-M03, CLZ-M04 and CLZ-M05.	The aquatic risk assessment is based on valid CATF data	X		
OAS does not have valid invertebrate ecotox studies for clomazone and the metabolites, CLZ-M03, CLZ-M04 and CLZ-M05.	The aquatic risk assessment is based on valid CATF data	X		
OAS does not have valid ecotox studies for the metabolite CLZ-M01exposed to *Chironomus riparus* in sediment.	The aquatic risk assessment is based on valid CATF data	X		
OAS does not provide data on effects on biological method for sewage treatment from exposure to clomazone.	A risk assessment was provide by CATF	X		

3.1.5 Issues that could not be finalised

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)**
Transport in air and the exposure of non-target off field plants (bleaching). See comments from co-RMS given in the fate and behaviour section.	This refers to all the representative uses.
The representativeness of the specification.	This refers to all the representative uses.

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)**
The active substance is proposed classified Repr 1B.	This refers to all the representative uses.

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		CATF (X^1)	OAS (X^1)
Operator risk	Risk identified	-	-
	Assessment not finalised	-	-
Worker risk	Risk identified	-	-
	Assessment not finalised	-	-
Bystander risk	Risk identified	-	-
	Assessment not finalised	-	-
Consumer risk	Risk identified	-	-
	Assessment not finalised	-	-
Risk to wild non target terrestrial vertebrates	Risk identified	-	-
	Assessment not finalised	-	-
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	-	-
	Assessment not finalised	-	-
Risk to aquatic organisms	Risk identified	-	-
	Assessment not finalised	-	-
Groundwater exposure active substance	Legal parametric value breached	-	-
	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**

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**
B.7.7, if results from a study from the open literature should be considered in MRL setting	It should be considered	Should not be considered

3.2 PROPOSED DECISION

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[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 taken into account to manage the risks identified

Proposed condition/risk mitigation measure	Relevance in relation to representative use(s)
[redacted]	[redacted]

3.4 APPENDICES

GUIDANCE DOCUMENTS USED IN THIS ASSESSEMENT

General

Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances.

Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for plant protection products.

Section Identity

None

Section Physical and Chemical Properties

ECHA (2017). Guidance on the Application of the CLP Criteria 2017 vers 5.0

UN recommendations on the Transport of Dangerous Goods (2015). Manual of tests and criteria Annex 6 2015 rev 6

Section Analytical Methods

SANCO/825/00 rev. 8.1, 16 November 2010, Guidance document on pesticide residue analytical methods.

Section Data on Application and Efficacy

SANCO/10054/2013 - rev. 3 (2013): Guidance document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products.

Section Toxicology

EFSA (2012), Guidance on Dermal Absorption, EFSA Panel on Plant Protection Products and their Residues (PPR), EFSA Journal 2012;10(4):2665

EFSA (2014), Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products, EFSA Journal 2014;12(10):3874

Section Residue and Consumer Risk Assessment

OECD (2009). Guidance Document on Overview of Residue Chemistry Studies (as revised in 2009). Environment, Health and Safety Publications. Series on Testing and Assessment No. 64 and Series on Pesticides No. 32

OECD (2011) Guidance Document on Crop Field Trials (Series on Testing and Assessment No. 164 and Series on Pesticides No. 66)

OECD (2008). Guidance document on magnitude of pesticide residues in processed commodities. Environment, Health and Safety Publications. Series on Testing and Assessment No. 96.

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3.5 REFERENCE LIST

List [in the conventional format] any references specifically cited in Volume 1 (i.e references to underpinning documents such as PPR-Panel Opinions, EFSA conclusions, national documents etc.).

Section identity, physical chemical and analytical methods

Section data on application and efficacy

Section toxicology

Section residue and consumer risk assessment

Section fate and behaviour in environment

Section ecotoxicology