Bayer CropScience

Document Title

Summary of the toxicological studies Iodosulfuron-methyl-sodium + Mesosulfuron-methyl +Mefenpyr-diethyl OD 42 (2+10+30 g/L)

Data Requirements

EU Regulation 1107/2009 & EU Regulation 284/2013
Document MCP
Section 7: Toxicological studies

According to the guidance document, SANCO 10181/2013, for preparing dossiers for the approval of a chemical active substance

M-489586-01-5

Date

2014/06/27

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Version history

Date	Data points containing amendments or additions[1] and brief description	Document identifier and version number

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

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Covers the point required in SANCO 10181/2013 format shown below

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IIIA 7 TOXICOLOGICAL STUDIES

In agreement with the Rapporteur Member State, the product dossier is submitted following the dRR format. All points required under the SANCO 10181/2013 are covered, although their naming might differ slightly.

IIIA 7.1 Acute Toxicity

IMS+MSM+MPR OD 42 (or Atlantis OD, Specification N° 102000008429) is an Oil Dispersion (OD) formulation containing 2 g/L iodosulfuron-methyl-sodium, 10 g/L mesosulfuron-methyl and the safener mefenpyr-diethyl (30 g/L). The formulated product is a herbicide for use in wheat, triticale and rye. Acute toxicity studies for this formulation were not evaluated as part of the EU review of iodosulfuron-methyl-sodium or mesosulfuron-methyl. Therefore all relevant data are provided in this document and are considered adequate.

The acute toxicology data package was performed on the formulated product IMS+MSM+MPR OD 42 also known as AE F115008 06 OD04 A1 (Specification N° 102000008369) which was found to be of low oral and dermal acute toxicity but was irritant to both skin (according to 2001/59/EC, not to CLP) and eyes. The formulation was found to be non-sensitising to skin. The results are summarised in the Table 7.1-1. The current product (Specification N° 102000008429) was produced by only minor changes to the original recipe and a bridging statement (M-281058-01-1, see Doc JCP) is available to demonstrate that the original acute toxicity data are relevant to the new specification and that further animal testing is not necessary.

Table 7.1-1: Summary of the Acute Toxicity of IMS+MSM+MPR OD 42

Study	Reference	Species (sex)	Results
Acute oral	[redacted] (2003) M-225480-01-1	Rat (Female)	LD_{50} >5000 mg/kg bw
Acute dermal	[redacted] (2003) M-225482-01-1	Rat (Male & Female)	LD_{50} > 4000 mg/kg bw
Acute skin irritation	[redacted]. (2004) M-227101-02-1	Rabbit (Female)	Irritant
Acute eye irritation	[redacted]. (2004) M-227104-01-1	Rabbit (Female)	Irritant
Buehler Skin sensitization	[redacted] (2004) M-227212-02-1	Guinea pig (Female)	Non sensitising

Therefore, according to the EC classification criteria (2001/59/EC Directive), the formulation iodosulfuron-methyl-sodium + mesosulfuron-methyl +mefenpyr-diethyl OD (50+7.5+250 g/L) is classified and should be labelled as follows:

- **EC classification criteria (2001/59/EC):**
  - **Xi, R36 "irritating to eyes" & Xi, R38 "irritating to skin".**
- **Regulation (EC) No 1272/2008 (CLP):**
  - **Eye Irritation Category 2; Warning: H319 "Causes serious eye irritation".**

IIIA 7.1.1 Acute oral toxicity

Report:	[redacted]9;[redacted];2003;M-225480-01
Title:	Mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 + 30 (AE F115008 06 OD04 A1 - Atlantis liquid) Acute toxicity in the rat after oral administration
Report No:	C038675
Document No(s):	M-225480-01-1
Guidelines:	**EU (=EEC): 67/548/EEC; OECD: 423; USEPA (=EPA): OPPTS 870.1100;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods

The formulation Mesosulfuron-methyl & Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 10 + 2 + 30 (batch number: AAIM01428) contained 10.44 g/L (measured: 10.63 g/L) of the active ingredient Mesosulfuron-methyl, 2 g/L (measured: 2.11 g/L) of the active ingredient Iodosulfuron-methyl-sodium, and 30 g/L (measured: 30.59 g/L) of the active ingredient Mefenpyr-diethyl.
The test material, a light brown liquid, was formulated in demineralised water and the administration volume was 10 mL/kg bw. A single dose (2000 mg/kg bw) of the test material was administered by gavage to 3 fasted female Wistar rats. Three additional animals were treated with the same dose.

Table 7.1.1-1: Acute oral toxicity in female rats

Dose (mg/kg bw)	Toxicological findings*	Duration of signs	Onset of death after (days)	LD_{50} (mg/kg bw)
(1st) 2000	0/3/3	35' - 3h	--	LD_{50} ≥5000
(2nd) 2000	0/3/3	25' – 3h	--	

* number of dead animals/number of animals with clinical signs/number of animals tested.

Findings

- Clinical signs observed were decreased motility and narrow palpebral fissures.
- Body weights: there were no toxicological effects on body weights or on body weight gain.
- Effects on organs: The necropsies performed at the end of the study revealed no particular findings.

Conclusion

The acute oral LD_{50} of the formulation iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30 g/L) in rats was ≥5000 mg/kg bw.

According to the EC classification criteria the formulation should be labelled as follows:

- **EC classification criteria (2001/59/EC):**
  - **None**
- **Regulation (EC) No 1272/2008 (CLP):**
  - **None**

IIIA 7.1.2 Acute percutaneous (dermal) toxicity

Report:	[redacted]q;[redacted];2003;M-225482-01
Title:	Mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 + 30 (AE F115008 06 OD04 A1 - Atlantis liquid) Acute toxicity in the rat after dermal administration
Report No:	C038677
Document No(s):	M-225482-01-1
Guidelines:	**EU (=EEC): 67/548/EEC; OECD: 402; USEPA (=EPA): OPPTS 870.1200;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods
The formulation Mesosulfuron-methyl & Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 10 + 2 + 30 (batch number: AAIM01428) contained 10.44 g/L (measured: 10.63 g/L) of the active ingredient Mesosulfuron-methyl, 2 g/L (measured: 2.11 g/L) of the active ingredient Iodosulfuron-methyl-sodium, and 30 g/L (measured: 30.59 g/L) of the active ingredient Mefenpyr-diethyl.

One day before the start of the treatment the back and flanks of 5 male and 5 female Wistar rats were shorn. They received a single dermal dose of 4000 mg/kg bw of the pure liquid test compound applied semi-occlusively. After an exposure time of 24 hours, the fixing bandage and the gauze strip were removed and the treated area was cleaned with soap and water.

Table 7.1.2-1: Acute dermal toxicity in rats

Sex	Dose (mg/kg bw)	Toxicological findings*	Duration of signs	Onset of death after (days)	LD_{50} (mg/kg bw)
Male	4000	0/5/5	2d – 15d	--	> 4000
Female	4000	0/5/5	2d – 15d	--	> 4000

* number of dead animals/number of animals with clinical signs/number of animals in the group

Findings
Mortality: no deaths occurred during the study.
Body weights and body weight gain were not affected in males whilst a slight transient decrease in body weight was observed on day 8 of the study in three females.
Clinical signs: local skin reactions were observed at the treatment area: partly reddening, partly formation of scale, partly encrustation, partly induration, partly swelling and partly ablation of skin.
Effects on organs: skin irritations were still evidenced at final necropsies. No other particular findings were found

Conclusion
The dermal LD_{50} of the iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30 g/L) in rats was > 4000 mg/kg bw.

According to the EC classification criteria the formulation should be labelled as follows:

- **EC classification criteria (2001/59/EC):**
  - **None**
- **Regulation (EC) No 1272/2008 (CLP):**
  - **None**

IIIA 7.1.3 Acute inhalation toxicity to rats

Since iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30 g/L) is commercialized in the form of an oil dispersible formulation, which is a liquid; no acute inhalation study is required. The formulation will not be used in a manner that is expected to pose any acute inhalation hazard. With respect to 94/79/EEC, testing for the acute inhalation toxicity of iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30 g/L) is not triggered because it:

- is not a gas or liquefied gas,
- is not a smoke generating formulation or fumigant,
- is not to be used with fogging equipment,
- is not a vapour releasing preparation,
- is not an aerosol,
- is not a powder, is dust-free, and hence does not contain a significant proportion of particles of diameter < 50 µm (> 1 % on a weight basis),
- is not to be applied from aircraft and
- does not contain active substances with a vapour pressure ≥ 1 x 10^{-2} Pa and
- is not to be used in a manner which generates a significant proportion of particles or droplets of diameter < 50 µm (>1% on a weight basis).

In the absence of the need to perform an acute inhalation toxicity study the iodosulfuron-methyl-sodium + mesosulfuron-methyl +mefenpyr-diethyl OD 42 (2+10+30 g/L) formulation need not be classified.

According to the EC classification criteria the formulation is labeled as follows:

- **EC classification criteria (2001/59/EC):**
  - **None**
- **Regulation (EC) No 1272/2008 (CLP):**
  - **None**

IIIA 7.1.4 Skin irritation

Report:	[redacted];2004;M-227101-02; Amended: 2004-07-21
Title:	Acute skin irritation / corrosion on rabbits Mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 +30 (AE F115008 06 OD04 A1 - Atlantis Liquid) 1st revised version of report AT00973
Report No:	C042947
Document No(s):	M-227101-02-1
Guidelines:	**EU (=EEC): 67/548/EEC, B.4, 67/548/EEC, Part B, B.4; OECD: 404;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods

The formulation Mesosulfuron-methyl & Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 10 + 2 + 30 (batch number: AAIM01428) contained 10.44 g/L (measured: 10.63 g/L) of the active ingredient Mesosulfuron-methyl, 2 g/L (measured: 2.11 g/L) of the active ingredient Iodosulfuron-methyl-sodium, and 30 g/L (measured: 30.59 g/L) of the active ingredient Mefenpyr-diethyl.

Approximately one day before the start of the treatment, fur was shorn from the right and left side of the dorso-lateral area of the trunk of each of the rabbits. A single application was performed to the shorn skin of 3 female KBL(NZW)BR White rabbits at a rate of 0.5 mL of the pure liquid test item/animal over a treated skin area of approximately 6 cm^2. After an exposure time of 4 hours, the dressing and patch were removed and the treated area was cleaned with water.

The individual findings of the treated skin areas at the various observation times are summarized in Table 7.1.4-1.

Table 7.1.4-1: Irritant Effects on the skin (Exposure: 4 hours)

Animal		24 hours	48 hours	72 hours	Mean scores	Response	Reversible (days)
2568	Erythema (redness) and Eschar formation	2	2	2	2	+	14
	Oedema Formation	0	0	0	0	-	NA
2556	Erythema (redness) and Eschar formation	2	2	2	2	+	14
	Oedema Formation	0	0	0	0	-	NA
2550	Erythema (redness) and Eschar formation	2	2	2	2		14
	Oedema Formation	0	0	0	0	-	NA

Abbreviations: No positive response: mean scores <2 = - NA= Not applicable
Positive response: mean scores ≥2 = +

Findings
After a 4 hour exposure (3 animals), Animal No. 2568 showed cracked skin at and around the application area on day 6 and 7 and animal No. 2556 on day 5 to 7. Mean scores over 24, 48 and 72 hours for each animal were 2.00, 2.00 and 2.00 for erythema and 0.00, 0.00 and 0.00 for oedema.

Conclusion
The test item, the iodosulfuron-methyl-sodium + mesosulfuron-methyl +mefenpyr-diethyl OD 42 (2+10+30 g/L) formulation, was moderately irritant when applied topically to rabbits with full reversibility within 14 days.

According to the EC classification criteria the formulation is labeled as follows:

- **EC classification criteria (2001/59/EC):**
  - **Xi, R38, "irritating to skin"**
- **Regulation (EC) No 1272/2008 (CLP):**
  - **None**

IIIA 7.1.5 Eye irritation

Report:	[redacted] ヨ; [redacted];2004;M-227104-01
Title:	Acute eye irritation/corrosion on rabbits - Atlantis liquid Mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl, OD 10 + 2 + 30 Code: AE F115008 06 OD04 A1
Report No:	C039670
Document No(s):	M-227104-01-1
Guidelines:	**EU (=EEC): 67/548/EEC, Part B, B.5; OECD: 405;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods
The formulation Mesosulfuron-methyl & Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 10 + 2 + 30 (batch number: AAIM01428) contained 10.44 g/L (measured: 10.63 g/L) of the active ingredient Mesosulfuron-methyl, 2 g/L (measured: 2.11 g/L) of the active ingredient Iodosulfuron-methyl-sodium, and 30 g/L (measured: 30.59 g/L) of the active ingredient Mefenpyr-diethyl.
The test was started with one of three rabbits. 100 µl of the pure liquid test substance was placed into the conjunctival sac of one eye of the first animal after having gently pulled the lower lid away from the eyeball. The lids were gently held together for about one second in order to prevent loss of the test compound. The other eye, which remains untreated, served as control. The eyes were not washed for at least 24 hours following instillation.
As no corrosive/irritating effect was observed after one hour the other two rabbits were treated.

The individual findings of the treated eyes at the various observation times are summarized in Table 7.1.5-1.

Table 7.1.5-1: Summary of irritant effect

Observations Animal 2589	1h	24h	48h	72h	Mean scores (24-48-72h)	Reversible (days)
Degree of cornea opacity	1	2	2	2	2.00 (+)	21
Iris	1	1	1	0	0.67 (-)	-
Redness conjunctivae	1	1	1	1	1.00 (-)	-
Chemosis conjunctivae	1	1	1	1	1.00 (-)	-

Observations Animal 2597	1h	24h	48h	72h	Mean scores (24-48-72h)	Reversible (days)
Degree of cornea opacity	1	2	2	2	2.0 (+)	21
Iris	1	1	1	1	1.0 (+)	5
Redness conjunctivae	1	1	1	1	1.0 (-)	-
Chemosis conjunctivae	1	2	2	2	2.0 (+)	6

Observations Animal 2600	1h	24h	48h	72h	Mean scores (24-48-72h)	Reversible (days)
Degree of cornea opacity	1	2	2	2	2.0 (+)	21
Iris	1	0	1	1	0.67 (-)	-
Redness conjunctivae	1	2	2	1	2.0 (-)	-
Chemosis conjunctivae	1	2	3	2	2.67 (+)	6

Response: corneal opacity: mean scores <2 = (-), ≥2<3 = (+), ≥3 = (++)
Iritis: mean scores <1 = (-), ≥1<2 = (+), = 2 =(++)
Conjunctival redness: mean scores <2.5 = (-), ≥2.5 = +
Conjunctival oedema: mean scores <2 = (-), ≥ 2 = +

Findings
The mean scores calculated using the two most sensitive animals 24, 48 and 72 hours were 2.33 for chemosis, 1.5 for redness of the conjunctiva, 0.83 for iris lesions and 2.0 for corneal opacity.

Conclusion
The test item, the iodosulfuron-methyl-sodium + mesosulfuron-methyl +mefenpyr-diethyl OD 42 (2+10+30 g/L) formulation, was moderately irritant when administered by the ocular route to rabbits with full reversibility within 21 days.

According to the EC classification criteria the formulation is labeled as follows:

- **EC classification criteria (2001/59/EC):**
    - **Xi, R36 “Irritating to eyes”.**
- **Regulation (EC) No 1272/2008 (CLP):**
    - **Eye Irritation Category 2; Warning H319.**

IIIA 7.1.6 Skin sensitisation

Report:	[redacted];[redacted];2004;M-227212-02; Amended: 2004-03-18
Title:	Study for the skin sensitization effect in guinea pigs (Buehler patch test) Code: AE F115008 06 OD04 A104
Report No:	C039780
Document No(s):	M-227212-02-1
Guidelines:	**EU (=EEC): EC 96/54, Method B.6; OECD: 406; USEPA (=EPA): OPPTS 870.2600;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods
Mesosulfuron-methyl & Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 10 + 2 + 30 (batch number: AAIM01428) contained 10.44 g/L (measured: 10.63 g/L) of the active ingredient Mesosulfuron-methyl, 2 g/L (measured: 2.11 g/L) of the active ingredient Iodosulfuron-methyl-sodium, and 30 g/L (measured: 30.59 g/L) of the active ingredient Mefenpyr-diethyl.

The test was performed on 30 female guinea pigs (20 animals for the test item group and 10 control animals). Two animals were used for dose-finding, where the test compound was formulated in physiological saline solution.

- Induction: the animals were dermally treated with the test item nine times over 3 weeks. The 1st to 9th inductions were performed with the 12% test item concentration. The volume applied per animal was 0.5 mL. The 1st to 4th induction and the 8th and 9th induction was carried out on the left flank and the 5th to 7th on the right flank, because of the strong skin effects after the 4th and 7th inductions. The occlusive patches were removed after an exposure period of 6 hours. The treatment areas were visually assessed 30 hours after initiation of exposure.

- Challenge: the challenge was performed four weeks after the first dermal induction. The backs and the flanks of the animals were shorn one day prior to challenge. A patch, loaded with 0.5 mL of the 6% test compound was applied and fixed to the right flank of the animals for an exposure period of 6 hours. The skin reactions were assessed 30 and 54 hours after the beginning of the challenge.

Findings

Table 7.1.6-1 Results of the proliferation assay:

Sex	Animal number	Control group			
		Test item patch		Control patch	
		30 hours*	54 hours*	30 hours*	54 hours*
Male	1	0	0	0	0
	2	0	0	0	0
	3	0	0	0	0
	4	0	0	0	0
	5	0	0	0	0
	6	0	0	0	0
	7	0	0	0	0
	8	0	0	0	0
	9	0	0	0	0
	10	0	0	0	0
		Treated group			
Male	11	0	0	0	0
	12	+	+	+	+
	13	0	0	0	0
	14	0	0	0	0
	15	0	0	0	0
	16	0	0	0	0
	17	0	0	0	0
	18	0	0	0	0
	19	0	0	0	0
	20	0	0	0	0
	21	0	0	0	0
	22	0	0	0	0
	23	0	0	0	0
	24	+	+		+
	25	0	0	0	0
	26	0	0	0	0
	27	0	0	0	0
	28	0	0	0	0
	29	0	0	0	0
	30	0	0	0	0

* : finding made 30 and 54 hours after start of exposure,
\+ : animal died

Mortality: Animal no 24 of the test item group died at day 10 of the study.

- Clinical signs: Animal no 12 of the test item group showed at day 13: laboured breathing, piloerection, pale and from day 14 to death at day 15: laboured breathing, piloerection, pale and apathy. Appearance and behaviour of other animals of the test item group were not different from the control group.

- Body weights: no difference was observed between the control group and the treated group.
- Dermal observations: no skin effects were recorded during the challenge phase with the 6%test item formulation.

Conclusion
The test item, the iodosulfuron-methyl-sodium + mesosulfuron-methyl +mefenpyr-diethyl OD 42 (2+10+30 g/L) formulation, was found to be non-sensitising when administered by the dermal route to guinea-pigs with both induction and challenge phases.
According to the EC classification criteria the formulation is labeled as follows:

- **EC classification criteria (2001/59/EC):**
  - **None**
- **Regulation (EC) No 1272/2008 (CLP):**
  - **None**

IIIA 7.1.7 Supplementary studies for combinations of plant protection products

Not relevant: the formulation is not recommended to be combined with other plant protection products.

IIIA 7.2 Short-Term Toxicity Studies

This is not an EC data requirement/ not required by Directive 91/414/EEC.

IIIA 7.3 Operator Exposure

IMS+MSM+MPR OD 42 (Atlantis OD®) is an Oil Dispersion (OD) formulation containing 2 g/L iodosulfuron-methyl-sodium, 10 g/L mesosulfuron-methyl and the safener mefenpyr-diethyl (30 g/L). The proposed use is as a post-emergence herbicide that controls grasses and broadleaf weeds in wheat triticale and rye. Applications will be achieved using field crop sprayers. Water will be the diluent/carrier in all situations. Usage information pertinent to operator exposure is summarised in Table 7.3-1.

Table 7.3-1: Worse case application parameters for IMS+MSM+MPR OD 42

Appl. techn.	Growth stage (BBCH)	Crop(s)	Maximum dose rate			Spray volume (L/ha)	No of trmt.
			L/ha (product)	(kg a.s./ha)			
				IMS	MSM		
FCS	20-32	Spring & Winter Wheat triticale, rye (end of winter to spring application)	1	0.003	0.015	100-400	1

IMS = Iodosulfuron-methyl-sodium, MSM = Mesosulfuron-methyl.
FCS = Field Crop Sprayer.

Dermal Absorption

No dermal absorption data are available for mesosulfuron in the Atlantis OD formulation. Therefore the default value of 75% (as proposed by the current EFSA guidance[1]) was used in the following risk assessments.

[1] EFSA Panel on Plant Protection Products and their Residues (PPR); Guidance on Dermal Absorption. EFSA Journal 2012;10(4):2665. [30 pp.] doi:10.2903/j.efsa.2012.2665.

Acceptable Operator Exposure Level

The AOEL for mesosulfuron-methyl of 0.2 mg/kg bw/day was established from a 90-day oral dog study (NOAEL of 574 mg/kg/day), an absorption correction factor of 3% and a safety factor of 100.

Operator exposure estimates

Operator exposure estimates were calculated using both the German model[2] and the UK-POEM[3]. Exposure calculations are performed without and with protective equipment. The application to winter cereals will be used for exposure calculations as it represents the highest application rate and thus the worst case scenario.

The results of the exposure calculations are summarised in Table 7.3-2.

Table 7.3-2: Predicted systemic exposure as a proportion of the AOEL

Substance	**PPE**	**Total systemic exposure (mg/kg bw/day)***	**AOEL (mg/kg/day)**	**% of AOEL**
German model Field crop sprayer application to cereals, 20 ha/day at a rate of 1.5 L product/ha, 70 kg operator				
MSM	No PPE 1)	0.01428	0.2	**7**
	With PPE 2)	0.00176		**1**
UK POEM Field crop sprayer application to cereals, 50 ha/day at a rate of 1.5 L product/ha, 100 L/ha. 60 kg operator				
MSM	No PPE 3)	0.128056	0.2	**64**
	With PPE 4)	0.083056		**42**

1) No PPE = lightly dressed operator, wearing a short sleeved T-Shirt, shorts and shoes.
2) With PPE = Gloves during mixing/loading and a coverall during application
3) No PPE UK POEM = operator wearing long sleeved shirt and long trousers.
4) With PPE UK POEM: operator wearing long-sleeved shirt, long trousers and gloves during Mixing/Loading.

*Dermal absorption value of 75%. Inhalation absorption was taken as 100%.

The BBA model estimates predict that IMS+MSM+MPR OD 42 can be used safely with Field Crop Sprayers even without the use of any personal protective equipment. Systemic exposure from the use of IMS+MSM+MPR OD 42 with Field Crop Sprayer without protection results in 7% of the mesosulfuron-methyl AOEL.

The UK POEM estimates predict that IMS+MSM+MPR OD 42 can be used safely with Field Crop Sprayers even without the use of any personal protective equipment. Systemic exposure from the use of IMS+MSM+MPR OD 42 with Field Crop Sprayer without protection results in 64% of the mesosulfuron-methyl AOEL.

[redacted] (1992): Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protections); Mitteilungen aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft, Berlin-Dahlem, n° 277, 1 - 112 (1992); (M-001230-02-1)

[3] Scientific Subcommittee on Pesticides and British Agrochemicals Joint Medical Panel., Estimation of Exposure and Absorption of Pesticides by Spray Operators (UK MAFF) 1986 and the Predictive Operator Exposure Model (POEM) – A User's Guide (UK MAFF); 1992, revised model 2003; (M-054618-01-1)

Overall conclusion
Exposure estimates predict acceptable risks for the intended use even without the use of personal protective equipment. To be consistent with good agricultural practices when handling pesticides, it is recommended that gloves be worn during mixing/loading and when handling contaminated surfaces.

IIIA 7.3.1 Estimation of operator exposure without personal protective equipment

a) Estimation according to the German model

Exposure is calculated for with the maximum dose rate. Lower doses will be covered by this calculation and separate evaluations are not made. The following assumptions were made:

Field crop sprayer
Treated area: 20 ha/day.
Max. dose rate: 1.5 L/ha plant protection product corresponding to 0.015 kg a.s./ha mesosulfuron-methyl

Exposure estimates based on the modified German model (with and without PPE) and proportions of the systemic AOEL are summarised in Table 7.3-2. Detailed calculations using the modified German model are presented in Table 7.3.1-1.

Table 7.3.1-1: Calculation of exposure to Mesosulfuron-methyl (MSM) of operators using IMS+MSM+MPR OD 42 at 1.5 L/ha; application with field crop sprayer (German model, without and with PPE) in 20 ha cereal fields.

Operator exposure estimate: German model. Tractor-mounted/trailed boom sprayer; hydraulic nozzles

Product:	Atlantis OD 42				
Active substance:	MSM	a.s. concentration:	10	[g/l or kg]	
Formulation:	Liquid	PPE during mix/loading:	Respiration:	None	
Dose [l or kg/ha]:	1.5		Hands:	Gloves	
Work rate [ha/day]:	20	PPE during application:	Respiration:	None	
Body weight [kg]:	70		Hands:	None	
Inhalation absorption [%]	100		Head:	None	
Dermal absorption [%]	75.0 (concentrate)		Body:	Standard protective coverall	
	75.0 (dilution)				

Calculation of route exposure:

Route	Specific exposure [mg/kg a.s.]	a.s. handled [kg/day]	Estimated exposure [mg/kg bw/day] No PPE	Reduction factor	with PPE	
						I = Inhalation
I_M =	0.0006	0.3	0.000003	1.0	0.000003	D = Dermal
$D_{M(H)}$ =	2.4	0.3	0.0103	0.01	0.000103	M = Mix/Loading
I_A =	0.001	0.3	0.000004	1.0	0.000004	A = Application
$D_{A(C)}$ =	0.06	0.3	0.0003	1.0	0.000257	H = Hands
$D_{A(H)}$ =	0.38	0.3	0.0016	1.0	0.001629	C = Head
$D_{A(B)}$ =	1.6	0.3	0.0069	0.05	0.000343	B = Body

Absorbed dose:

Route		Absorption [%]	No PPE: Estimated route exposure [mg/kg bw/day]	No PPE: Systemic exposure [mg/kg bw/day]	With PPE: Estimated route exposure [mg/kg bw/day]	With PPE: Systemic exposure [mg/kg bw/day]
Dermal:	Mix/Loading	75.0	0.010286	0.007714	0.000103	0.000077
	Application	75.0	0.008743	0.006557	0.002229	0.001671
Inhalation:	Mix/Loading	100	0.000003	0.000003	0.000003	0.000003
	Application	100	0.000004	0.000004	0.000004	0.000004
		Total =		**0.014278**		**0.001755**

b) Estimation according to the UK-POEM

Using the UK-POEM, the highest exposure for each application type is calculated if the maximum dose rates and the minimum spray volumes are used. Lower dose rates and higher spray volumes for crops which are treated with the same application type will be covered by this calculation and separate evaluations are not made. The following assumptions have been made:

Field Crop Sprayer application (cereals)

Treated area:	50 ha per day.
Max. dose rate:	1.5 L/ha plant protection product corresponding to 0.015 kg MSM/ha.
Applied volume:	100 L/ha
Duration of work:	6 hours
Container size:	10 L, 63 mm closure.

Detailed calculations with the UK POEM are presented in Table 7.3.1-2.

Table 7.3.1-2: Calculation of exposure to mesosulfuron-methyl-sodium (MSM) of operators using IMS+MSM+MPR OD 42 at 1.5 L/ha; application with field crop sprayer (UK POEM, with and without PPE) in 50 ha cereal fields.

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**Atlantis OD 42**	Active substance	**MSM**
Formulation type	organic solvent based	a.s. Concentration	**10** mg/ml
Dermal absorption from product	**75** %	Dermal absorption from spray	**75** %
Container	10 litres 63 mm closure		
PPE during mix/loading	Gloves	PPE during application	None
Dose	**1.5** L/ha	Work rate/day	**50** ha
Application volume	**100** L/ha	Duration of spraying	**6** h

EXPOSURE DURING MIXING AND LOADING									
Container size	10	litres							
Hand contamination/operation	0.05	ml							
Application dose	1.5	litres product/ha							
Work rate	50	ha/day							
Number of operations	8	/day							
Hand contamination	0.4	ml/day							
Protective clothing	None					Gloves			
Transmission to skin	100	%				10	%		
Dermal exposure to formulation	0.400	ml/day				0.040	ml/day		

DERMAL EXPOSURE DURING SPRAY APPLICATION									
Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles								
Application volume	100	l/ha							
Volume of surface contamination	10	ml/h							
Distribution	Hands		Trunk		Legs				
	65%		10%		25%				
Clothing	None	Permeable	Permeable			None	Permeable	Permeable	
Penetration	100%	5%	15%			100%	5%	15%	
Dermal exposure	6.5	0.05	0.375	ml/h		6.5	0.05	0.375	ml/h
Duration of exposure	6	h				6	h		
Total dermal exposure to spray	41.550	ml/day				41.550	ml/day		

ABSORBED DERMAL DOSE								
	Mix/load		Application		Mix/load		Application	
Dermal exposure	0.4	ml/day	41.55	ml/day	0.04	ml/day	41.55	ml/day
Concen. of a.s. product or spray	10	mg/ml	0.15	mg/ml	10	mg/ml	0.15	mg/ml
Dermal exposure to a.s.	4	mg/day	6.233	mg/day	0.4	mg/day	6.2325	mg/day
Percent absorbed	75	%	75	%	75	%	75	%
Absorbed dose	3	mg/day	4.674	mg/day	0.3	mg/day	4.674	mg/day

INHALATION EXPOSURE DURING SPRAYING		
Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	0.15	mg/ml
Inhalation exposure to a.s.	0.009	mg/day
Percent absorbed	100	%
Absorbed dose	0.009	mg/day

PREDICTED EXPOSURE	No PPE		With PPE	
Total absorbed dose	7.683	mg/day	4.983	mg/day
Operator body weight	60	kg	60	kg
Operator exposure	0.12805625	mg/kg bw/day	0.083056	mg/kg bw/day

AOEL	0.200	mg/kg bw/day
%AOEL	64.0 %	41.5 %

IIIA 7.3.2 Estimation of operator exposure using personal protective equipment

Presented in the previous section.

IIIA 7.3.3 Measurement of operator exposure

Since the exposure estimate carried out indicated that the health-based limit values (AOEL) will not be exceeded under practical conditions of use, a study to provide a measure of operator exposure was not necessary and was therefore not carried out.

IIIA 7.4 Bystander Exposure

Bystander exposure to IMS+MSM+MPR OD 42 was not evaluated as part of the EU review of mesosulfuron-methyl. Therefore, all relevant data and risk assessments are provided here and are considered adequate.

No EU-wide accepted official model is available for estimation of bystander exposure. Some proposals were given by the EUROPOEM Bystander Working Group but the report is still a draft and not officially published because slight changes may still be anticipated following comments provided by the members of the working group.

Therefore, as long as there is no official guidance on how to estimate bystander exposure an approach is presented in this document that considers both dermal exposure, derived from available drift data – and inhalation exposure – derived from an operator exposure model simulating a bystander who is exposed in a similar way as an unprotected operator spraying in the field. Additionally, exposure to residents is assessed as well.

This approach is following a guidance of the German Federal Institute for Risk Assessment (BfR)[4] and is in line with what has been published by US EPA and PSD recently. All technical details with regard to figures and assumptions are provided in this guidance.

Exposure estimates and proportions of the systemic AOEL accounted for by the estimates are summarised in the following table. Detailed information and calculations are presented in chapter CPI 7.4.1.

[4] [redacted]; Guidance for Exposure and Risk Evaluation for Bystanders and Residents exposed to Plant Protection Products during and after Application, Journal für Verbraucherschutz und Lebensmittelsicherheit *Journal of Consumer Protection and Food Safety* (2008, in preparation)

Table 7.4-1: Predicted systemic exposures as a proportion of the AOEL

Substance	Scenario	Total systemic exposure* (mg/kg bw/day)	AOEL (mg/kg bw/day)	% of AOEL
Bystander of field crop application (tractor-mounted)				
MSM	Bystander: adult	0.000055	0.2	0.028
	Bystander: child	0.000044		0.022
MSM	Resident: adult	0.0000040	0.2	0.0020
	Resident: child	0.0000053		0.0023

* Assumes a 60 kg bystander for an adult and 16.15 kg for a child.
Dermal absorption value of 75% used. Inhalation absorption was taken as 100% for both compounds.

Assessment
The results of the calculations reveal that the situation with respect to bystander and resident exposure is favourable for the intended use of IMS+MSM+MPR OD 42.

IIIA 7.4.1 Estimation of bystander exposure without personal protective equipment

The following definitions and assumptions for bystanders and residents may be applied.

Bystanders and residents are not involved in application or handling plant protection products or the professional handling of treated crops. The question arises whether it is necessary to distinguish between bystanders and residents in terms of the potential for exposure and health risks. However, because the circumstances of this exposure could differ with respect to amount, frequency and duration, this seems to be reasonable.

Bystanders may inadvertently be present within or directly adjacent to an area for a short period of time, typically a matter of minutes, where application of a plant protection product is in progress or has recently taken place. They may be exposed to plant protection products mainly *via* the dermal route from spray drift and by inhalation of drifting spray droplets. Hand held application is considered to be worse case compared to field crop sprayer.

Residents may live or work near areas of the application of plant protection products (e.g. standing, working or sitting in a garden in the vicinity of the application). They may be exposed to plant protection products mainly *via* the dermal route from spray drift deposits and by inhalation of vapour drift (depending on the vapour pressure of the active substance). For infants and toddlers exposure might also occur orally (e.g. through hand-to-mouth transfer and/or object-to-mouth transfer).

Table 7.4.1-1: Percent Drift Values for Different Crops (Rautmann *et al.* 2001, current version 27.03.2006) – 1 application only

Crop, Distance 10 m	Percent Drift (1 application) (90^{th} percentile values)
Field crops	0.29
Fruit crops, early	1.81
Fruit crops, late	3.60
Grapes	1.23
Hops	2.77
Vegetables, ornamentals & small fruit:	
< 50 cm	0.29
> 50 cm	1.23

Exposure calculations are performed according to the following equations:

a) Bystander exposure to Mesosulfuron-methyl-sodium

Dermal exposure due to spray drift following 1 low crop application using a tractor mount field sprayer:

$SDE_B = (AR \times D \times BSA \times DA) / BW$

Where:

SDE_B	= Systemic Exposure of Bystanders via the Dermal Route (mg/kg bw/day).	
AR	= Application Rate (mg/m²)	0.015 kg a.s./ha = 1.5 mg/m².
D	= Drift (%)	0.29% (10 m distance) for 1 application.
BSA	= Exposed Body Surface Area (m²)	1 m² (adult), 0.21 m² (child).
DA	= Dermal Absorption (%)	75%.
BW	= Body Weight (kg/person)	60 kg (adult), 16.15 kg (child).

Inhalation exposure due to spray drift:

$SIE_B = (I_A^* \times AR \times A \times T \times IA) / BW$

Where:

SIE_B	= Systemic Exposure of Bystanders via the Inhalation Route (mg/kg bw/day).	
I_A^*	= Specific Inhalation Exposure (mg/kg a.s. handled per day)	0.001 mg/kg a.s. (field crop sprayer).
AR	= Application Rate (kg a.s./ha)	0.015 kg a.s./ha.
A	= Area Treated (ha/day)	20 ha (field crop sprayer).
T	= Time [Duration] (min)	5 min.

IA	= Inhalation Absorption (%)	100%.
BW	= Body Weight (kg/person)	60 kg (adult), 16.15 kg (child).

Total Systemic Exposure of Bystanders

Adults and Children: $SE_B = SDE_B + SIE_B$ (mg/kg bw/day).

Where:
SE_B = Systemic Exposure of Bystanders (mg/kg bw/day).
SDE_B = Systemic Dermal Exposure of Bystanders (mg/kg bw/day).
SIE_B = Systemic Inhalation Exposure of Bystanders (mg/kg bw/day).

Table 7.4.1-2: Calculations for bystander exposure to mesosulfuron-methyl

Adults	Children
Bystander of field crop application (tractor-mounted)	
Dermal Exposure $SDE_B = (AR \times D \times BSA \times DA)/BW$ $SDE_B = (\ 1.5 \times 0.0029 \times 1 \times 0.75\ ) / 60$ $SDE_B = 0.000054$ mg/kg/day	Dermal Exposure $SDE_B = (AR \times D \times BSA \times DA)/BW$ $SDE_B = (\ 1.5 \times 0.0029 \times 0.25 \times 0.75\ ) / 16.15$ $SDE_B = 0.000042$ mg/kg/day
Inhalation Expsoure $SIE_B = (I_A * AR \times A \times T \times IA)/BW$ $SIE_B = (\ 0.001 \times 0.015 \times 20 \times 0.1667 \times 1.00\ ) / 60$ $SIE_B = 0.00000083$ mg/kg/day	Inhalation Exposure $SIE_B = (I_A * AR \times A \times T \times IA)/BW$ $SIE_B = (\ 0.000575 \times 0.015 \times 20 \times 0.1667 \times 1.00\ ) / 16.15$ $SIE_B = 0.00000178$ mg/kg/day
Total Sytemic Exposure $SE_B = SDE_B + SIE_B$ $= 0.000055$ mg/kg/day	Total Sytemic Exposure $SE_B = SDE_B + SIE_B$ $= 0.000044$ mg/kg/day
%AOEL = 0.0276	**%AOEL = 0.0221**

b) Residential exposure to Mesosulfuron-methyl

Dermal exposure *via* deposits caused by spray drift

$SDE_R = (AR \times D \times TTR \times TC \times H \times DA) / BW$

Where:

SDE_R	= Systemic Exposure of Residents via the Dermal Route (mg/kg bw/day).	
AR	= Application Rate (mg/cm²).	0.015 kg a.s./ha = 0.00015 mg/cm².
D	= Drift (%)	0.29% (10 m distance) for 1 application.
TTR	= Turf Transferable Residues (%)	5%.
TC	= Transfer Coefficient (cm²/hour)	7300 cm²/h (adult), 2600 cm²/h (child).
H	= Exposure Duration (hours)	2 h.
DA	= Dermal Absorption (%)	75%.
BW	= Body Weight (kg/person)	60 kg (adult), 16.15 kg (child).

Inhalation exposure due to vapour drift

$SIE_R = (AC_V \times IR \times IA) / BW$

Where:

SIE_R	= Systemic Exposure of Residents via the Inhalation Route (mg/kg bw/day).	
AC_V	= Airborne Concentration of Vapour (mg/m³): 0 mg/m³ (vapour pressure of a.s. < 10^{-5} Pa).	
IR	= Inhalation Rate (m³/day)	16.57 m³/day (adult), 8.31 m³/day (child).

IA	= Inhalation Absorption (%)	100%.
BW	= Body Weight (kg/person)	60 kg (adult), 16.15 kg (child).

As the vapour pressure of mesosulfuron-methyl is 1.1×10^{-11} Pa @ 25°C the product is considered as non-volatile and therefore $AC_V = 0$ and $SIE_R = 0$.
In addition, oral exposure of children is estimated as well by the following equations.
Children's hand-to-mouth transfer:

$$SOE_H = (AR \times D \times TTR \times SE \times SA \times Freq \times H \times OA) / BW$$

Where:

SOE_H	= Systemic Oral Exposure via the Hand to Mouth Route (mg/kg bw/day).	
AR	= Application Rate (mg/cm^2)	0.015 kg a.s./ha = 0.00015 mg/cm².
D	= Drift (%)	0.29% (10 m distance) for 1 appln.
TTR	= Turf Transferable Residues (%)	5%.
SE	= Saliva Extraction Factor (%)	50% (EPA default value).
SA	= Surface Area of Hands (cm^2)	20 cm^2.
Freq	= Frequency of Hand to Mouth (events/hour)	20 events/h.
H	= Exposure Duration (hours)	2 h.
OA	= Oral Absorption (%)	3%.
BW	= Body Weight (kg/person)	16.15 kg (child).

Children's object-to-mouth transfer

$$SOE_O = (AR \times D \times DFR \times IgR \times OA) / BW$$

Where:

SOE_O	= Systemic Oral Exposure via the Object to Mouth Route (mg/kg bw/day).	
AR	= Application Rate (mg/cm^2)	0.015 kg a.s./ha = 0.00015 mg/cm².
D	= Drift (%)	0.29% (10 m distance) for 1 appln.
DFR	= Dislodgeable Foliar Residues (%)	20%.
IgR	= Ingestion Rate for Mouthing of Grass/Day (cm^2)	25 cm^2/day.
OA	= Oral Absorption (%)	3%.
BW	= Body Weight (kg/person)	16.15 kg (child).

Total systemic exposure of residents is then estimated for:

Adults: $SE_R = SDE_R + SIE_R$ (mg/kg bw/day)
Children: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$ (mg/kg bw/day)

Where:

SE_R	= Systemic Exposure of Residents (mg/kg bw/day).
SDE_R	= Systemic Dermal Exposure of Residents (mg/kg bw/day).
SIE_R	= Systemic Inhalation Exposure of Residents (mg/kg bw/day).
SOE_H	= Systemic Oral Exposure via the Hand to Mouth Route (mg/kg bw/day).
SOE_O	= Systemic Oral Exposure via the Object to Mouth Route (mg/kg bw/day).

Table 7.4.1-3: Calculations for resident exposure to mesosulfuron-methyl

Adults			Children		
Resident: Exposure after application with Field Crop, tractor mounted/trailed					
Dermal exposure:			Dermal exposure:		
SDE_R = (AR x D x TTR x TC x H x DA) / BW			SDE_R = (AR x D x TTR x TC x H x DA) / BW		
(0.00015 x 0.29% x 5% x 7300 x 2 x 75%) / 60			(0.00015 x 0.29% x 5% x 2600 x 2 x 75%) / 16.15		
Absorbed dose:	0.00000397	mg/kg bw/d	Absorbed dose:	0.00000525	mg/kg bw/d
Inhalation exposure:			Inhalation exposure:		
SIE_R = (AC_V x IR x IA) / 1000 x BW			SIE_R = (AC_V x IR x IA) / BW		
(0 x 16.57 x 100%) / 60			(0 x 8.31 x 100%) / 16.15		
Absorbed dose:	0.0	mg/kg bw/d	Absorbed dose:	0.0	mg/kg bw/d
			Oral exposure (hand-to-mouth transfer):		
			SOE_H = (AR x D x TTR x SE x SA x Freq x H x OA) / BW		
			(0.00015 x 0.29% x 5% x 50% x 20 x 20 x 2 x 3%) / 16.15		
			Absorbed dose	0.00000002	mg/kg bw/d
			Oral exposure (object-to-mouth transfer):		
			SOE_O = (AR x D x DFR x IgR x OA) / BW		
			(0.00015 x 0.29% x 20% x 25 x 3%) / 16.15		
			Absorbed dose	0.000000004	mg/kg bw/d
Total systemic exposure:			**Total systemic exposure:**		
SE_R = SDE_R + SIE_R			**SE_R = SDE_R + SIE_R + SOE_H + SOE_O**		
Total absorbed dose:	**0.00000397**	mg/kg bw/d	**Total absorbed dose:**	**0.00000527**	mg/kg bw/d
% of AOEL:	**0.0020**		**% of AOEL:**	**0.0026**	

IIIA 7.4.2 Measurement of bystander exposure

Since the exposure estimate carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under practical conditions of use, a study to provide a measure of bystander exposure was not necessary and was therefore not carried out.

IIIA 7.5 Worker Exposure

According to the application parameters of IMS+MSM+MPR OD 42 the only intended use is spray application to cereals at early growth stages (BBCH up to 32). At these growth stages no re-entry exposure would be expected due to the relative height (very low) of the crop. However, the potential exposure due to scouting procedures is provided in the following section.

IIIA 7.5.1 Estimation of worker exposure without personal protective equipment

The greatest potential for worker exposure following re-entry will be contamination *via* the skin. Risk of inhalation exposure during re-entry is generally confined to a brief period after application, while the product is drying, which will be rapid under outdoor conditions and would generally be avoided according to good agricultural practices. Exposure to workers entering treated areas are predicted

using an exposure model proposed by [redacted] *et al*,[5] (1998) and [redacted]s *et al.* [6](2001). The following assumptions are made;

- Re-entry exposure is predominantly *via* the dermal route (contact with the foliage)
- Residues on the foliage depend on:
  - i) application rate
  - ii) extent of remaining residues from previous applications
  - iii) the Leaf Area Index (LAI) [total size of foliage compared to surface area]
- Transfer of residues from foliage to the clothes or skin of workers depends mainly on the intensity of contact with the foliage.
- Activities with a similar pattern can be grouped and a generic Transfer Coefficient (TC) applied
- Dislodgeable Foliar Residue (DFR) is calculated using a default value of 3 µg as/cm² per kg as/ha. This figure is based [redacted] *et al*[7] (2001)
- Workers re-enter the treated culture shortly after the spray has dried on plant surfaces, nevertheless it is now recommended to use the higher dermal absorption values amongst neat and diluted values.

The dermal exposure calculation is performed according to the following equation:

$$D = DFR \times TC \times WR \times AR \times P$$

Where:

DFR = Dislodgeable foliar residues (µg as/ cm²).
TC = Transfer Coefficient (cm²/person/h).
WR = Work rate (hours/day).
AR = Application rate (kg as/ha).
P = Protection factor for PPE (P = 1 no PPE, just a long sleeved shirt, or 0.1 when adequate clothing and gloves are worn).

DFR values:

A single application is considered in this risk assessment resulting in an estimated worst case DFR of 3 µg as/cm² per kg as/ha.

Transfer Coefficient values:

Hoernicke *et al* (1998) propose that a transfer coefficient (TC) of 30,000 (cm²/person/h) be used for the transfer of residues from foliage to the clothes or skin of a worker in initial estimates of exposure. This value is considered to represent a worst case for worker exposure, being derived from tasks requiring intensive contact with foliage and representing an unprotected worker.

As no specific TCs are available in Europe to assess re-entry activities performed in cereals a conservative value of 2500 cm²/person/h has been used in this risk assessment. This value was obtained from the Europoem II data for vegetables which are believed to be the most reasonable surrogate from the available data for scouting activities in young cereal crops.

[5] [redacted].: Label instructions for the protection of workers re-entering crop growing areas after application of plant protection products, Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), (1998), 267 - 269 (document no. M-107544-01-1)

[6] [redacted](2001) Uniform principles for safeguarding the health of workers re-entering crop growing areas after application of plant-protection products, Worker exposure to agrochemicals, Ed. R.C. Honeycutt and E.W. Day, chapter 8, 107- 117, CRC Press (2001), (document no.: M-209388-01-1)

[7] [redacted].: (2001); Modeling re-entry exposure estimates: techniques and application rates; Worker exposure to agrochemicals, Ed. R.C. Honeycutt and E.W. Day, chapter 9, 119- 138, CRC Press (2001), (document no.: M-128767-01-1)

Predicted exposures are compared with the AOEL for mesosulfuron-methyl. Systemic exposure values assume the highest dermal absorption value (default 75%). A body weight of 60 kg is assumed for the re-entry worker. Exposure estimates based proportions of the systemic AOELs accounted for by the estimates are summarised in the following Table. Detailed calculations are presented on the following pages.

Table 7.5.1-1: Summary of predicted mesosulfuron worker exposures arising from the use of IMS+MSM+MPR OD 42 and comparison with the respective AOELs

Active substance	Systemic exposure* (mg/kg bw/day)	AOEL (mg/kg bw/day)	% of AOEL
MSM	0.002812 5	0.2	1.4

*75% dermal absorption for MSM, 60 kg worker.

Assessment

The exposure to mesosulfuron of workers entering treated areas is well within acceptable levels following application of IMS+MSM+MPR OD 42.

Detailed calculations of worker exposure during re-entry:

Product Name: Atlantis OD 42
Active substance: MSM

D		DFR	x	TC	x	WR	x	AR	x	P
		µg/cm²		cm²/pers/h		hrs/day		kg/ha		
D	=	3	x	2500	x	2	x	0.015	x	1
D	=	225 µg a.s./pers/day								
	=	0.225 mg a.s./pers/day								
	=	0.00375 mg/kg bw/day								

using 75.00% dermal absorption (highest value)

S	=	0.00375	x	0.7500
	=	0.002813 mg/kg bw/day		

IIIA 7.5.2 Estimation of worker exposure using personal protective equipment

Considered to be not required (see CP1 7.5).

IIIA 7.5.3 Estimation of worker exposure assuming personal protective equipment is used and using dislodgeable residues data

Considered to be not required (see CP1 7.5).

IIIA 7.5.4 Measurement of worker exposure

Considered to be not required (see CP1 7.5).

IIIA 7.6 Dermal Absorption

In the absence of a dermal absorption study for the Atlantis OD 42 formulation the default value of 75% was used.

IIIA 7.6.1 Dermal absorption, in vivo in the rat

No relevant study available.

IIIA 7.6.2 Comparative dermal absorption, in vitro using rat and human skin

No relevant study available.

IIIA 7.7 Dislodgeable Residues

Point not covered under Guidance Document SANCO 10181/2013.

IIIA 7.7.1 Dislodgeable Residues - foliar

IIIA 7.7.2 Dislodgeable Residues - soil

IIIA 7.7.3 Dislodgeable Residues - indoor surface re-volatilization

IIIA 7.8 Epidemiology

Point not covered under Guidance Document SANCO 10181/2013.

IIIA 7.9 Data on Formulants

CONFIDENTIAL information - data provided separately (Doc JCR).

IIIA 7.9.1 Material safety data sheets for each formulant

IIIA 7.9.2 Available toxicological data for each formulant

IIIA 7.10 Domestic Animal/Livestock Safety

Point not covered under Guidance Document SANCO 10181/2013.