

Draft Renewal Assessment Report  
under Regulation (EC) 1107/2009



**FORAMSULFURON**  
**Volume 3 – B.6 (PPP) – Equip**

Rapporteur Member State: Finland  
Co-Rapporteur Member State: Slovakia

March 2015

## Volume 1

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## Volume 3

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**Annex C: Confidential information and, where relevant, details of any task force formed for the purpose of generating tests and studies submitted**

## List of Endpoints

**Version History**

<b>When</b>	<b>What</b>
2015/March	First Draft RAR

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## **B.6. TOXICOLOGY AND METABOLISM DATA AND ASSESSMENT OF RISKS FOR HUMANS**

In this renewal submission, a previous evaluation/comments box has been inserted above each study to indicate studies already evaluated in the original RAR. Additional studies/information have been submitted and evaluated in this revised RAR. New evaluations and changes to the text are highlighted in yellow.

### **B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT**

Equip (AE F130360 01 1K05 A3xx) is a postemergence herbicide formulated as a suspension concentrate (SC). It contains 22.5 g/l foramsulfuron and in addition to the active substance the safener Isoxadifen-ethyl (22.5 g/l).

The acute toxicity of Equip was low irrespective of the route of exposure (oral, dermal and inhalation). For both sexes the rat oral LD<sub>50</sub> was greater than 5000 mg/kg body weight, the highest international regulatory limit dose. Clinical signs observed following oral dosing were non-specific and included piloerection, hunched posture, waddling/unsteady gait, lethargy, walking on toes, pallid extremities, partially closed eyelids and a thin and ungroomed appearance. All reactions had resolved by Day 9 post-dosing.

Similarly, the rat acute dermal LD<sub>50</sub> was greater than 5000 mg/kg body weight for both sexes. No signs of systemic toxicity were observed, but erythema, oedema and desquamation occurred at the test site. All responses had resolved by Day 12.

The acute inhalation (4-hour) LC<sub>50</sub> to the rat was >5.25 mg/l air, which did not cause mortality and was the highest achievable concentration. The principal clinical signs observed included wet fur, hunched posture, piloerection, red/brown staining of the snout, increased respiratory rate and noisy respiration. They had resolved by 2 days in all but one animal which had recovered 5 days post-exposure.

Equip was moderately irritating to rabbit skin, causing slight to moderate/severe erythema and slight to moderate oedema with desquamation and thickening of the skin in all the animals. The test material was slightly and reversibly irritating to rabbit eyes causing conjunctival reddening, chemosis and a discharge. All signs of irritancy had completely resolved within 4 days.

No evidence of skin sensitisation was seen in a 3-induction guinea pig Buehler test and a modified Buehler test with 9 induction applications. In addition, foramsulfuron was tested in a local lymph node assay (LLNA) which is not considered to be acceptable due to shortcomings in performance of the study.

**Table B.6.1-1: Results of acute toxicity testing of Equip**

Type of study	Species	Sex	Result
Acute oral toxicity	Rat	Male & Female	LD <sub>50</sub> > 5000 mg/kg
Acute dermal toxicity	Rat	Male & Female	LD <sub>50</sub> > 5000 mg/kg
Acute inhalation toxicity	Rat	Male & Female	LC <sub>50</sub> > 5.25 mg/l air
Skin irritancy	Rabbit	Male	Irritating
Eye irritancy	Rabbit	Male	Not irritating
Skin sensitisation (3-induction Buehler)	Guinea pig	Female	Not sensitizing
Skin sensitisation (9-induction Buehler)	Guinea pig	Male & Female	Not sensitizing

Local lymph node assay (LLNA)	Mouse	Female	Study not acceptable
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**Classification:**

With respect to the ~~prevailing EU classification schemes~~ Directive 1999/45/EC, Equip should be classified as "irritating to skin" (Xi, R 38)

Additionally labelling with Xn, R65 "Harmful: may cause lung damage if swallowed" is necessary because of the toxicological data of one of the co-formulations: Solvesso 200). The label of the product shall bear the statement "Contains isoxadifen-ethyl. May produce an allergic reaction."

According to the CLP Regulation (EC) 1272/2008, the product Equip is classified as Skin Irrit. 2 - H315 "Causes skin irritation". Due to a solvent co-formulant (e.g. Solvesso 200 ND), Equip is classified as Asp. Tox. 1 - H304 "May be fatal if swallowed and enters airways". The label of the product shall bear the statement "EUH208 - Contains isoxadifen-ethyl. May produce an allergic reaction."

**B.6.1.1. Oral**

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. Conclusion has not been changed. Classification is not required according to CLP Regulation (EC) No 1272/2008.
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**Report:**

██████████ 1999e:  
 Rat acute oral toxicity; AE F130360 + AE F122006, 22.5 +22.5 g/l Oil flowable, Code: AE F130360 01 1K05 A304;  
 Report No.: Tox/99/262-57; Doc. No. (Aventis): C005915;  
 Study No.: Tox 95126; unpublished.  
 Testing facility: ██████████;  
 Experimental phase of study: 15 June 1999 to 5 July 1999.

**Test Material:**

AE F130360 01 1K05 A304, batch number KD945/990301;  
 (AE F130360: 2.42% w/w; AE F122006: 2.44% w/w)

**Test Animals:**

Hsd:Sprague-Dawley (CD) rats;  
 Source: ██████████

**GLP:**

Yes

**Test Method:**

OECD 401, adopted 24 February 1987 (Limit test)

**Deviations:**

None

**Acceptability:**

The study is considered to be acceptable.

**Material and Methods:**

Sprague Dawley CD rats, approximately 8 to 11 weeks old and weighing from 237 to 259 g (males) and from 205 to 215 g (females) at the time of treatment, were used. They were acclimatised for 11 days prior to dosing and caged by sex in groups of 5.

Groups of 5 male and 5 female fasted rats were given a single oral dose, by gavage, of 5000 mg/kg body weight of Equip, as supplied i.e. undiluted, at a dose volume of 5.26 ml/kg. The dose level was chosen after review of preliminary study findings. Animals were observed at least twice daily for mortality. Observations for clinical signs of toxicity were carried out soon after dosing, at frequent intervals on the remainder of the day of dosing (Day 1), twice daily for 14 days and once at Day 15, the day of termination. Individual body weights were recorded prior to dosing and at Days 8 and 15 (or death). All animals were killed at Day 15 and examined for macroscopic abnormalities. This consisted of opening the thorax and abdominal cavities and the cranial cavity in 8 of the animals. The macroscopic appearance of all organs and tissues was recorded.

#### Findings:

At 5000 mg/kg, 1/5 males and 1/5 females died within a few minutes of dosing.

The principal clinical signs of toxicity observed in both sexes included piloerection, hunched posture, waddling/unsteady gait, lethargy, walking on toes and pallid extremities. Less commonly observed signs were partially closed eyelids and thin and/or ungroomed appearance. The onset of signs (piloerection and hunched posture) was within 10 minutes of dosing, and recovery of surviving rats was complete by Day 9.

Body weight gain was unaffected in the majority of animals, although one female showed a low gain at Day 15 compared with its cagemates.

Macroscopic examination of decedents revealed some minimal darkened tissue and prominent blood vessels in the lungs. Examination of 6 out of 8 animals killed at termination revealed thickening of the stomach wall accompanied, in 2 females, by gaseous distension of the duodenum. There were no findings in the remaining two animals.

**Table B.6.1-2: Mortality and clinical signs in rats given a single oral dose of Equip**

Parameter	Dose Level (mg/kg)	
	5000	5000
	Males	Females
<b>Mortality:</b>	1/5	1/5
<b>Clinical signs:</b>		
Piloerection	4/5	4/5
Hunched posture	4/5	4/5
Waddling/unsteady gait	4/5	4/5
Lethargy	4/5	4/5
Walking on toes	1/5	4/5
Pallid extremities	2/5	4/5
Partially closed eyelids	3/5	0/5
Thin appearance	1/5	2/5
Ungroomed appearance	1/5	2/5

#### Conclusion:

The acute oral LD<sub>50</sub> for Equip in both male and female Sprague Dawley rats was >5000 mg/kg body weight, the highest international limit dose.

#### B.6.1.2. Dermal

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. Conclusion has not been changed.
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	Classification is not required according to CLP Regulation (EC) No 1272/2008.
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**Report:**

██████████ 2000a:  
Rat acute dermal toxicity; AE F130360 + AE F122006  
22.5 +22.5 g/l, Oil flowable, Code: AE F130360 01 1K05 A3;  
Report No.: Tox/00/262-58; Doc. No. (Aventis): C005916;  
Study No.: Tox 95127; unpublished.  
Testing facility: ██████████;  
Experimental phase of study: 17 June 1999 to 1 July 1999.

**Test Material:**

AE F130360 01 1K05 A304, batch number KD945/990301  
(AE F130360: 2.42% w/w; AE F122006: 2.44% w/w)

**Test Animals:**

Hsd:Sprague-Dawley (CD) rats;  
Source: ██████████

**GLP:**

Yes

**Test Method:**

OECD 402, adopted 24 February 1987 (Limit test)

**Deviations:**

None

**Acceptability:**

The study is considered to be acceptable.

**Material and Methods:**

A group of five male and five female Sprague Dawley CD rats, approximately 8 to 11 weeks old and weighing 218 to 242 g (males) and 208 to 241 g (females) at the time of treatment (Day 1) was used. They were acclimatised for 7 days prior to treatment and caged by sex in groups of 5.

Each rat received a single 24-hour topical occluded application to the shaved intact dorso-lumbar skin of 5000 mg/kg body weight of Equip, as supplied i.e. undiluted.

Animals were checked at least twice daily for mortality. Observations for clinical signs of toxicity were carried out soon after dosing, at frequent intervals during the rest of the day of dosing (Day 1), twice daily for 14 days and once at Day 15, the day of termination. Dermal responses were assessed daily. Individual body weights were recorded prior to dosing and at Days 8 and 15. All animals were killed at Day 15 and examined for macroscopic abnormalities. This consisted of opening the thorax and abdominal cavities and the cranial cavity in 8 of the animals. The macroscopic appearance of all the organs and tissues was recorded.

**Findings:**

There were no cases of mortality and no clinical signs of systemic reaction to treatment.

Slight to well-defined skin irritation at the treatment site (up to moderate erythema and up to well-defined oedema) was seen in all rats at Day 2 and Day 3 before ameliorating in most instances by Day 8. These responses had resolved in all animals by Day 10. Desquamation (indicative of repair and characterised by spots and/or scabbing, dryness, sloughing and/or scaling) was also seen in the majority of animals at Day 4, resolving in all instances by Day 12.

Body weight gains were satisfactory throughout the study in the majority of animals, although two females showed low gains and another female had lost weight by Day 8.

No macroscopic abnormalities were observed in any animal at necropsy.



**Conclusion:**

The acute dermal LD<sub>50</sub> value in Sprague Dawley rats of Equip was >5000 mg/kg body weight, the highest international regulatory limit dose.

**B.6.1.3. Inhalation**

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. Conclusion has not been changed. After the study was performed, a new version of the OECD Test Guideline 403 has been adopted 7th September, 2009. The study practically fulfils the current data requirements. Classification is not required according to CLP Regulation (EC) No 1272/2008.
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**Report:**

██████████ 1999a:  
 Rat acute inhalation toxicity; AE F130360 + AE F122006, 22.5 +22.5 g/l Oil flowable, Code: AE F130360 01 1K05 A3;  
 Report No.: Tox/99/262-54; Doc. No. (Aventis): C005786;  
 Study No.: Tox 99207; unpublished.  
 Testing facility: ██████████;  
 Experimental phase of study: 9 August 1999 to 2 September 1999.

**Test Material:**

AE F130360 01 1K05 A304, batch number KD945/990301  
 (AE F130360: 2.42% w/w; AE F122006: 2.44% w/w)

**Test Animals:**

Sprague-Dawley Crl:CD BR rats;  
 Source: ██████████

**GLP:**

Yes

**Test Method:**

OECD 403, adopted 12 May 1981 (Limit test)

**Deviations:**

None

**Acceptability:**

The study is considered to be acceptable.

**Material and Methods:**

Equip<sup>®</sup> (AE F130360 01 1K05 A304, batch number KD945/000301) containing analysed quantities of 2.42% w/w of foramsulfuron was used.

A group of five male and five female Sprague Dawley CD rats, approximately 8 to 10 weeks old and weighing 300 to 325 g (males) and 224 to 240 g (females) immediately prior to exposure was used. They were acclimatised for at least 5 days prior to treatment and caged by sex in groups of 5 except during exposure when they were placed in individual restraining tubes.

Each rat received a single 4-hour nose-only exposure to a chemically analysed mean chamber atmosphere concentration of 5.25 mg/l (based on formulation) of air. The atmosphere was generated using a glass concentric jet nebuliser located at the top of the exposure chamber and connected to both a glass syringe attached to an infusion pump (which provided a continuous supply of test material under pressure) and a metered compressed air supply. The chamber atmosphere equilibrated prior to exposure of the animals. Before the start of the study, exposure chamber atmospheres were generated by varying the amount of test material input in order to achieve the optimum atmospheric conditions.

Animals were observed for clinical signs at hourly intervals during exposure, immediately on removal from the restraining tube at the end of exposure and once daily thereafter for 14 days. Individual body weights were recorded prior to treatment and at Days 7 and 14. All animals were killed at Day 15 and examined externally and internally for macroscopic abnormalities. The respiratory tract was examined thoroughly for signs of local irritation or toxicity. Any macroscopic abnormalities were recorded.

Throughout the exposure period the chamber was monitored for temperature, relative humidity and oxygen concentration. In addition, the achieved atmosphere concentration of the test material was analysed chemically for the content of foramsulfuron and AE F122006 in the formulation. The nominal concentration of the formulation was measured gravimetrically. Particle size distribution was also determined.

#### Findings:

There were no cases of mortality. During exposure clinical signs of wet fur and incidents of increased or decreased respiratory rate were recorded. On removal from the chamber all animals showed wet fur, hunched posture, piloerection, increased respiratory rate and red/brown staining around the snout. At 1 hour post-exposure hunched posture, piloerection, increased respiration and red/brown staining around the snout were still present. However, 1 day post-exposure only increased respiration predominated with isolated incidents of hunched posture and piloerection. All animals had recovered 48 hours after exposure, with the exception of one male which continued to exhibit noisy respiration until day 5 post-exposure. Body weight gain was unaffected by treatment and no abnormalities were detected at necropsy.

The chemically analysed achieved concentration of Equip was 5.25 mg/l. This was based on the concentration of foramsulfuron, which was slightly lower than that of AE F122006. The mass median aerodynamic diameter (MMAD) of the particles was 4.64 µm and 42.3% of these were < 4 µm. The nominal (gravimetric) concentration was 77.0 mg/l.

#### Conclusion:

The 4-hour acute inhalation median lethal concentration (LC<sub>50</sub>) of Equip to Sprague Dawley rats was > 5.25 mg/l, which did not cause mortality and was the highest achievable concentration.

#### B.6.1.4. Skin irritation

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. After the study was performed, a new version of the OECD Test Guideline 404 has been adopted 24th April, 2002. The study fulfils the current data requirements. Conclusion has not been changed. Formulation is classified as Skin Irrit. 2 - H315 "Causes skin irritation" according to CLP Regulation (EC) No 1272/2008.
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#### Report:

██████████ 1999f:  
 Rabbit skin irritancy; AE F130360 + AE F122006, 22.5 +22.5 g/l Oil flowable, Code: AE F130360 01 1K05 A3;  
 Report No.: Tox/99/262-59; Doc. No. (Aventis): C005917;  
 Study No.: Tox 95128; unpublished.  
 Testing facility: ██████████  
 Experimental phase of study: 14 June 1999 to 27 June 1999.

**Test Material:** AE F130360 01 1K05 A304, batch number KD945/990301  
(AE F130360: 2.42% w/w; AE F122006: 2.44% w/w)

**Test Animals:** New Zealand White rabbits;  
Source: [REDACTED]

**GLP:** Yes

**Test Method:** OECD 404, 17 July 1992

**Deviations:** None

**Acceptability:** The study is considered to be acceptable.

#### Material and Methods:

Three male New Zealand White rabbits at least 11 weeks old prior to treatment and weighing 2.3 to 2.6 kg were used. They were housed individually throughout and had been acclimatised for 5 days prior to dosing.

An 0.5 ml aliquot of undiluted Equip was applied for 4 hours to the clipped intact dorso-lumbar skin under a 2-ply 25 mm x 25 mm gauze pad of each rabbit which was covered with a semi-occlusive adhesive dressing. At the end of the exposure period the dressing and gauze were removed and the skin washed with warm water to remove any residual test material, then blotted dry.

Rabbits were observed daily for clinical signs and mortality. Skin responses were evaluated at Day 1 approximately 60 minutes after removal of the bandage, 24, 48 and 72 hours post-exposure, then at Days 5 through 11 for all three animals and at Days 12 through 14 for one.

#### Findings:

Well-defined to moderate erythema (Grade 2 to 3) and slight to moderate oedema (Grade 2 1-to 3) were observed in all three rabbits from bandage removal to Day 8. Thereafter both conditions ameliorated in all animals to very slight and resolved in two animals by Day 8. Desquamation (characterised by dryness and sloughing) and thickening of the skin, indicative of repair, were present from Day 5 resolving in 2 of the 3 animals by Day 11. Thickening and very slight erythema were still evident in one animal at termination at Day 15.

**Table B.6.1-3: Skin irritation scores after testing with Equip in rabbits**

Animal		Day post application				
		1*	2	4	8	14
Male #1	erythema	2	2	3	2b	1b
	oedema	2	3	2	1	0
Male #2	erythema	2	2	3	2a	-
	oedema	2	3	3	2b	-
Male #3	erythema	2	2	2	2a	-
	oedema	1	2	2	1b	-

\* Approximately 60 min after removal of the dressing

a Desquamation (characterised by dryness and sloughing)

b Thickening of the skin

#### Conclusion:

Equip was moderately and reversibly irritating to rabbit skin (with scores up to 3). According to the EU Commission Directive 93/21/EEC, this formulation requires classification and labelling with risk phrase R38 “irritating to skin”.

According to the Regulation (EC) No 1272/2008, this formulation is classified as Skin Irrit. 2 - H315 "Causes skin irritation".

#### B.6.1.5. Eye irritation

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. At the moment of the AIR-3 dossier submission, a new version of the OECD Test Guideline 405 (adopted 24th April, 2002) should have been followed. The study fulfils these data requirements. Conclusion has not been changed. Classification is not required according to CLP Regulation (EC) No 1272/2008.
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**Report:** [REDACTED] 2000b:  
 Rabbit eye irritancy; AE F130360 + AE F122006, 22.5 +22.5 g/l Oil flowable, Code: AE F130360 01 1K05 A3;  
 Report No.: Tox/00/262-60; Doc. No. (Aventis): C005918;  
 Study No.: Tox 95129; unpublished.  
 Testing facility: [REDACTED];  
 Experimental phase of study: 21 June 1999 to 17 July 1999.

**Test Material:** AE F130360 01 1K05 A304, batch number KD945/990301  
 (AE F130360: 2.42% w/w; AE F122006: 2.44% w/w)

**Test Animals:** New Zealand White rabbits;  
 Source: [REDACTED]

**GLP:** Yes

**Test Method:** OECD 405, adopted 24 February 1987

**Deviations:** None

**Acceptability:** The study is considered to be acceptable.

#### Material and Methods:

A total of 4 New Zealand White rabbits was used; 3 for the main study and one (screen animal) for initial screening for the severity of any irritant response. They were at least 12 weeks old, had been acclimatised for at least 5 days and weighed 2.4 to 2.6 kg immediately prior to the treatment of the first main study animal (Day 1). All rabbits were housed individually.

A volume of 0.1 ml of Equip was instilled into the right eye. The left eye was untreated and served as the control. One main study animal (pilot animal) was treated in advance of the others to check whether a severe response was likely. In addition, prior to the main study, one rabbit (screen animal) was treated in advance to ensure that, if the response was severe, no further animals would be exposed. Thirty seconds after instillation, the treated eye of this animal was rinsed thoroughly with distilled water for 30 seconds.

Animals were observed daily for clinical signs whilst body weight was recorded immediately prior to dosing. The eyes of each animal were examined 1 hour after dosing, and then at 1, 2, 3, and 4 days after instillation.

**Table B.6.1-4: Eye irritation scores after testing with Equip in rabbits**

Animal			Time after instillation [days]				
			1 hour	1	2	3	4
Male 1	Cornea	Density	0	0	0	0	-
		Area	0	0	0	0	-
	Iris		0	0	0	0	-
	Conjunctivae	Redness	2	2	1	0	-
		Chemosis	1	0	0	0	-
		Discharge	3	0	0	0	-
Male 2	Cornea	Density	0	0	0	0	0
		Area	0	0	0	0	0
	Iris		0	0	0	0	0
	Conjunctivae	Redness	2	2	2	1	0
		Chemosis	1	1	0	0	0
		Discharge	3	0	0	0	0
Male 3	Cornea	Density	0	0	0	0	0
		Area	0	0	0	0	0
	Iris		0	0	0	0	0
	Conjunctivae	Redness	2	2	1	1	0
		Chemosis	2	1	0	0	0
		Discharge	2	0	0	0	

#### Findings:

A diffuse, crimson coloration (Grade 1 to 2) of the conjunctivae and swelling up to partial eversion (Grade 0 to 1) of the eyelids was seen in all main study animals from 1-hour post-instillation. A considerable discharge (Grade 2 to 3) was seen in all animals 1-hour post-instillation only. Reactions had resolved in all instances 4 days after instillation.

#### Conclusion:

Equip was slightly and reversibly irritating to the rabbit eye. According to the EU Commission Directive 93/21/EEC, classification and labelling is not required.

According to the Regulation (EC) No 1272/2008, classification is not required.

#### B.6.1.6.1 Skin sensitization

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. Conclusion has not been changed. Classification is not required according to CLP Regulation (EC) No 1272/2008.
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#### Report:

1999b:  
Guinea pig skin sensitisation (3-induction Buehler test); AE F130360 + AE F122006, 22.5 +22.5 g/l Oil flowable,  
Code: AE F130360 01 1K05 A3;

Report No.: Tox/99/262-69; Doc. No. (Aventis): C005974;  
Study No.: Tox 95130; unpublished.  
Testing facility: [REDACTED]  
Experimental phase of study: 31 May 1999 to 8 July 1999.

**Test Material:** AE F130360 01 1K05 A304, batch number KD945/990301  
(AE F130360: 2.42% w/w; AE F122006: 2.44% w/w)

**Test Animals:** Dunkin/Hartley albino guinea pigs;  
Source: [REDACTED]

**GLP:** Yes

**Test Method:** OECD 406, adopted 17 July 1992

**Deviations:** None

**Acceptability:** The study is considered to be acceptable.

#### **Material and Methods:**

Thirty female Dunkin/Hartley guinea pigs were used. They were approximately 4 to 7 weeks old at arrival, housed in groups of 5, were acclimatised for 5 days and weighed 349 to 426 g at the start of treatment of the main study. Four extra animals were used for preliminary dose ranging investigations. Ten control and 20 test animals were used for the main study.

Preliminary study: The topical irritancy of a range of concentrations (25% w/w to undiluted compound) in sterile water was evaluated to identify where possible, a) a concentration that would produce irritation suitable for the induction phase of the main study and b) a maximum non-irritant concentration for the challenge phase.

Main study: Based on the results of the preliminary study, the following concentrations were used:  
Induction phase topical applications: as supplied, because this caused irritancy but did not adversely affect the animals.  
Challenge phase topical applications: 25% v/v in sterile water, which was the highest concentration that did not produce irritancy.

#### **i) Induction phase:**

On study Day 1, each of the 20 test guinea pig received a 6-hour topical induction application of approximately 0.5 ml undiluted Equip on a 20 mm x 20 mm surgical gauze placed on a area of shaved skin over the left shoulder. The treatment site was occluded for the exposure period with impermeable adhesive tape and secured with plaster. At the end of the exposure period, the dressing was removed. Skin responses observed approximately 24 hours later. The process was repeated twice more at weekly intervals (at Days 8 and 15) over three weeks so that in total each animal received 3 applications. The 10 control group animals were similarly treated, except that no test compound was applied to the dry sterile gauze.

#### **ii) Challenge phase:**

Two weeks after the last induction application all the test and control guinea pigs were challenged topically. A topical 6-hour challenge of a 25% v/v dilution of the test material in sterile water on a 20 x 20 mm gauze patch was applied to area of the shaved skin of the right flank. Skin responses at the challenge sites were evaluated 24 and 48 hours after removal of the dressing. A test animal was considered to show positive evidence of skin sensitisation if the reactions at challenge were definitely more marked and/or more persistent than the maximum reaction in the controls. If the reactions were slightly more marked and/or more persistent but not clearly distinguishable from

controls, the animal was classified as inconclusive. If the reactions were similar to or less marked than the maximum response in the controls, the test animal was considered to show no evidence of skin sensitisation.

All animals were observed daily for signs of ill-health or toxicity. Body weights were recorded on Study Day 1 (the first day of topical application) and on the last day observations of dermal responses were made (Day 34).

#### Findings:

Main study: There were no signs of ill-health or toxicity and expected body weight increases were recorded for all guinea pigs.

#### i) Induction phase:

Slight to moderate erythema and slight to well-defined oedema was observed in all test animals following the induction applications. Thickening, dryness and sloughing of the epidermis at the test site was also observed in 3/20 animals after the second application and a necrotic patch in 6/20 guinea pigs after the third induction. No dermal reactions were seen in any control animal during this period.

#### ii) Challenge phase:

No dermal reactions were seen in eighteen of the twenty test or control animals. Therefore these eighteen animals gave negative responses for sensitisation.

The two remaining test animals gave positive responses.

#### Conclusion:

Equip was not a skin sensitizer in this 3-induction guinea pig Buehler test. Because the active ingredient foramsulfuron was tested in a Maximisation test to be not a sensitizer, on this basis a classification and labelling of Equip should not be required.

#### B.6.1.6.2 Skin sensitization

**Report:** [REDACTED] 2001:  
 EQUIP (AE F130360 01 1K05 A3xx) - Sensitising potential in the guinea-pig - Modified Buehler Test (9 induction applications)  
 Study No. 198/131  
 Testing facility: [REDACTED]  
 Date: 18 September 2001

**Test Material:** AE F130360 01 1K05 A304 or AE F130360 01 1K05 A3,  
 batch number 210700 and KD945/990301  
 (AE F130360: 2.43% w/w; AE F122006: 2.41% w/w)

**Test Animals:** Hartley guinea pigs;  
 Source: [REDACTED]

**GLP:** Yes

**Test Method:** OECD 406, adopted 17 July 1992

**Deviations:** Application site was changed at Day 7 as erythema (score 2) and oedema (score 1) were observed in all animals at Day 4. At Day 14, application site was changed back to the first site. As skin reactions increased in severity and were observable throughout the study, this deviation is not considered to have affected the outcome of the study.



**Acceptability:** The study is considered to be acceptable.

**Material and Methods:**

EQUIP (AE F130360 01 1K05 A3xx) was tested for skin sensitising properties in the modified Buehler test with 9 induction applications. Test article in 100, 50, 25 and 10 % (v/v) solutions in water were tested in preliminary studies. Test article concentration of 50 % was found to cause slight erythema in 4/4 animals after 24 hours and slight erythema in 1/4 animal after 48 hours. Concentration of 25 % caused erythema in 1/4 animals after 24 hours and no reactions after 48 hours. No reactions were observed at 10 % concentration.

In the main study, 9 occlusive topical applications of the test article at concentration of 50 % (minimally irritant concentration) were given for 6 hours to the clipped and shaved skin of the back of 20 guinea-pigs (10 males and 10 females). The test article was applied on days 0, 2, 4, 7, 9, 11, 14, 16 and 18. Application site was changed at Day 7 as erythema of score 2 was observed in all animals. At Day 14, application site was changed back to the first site. After 10 days rest period, animals were exposed topically for 6 hours at test article concentration of 10 % (the highest non-irritating dose). A control group of 10 guinea-pigs (5 males and 5 females) were exposed to water alone. Skin reactions were examined 24 and 48 hours after removal of the occlusive dressing.

**Results:**

No mortality was observed during the study. Body weight changes in the treated animals were not influenced by treatment when compared with controls. Skin reactions during induction are shown in Table 6.1-5.

**Table 6.1-5: Observations during induction phase in the treated group**

	Number of animals affected								
	Day 0 Site 1	Day 2 Site 1	Day 4 Site 1	Day 7 Site 2	Day 9 Site 2	Day 11 Site 2	Day 14 Site 1	Day 16 Site 1	Day 18 Site 1
No erythema	0	0	0	10	0	0	0	0	0
Erythema (score 1)	20	0	0	10	0	0	20	20	0
Erythema (score 2)	0	20	20	0	20	20	0	0	20
Oedema (score 1)	0	0	20	0	0	20	0	0	20

After the challenge with test article in 10 % (v/v) solution, erythema (score 1) was observed in one male and one female animal 24 hours after application.

No skin reactions were noticed in the control group. Applicability of the test system was tested with 1-chlor-2,4-dinitrobenzol in the test laboratory eight months before the study with EQUIP.

**Conclusion:**

EQUIP elicited a positive reaction in 2/20 animals challenged with the test article at concentration of 10 % (v/v). The result of the study is negative and the product EQUIP is considered to be non-sensitising.

**B.6.1.6.3 Skin sensitization**

**Report:** [REDACTED] 2004



AEF 130360 - Evaluation of potential dermal sensitization in the local lymph node assay (LLNA)

Report No: C039527

Study No: SA 03305

Testing facility:

Date: 23 January 2004

**Test Material:** AE F130360 01 1K05 A9

**Test Animals:** Charles River CBA mice,

Source:

**GLP:** Yes

**Test Method:** OECD 429, adopted 24 April 2002

**Deviations:** No positive control group was included in the study and no historical control data was shown. Data summarised only the mean DPM (disintegrations per minute) values but neither individual values nor the range of values were reported.

On the first day of the treatment period, the animals were 6 weeks old at the most. Animals should be 8-12 weeks old at the start of the study. Body weights were not measured.

**Acceptability:** Due to deviations mentioned above, the study is not acceptable.

#### Material and methods

Sixteen female Charles River CBA mice were allocated in 4 groups of four animals each. Three groups received the test substance at the concentrations of 5, 10 and 20 % (the highest concentration maximising exposure whilst avoiding systemic toxicity and excessive local skin irritation). One control group received the vehicle dimethylformamide (DMF). Mice were dosed with 25 µl of the test substance at appropriate concentration or the vehicle on external surfaces of each ear on days 0, 1 and 2. Animals were checked for clinical signs and mortality approximately one hour after dosing and at least once a day until the completion of the study. On Day 5, each mouse was intravenously injected via the tail vein with 250 µl of sodium chloride (0.9 %) containing 20 µCi of <sup>3</sup>H-methyl thymidine. Five hours later, animals were killed and two auricular lymph nodes were removed from each mouse. Nodes from each group were pooled in a tube containing physiological saline and were disaggregated by crushing with a plastic piston. Cell suspensions were washed with physiological saline and pellets re-suspended in trichloroacetic acid (TCA) and stored overnight at +4 °C. Incorporation of <sup>3</sup>H-methyl thymidine was measured by a beta-counter. The results were expressed as disintegrations per minute (DPM) per node (DPN) for each experimental group. Proliferation Indices (PI) were calculated according to the following formula:  $PI = \text{DPN of treated group} / \text{DPN of control group}$ .

A test substance is regarded as a skin sensitizer if one concentration of the test substance results in an increase of <sup>3</sup>H-TdR incorporation of three-fold or greater when compared to control values in the absence of skin irritation and if there is dose related response.

#### Results:

No mortality and no clinical signs of systemic toxicity were observed during the study. No cutaneous reactions were observed in the vehicle and all treated groups. Negative lymphoproliferative responses ( $PI < 3$ ) were noted at all tested concentrations. Results of proliferation assay are summarized in Table B.6.1-6.

**Table B.6.1-6: Results of proliferation assay**

	Treatment, concentration (%)	Disintegrations per minute (DPM)	Disintegrations per node (DPN)	Proliferation Index (PI)
DMF	-	3784	473	-
AEF 130360	5	9546	1193	2.5
AEF 130360	10	8441	1055	2.2
AEF 130360	20	9998	1250	2.6

**Conclusion:**

Negative lymphoproliferative responses ( $PI < 3$ ) were noted at all tested concentrations. Due to deviations mentioned above, the study is not acceptable.

**B.6.1.6. Supplementary studies on the plant protection product**

No supplementary studies have been performed.

**B.6.1.7. Supplementary studies for combinations of plant protection products**

As the notifier informed to this issue, no supplementary studies have been conducted because Equip will not be registered as a tank-mixture partner with other plant protection products for the intended uses. But it is advisable to carry out preliminary tests in the case of tankmixes with other plant protection products. In this connection a warning was formulated by the notifier (Doc. C): "Longer preharvest intervals must be observed when tankmixes with other products are applied. In this case, employ the safety measures prescribed for the more highly toxic products. If symptoms of poisoning occur, inform the physician about the complete mixture."

Effects such as the incompatibility with organophosphates - ..."this would slow down the degradation of the active ingredient in the maize plant" should be discussed for relevance in human toxicity and assessed if such tank-mixes are defined.

**B.6.2. DERMAL ABSORPTION****B.6.2.1 Dermal absorption *in vivo* studies**

Foramsulfuron was shown to have a low potential for dermal absorption following the application of an SC formulation to the skin of male rats. The total amount absorbed over a 24-hour period was less than 1.7% of the applied dose either as neat (undiluted) formulation or as the spray dilution.

<b>Previous evaluation</b>	This study was evaluated in the original DAR. No new evaluation has been performed. After the study was performed, the OECD Test Guideline 427 has been adopted 13th April, 2004. The study practically fulfils the current data requirements and the outcome of the interpretation is considered to be in line with the EFSA Guidance on Dermal Absorption (2012). Conclusion has not been changed.
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**Report:**

1999 (TOX2000–1071)  
(14C)-AE F130360 : *In vivo* dermal absorption study in the male rat.

Report No. TOX/99/262-46, Doc.No. (Aventis): C006428, unpublished  
Testing facility: [REDACTED]  
(Experimental work: 22 April to 16 December 1999)

**Test Material:** Foramsulfuron: undiluted SC formulation (nominally 22.5 g/l) and aqueous spray dilution (nominally 0.225 g/l).  
Formulation code No.: AE F130360 01 1K05 A3 (Equip)

**Test Animals:** Rats

**GLP:** Yes

**Test Method:** OECD draft guideline 1996

**Deviations:** None

**Acceptability:** The study is considered to be acceptable.

**Material and Methods:**

Foramsulfuron was applied to the skin of male rats as a single application of an undiluted SC formulation (nominally 22.5 g/l) and as an aqueous spray dilution (nominally 0.225 g/l). The dose area was enclosed using a silicone rubber saddle covered with semi-occlusive gauze to mimic clothing and for protection against loss of formulation. The formulation was in contact for a maximum of 10 hours before being washed off by swabbing with 1% Tween 80 detergent in distilled water. The period of 10 hours was chosen to represent the maximum duration of a working day.

Urine, faeces and cage washes were collected at pre-determined time points and analysed for radioactive content. Groups of 4 rats were killed at 3, 5, 10, 24, 72, and 120 hours after dosing and the radioactivity present in the treated skin (dose area), untreated skin, carcass, and blood was determined.

**Findings:**

The overall absorption of foramsulfuron was found to be very low with only 0.23% of the spray dilution and 1.69% of the neat formulation being absorbed over the first 10 hour period. After the wash at 10 hours, the cumulative amount absorbed from the application site gradually increased to 0.82% of the dose over the subsequent 110 hours for the diluted formulation but did not increase for the neat formulation. The dose was virtually eliminated by 120 hours after application with less than 0.1% remaining in the tissues at this time.

The amount of dose associated with the application site (approximately 20% of the dose at the diluted formulation and 5% at the neat formulation) did not decrease significantly over the 110 hours following the swabbing procedure showing that this was not absorbed to any significant degree over this time. It is probable that this material would be eventually lost externally by skin contact or associated with desquamated cells, and it should therefore not be considered as being available for absorption. The proportions of dose present in the excreta, carcass, washes, and at the application site are given in Table B.6.2-1.

**Table B.6.2-1: Distribution of radioactivity after dermal application of radiolabelled foramsulfuron (as formulation concentrate or spray dilution)**

Sample	Amount of applied dose (as % applied) at timepoint:-					
	Formulation concentrate			Spray Dilution		
	10 h	24 h	120 h	10 h	24 h	120 h
Excreted (urine, faeces, cage wash)	0.46	0.87	1.56	0.08	0.19	0.76
Carcass + excretory organs, untreated skin, blood	1.23	0.60	0.02	0.14	ND	0.07
<b>Total Absorbed</b>	<b>1.69</b>	<b>1.47</b>	<b>1.58</b>	<b>0.23</b>	<b>0.19</b>	<b>0.82</b>
Application Site	5.17	5.30	4.98	21.56	23.40	19.19
Swab, saddle, gauze and tapes	93.61	92.02	92.15	68.66	68.99	70.03
<b>Total Recovery</b>	<b>100.47</b>	<b>98.79</b>	<b>98.71</b>	<b>90.45</b>	<b>92.58</b>	<b>90.04</b>

**Conclusion:**

Foramsulfuron has a very low potential for absorption through rat skin when applied either as a neat SC formulation or as an aqueous spray dilution. Following a 10-h application period, the total amount absorbed within 24 hours was less than 1.7% of the applied dose for either the neat formulation or the spray dilution.

Therefore it is appropriate to use the experimentally determined dermal absorption value of 2% in calculations of operator exposure as a worst case figure. The *in vivo* dermal penetration study in rats provided an acceptable margin of safety and consequently a comparative *in vitro* study is not required.

**B.6.3. AVAILABLE TOXICOLOGICAL DATA RELATING TO CO-FORMULANTS**

Besides its active ingredient foramsulfuron, the SC formulation Equip (AE F130360 01 1K05 A3) contains the safener isoxadifen-ethyl (AE F122006) and different co-formulants. The respective data are given in Safety Data Sheets. The possible acute toxic, irritating and skin sensitising properties of all co-formulants are covered by the studies with the preparation. Additionally due to the presence of one of the solvents in the product (Solvesso 200; conc. >10%; SDS: R 65), for Equip the indication of danger "Harmful: may cause lung damage if swallowed (Xn, R 65)" is required. Due to this solvent, classification of Equip according to the CLP Regulation (EC) 1272/2008 is additionally Asp. Tox. 1 - H304. According to the applicant, isoxadifen-ethyl is classified as skin sensitising (Skin Sens. 1 - H317). The product Equip was not skin sensitising in animal tests but the label of the product shall bear the statement "EUH208 - Contains isoxadifen-ethyl. May produce an allergic reaction."

**B.6.4. EXPOSURE DATA**

Equip is a post-emergence herbicide for the control of annual weeds and grasses in grain maize and fodder maize formulated as a suspension concentrate (SC). Equip contains 22.5 g/l foramsulfuron and in addition to the active substance the safener isoxadifen-ethyl in the same concentration of 22.5 g/l. Equip is applied by overall spraying on maize from the 2-leaf to the 6/8-leaf stage of the crop at a maximum rate of 2.67 l product per hectare (60 g ai/ha).

### B.6.4.1. Operator exposure

#### B.6.4.1.1. Estimation of operator exposure assuming personal protective equipment is not used

Exposure to the product was calculated using the German model and the UK-POEM.

- 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;
- 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) (UK MAFF) 1992.

Operator exposure related to the AOEL, to provide an estimate of the extent to which the AOEL is accounted for. **The proposed AOEL<sub>systemic</sub> for foramsulfuron is 0.1 mg/kg bw/d**, based on the NOEL in the rabbit developmental toxicity (teratogenicity) study of 50 mg/kg/day and a 100-fold safety factor adjusted by a factor of 5 for the oral absorption rate of 20% (see B.6.10).

The notifier also proposed an AOEL based on the NOEL of 50 mg/kg/day from the rabbit developmental toxicity (teratogenicity) study, but used a 25-fold safety factor. In addition, although the notifier stated that "... Since absorption was only 20% of the administered dose by the oral route, the AOEL is corrected to 0.4 mg/kg bw/d", a value of 2.0 mg/kg bw/d marked as AOEL<sub>systemic</sub> was used for the operator exposure assessment.

By the rapporteur, the absorbed dose was determined on the basis of 2% percutaneous absorption (concentrate and diluted product) for both calculation models. (i.e. a dermal tolerated exposure of 5 mg/kg bw/d) and an assumed body weight of 70 kg for the operator.

The notifier derived a specific dermal AOEL of 40 mg/kg bw/d (rat, 28-d dermal toxicity study: NOEL 1000 mg/kg bw/d; SF 25) but did not use this figure in the risk assessment. In both of the models, the notifier calculated with the dermal absorption rate of 2%.

The estimated operator exposure values, determined on the basis of the model scenarios without protective clothing, are set out in Table B.6.4-1, where they are also shown as percentages of the systemic AOEL.

**Table B.6.4-1: Estimations of operator exposure (absorbed dose) in relation to the AOEL – no protective clothing and equipment used**

Model	Exposure (mg/kg bw/day)	% of AOEL used by the notifier [2.0 mg/kg bw/d]	% of AOEL <sub>systemic</sub> [0.1 mg/kg bw/d]
German model	0.0015	0.08%	1.5%
UK-POEM	0.009	0.45%	9.4%

The calculations show that in the worst case, less than 10% of the AOEL<sub>systemic</sub> is used (UK-POEM, smallest pack size, with large use rate of 50 ha/day, and no protective clothing).

The calculations were based on the parameters set out below, which are specific to Equip:

#### Worst-case scenario for the German model:

- a maximum application rate of 2.67 litres product per hectare (60 g ai/ha),
- a work rate of 20 hectares per day,

- iii. liquid formulation applied with a tractor-mounted sprayer in a field crop,

Worst-case scenario for the UK-POEM:

- i. a maximum application rate of 2.67 litres product per hectare (60 g ai/ha),
- ii. a spray volume of 100 to 200 litres per hectare, with 100 litres as the most concentrated spray solution and hence the worst-case for operator exposure,
- iii. a work rate of 50 hectares per day,
- iv. a wide-neck 5-litres container,
- v. liquid (SC) formulation applied with tractor-mounted boom equipment with hydraulic nozzles.

The actual calculations are presented in Table B.6.4-2 and Table B.6.4-3. The calculations were done assuming operators weighing 70 kg, which is 10 kg higher than normally used for the UK-POEM. It was believed by the notifier that the higher figure represents a more realistic body weight for operators. The use of this higher figure also serves to adjust the model inputs.

**Table B.6.4-2: Estimated operator exposure – German model**

Product:			EQUIP®	
Formulation type			Liquid	
Active ingredient (ai):			Foramsulfuron	
Concentration:			22.5 g/l	
NOEL <sub>oral</sub> :			50 mg/kg/day	
Maximum rate:			0.06 kg ai/ha	
Area treated:			20 ha	
Amount of product handled per day:			20 ha x 0.06 kg ai/ha = 1.2 kg ai/day	
EXPOSURE FOR TRACTOR SPRAYER WITH BOOM & HYDRAULIC NOZZLES, FIELD CROP				
Route			Specific exposure [mg/kg ai]	Foramsulfuron x 1.2 kg ai/day [mg/person <sup>1</sup> and day]
Mixing/loading	inhalation	I <sub>m</sub>	0.0006	0.00072
	dermal	D <sub>m</sub>	2.4	2.88
Spray application	inhalation	I <sub>a</sub>	0.001	0.0012
	dermal - head	D <sub>a(c)</sub>	0.06	0.072
	dermal - hand	D <sub>a(h)</sub>	0.38	0.456
	dermal - body	D <sub>a(b)</sub>	1.6	1.92
ESTIMATED EXPOSURE (WITHOUT PROTECTIVE CLOTHING AND EQUIPMENT):				
Inhalation:	mix/load		0.00072	mg/person <sup>1</sup> /day
	spray		0.0012	mg/person/day
Dermal:	mix/load		2.88	mg/person/day
	spray		2.448	mg/person/day
Systemic <sup>2</sup> :	mix/load		0.05832	mg/person/day
	spray		0.05016	mg/person/day
Total <sub>systemic</sub>			0.108	mg/person/day
:			= 0.0015	mg/kg bw/day

<sup>1</sup> Operator exposure calculations performed assuming 70 kg body weight

<sup>2</sup> assuming 100% absorption of inhaled exposure and 2% dermal penetration

Table B.6.4-3: Estimated operator exposure – UK-POEM

A. PRODUCT DATA				
1	Product name	EQUIP®		
2a	Active ingredient	Foramsulfuron		
2b	Concentration (mg/ml)	22.5		
3	Formulation type	sc		
4a	Main solvent			
4b.	Concentration of solvent	na		
5.	Maximum in-use ai concentration (mg/ml)	0.601		
B. EXPOSURE DURING MIXING AND LOADING				
1a.	Container size (litres)	5 litres		
1b.	Hand contamination/operation	0.01 ml		
2.	Application dose (litres product/ha)	2.67		
	(kg ai/day)	3.00375		
3.	Work rate (ha/day)	50		
4.	Number of operations (/day)	27		
5.	Hand contamination (ml/day)	0.27		
6.	Protective clothing	NONE	GLOVES	
7.	Transmission to skin (%)	100	5	
8.	Dermal exposure to formulation (ml/day)	0.27	0.014	
9.	Concentration of ai (mg/ml)	22.5	22.5	
10.	Dermal exposure to ai (mg/day)	6.075	0.304	
11.	Percent absorbed (%)	2	2	
12.	Absorbed dose (mg/kg bw/day)	0.002	0.00009	
C. EXPOSURE DURING SPRAY APPLICATION				
1.	Application technique	Vehicle with cab boom hydraulic nozzles		
2.	Application volume (spray/ha)	100		
3.	Volume of surface contamination (ml/h)	10		
4.	Distribution (%)	Hands 65	Hands 65	Trunk 10 Legs 25
5.	Clothing	NONE	GLOVES	PERMEABLE PERMEABLE
6.	Penetration (%)	100	10	5 15
7.	Dermal exposure (ml/h)	6.5	0.65	0.05 0.375
8.	Duration of exposure (h)	6		
	PPE	NONE		GLOVES
9	Total dermal exposure to spray (ml/day)	41.55		6.45
10.	Concentration of ai (mg/ml)	0.601		0.601
11.	Dermal exposure to ai (mg/day)	24.961		3.875
12.	Percent absorbed (%)	2		2
13.	Absorbed dose (mg/kg bw/day)	0.0071		0.0011



<b>D. INHALED EXPOSURE DURING SPRAY APPLICATION</b>	
1. Inhalation exposure (ml/h)	0.01
2. Duration of exposure (h)	6
3. Concentration of ai (mg/ml)	0.601
4. Inhalational exposure to ai (mg/day)	0.036
5. Percent absorbed (%)	100
6. Absorbed dose (mg/kg bw/day)	0.0005
<b>E. PREDICTED EXPOSURE (assumed body weight of an operator: 70 kg)</b>	
1. No gloves	0.009 mg/kg bw/day
2. Gloves only when mixing/loading	0.008 mg/kg bw/day
3. Gloves only during spray application	0.003 mg/kg bw/day
4. Gloves during spray appl. & mix/loading	0.002 mg/kg bw/day

**Conclusion:**

According to the relation of the estimated exposures (German model: 0.0015 mg/kg bw/d; UK-POEM: 0.009 mg/kg bw/d) and the systemic AOEL of 0.1 mg/kg bw/d, operator exposure to Equip, during mixing, loading and spraying does not involve a significant risk to the health of the operators concerned, even if no protective clothing and equipment is used (Table B.6.4-1). The safener isoxadifen-ethyl contained in the formulation in the same concentration as the active ingredient was not a matter of the exposure assessment but according to the applicant the safener is skin sensitising. As the product is classified as Skin Irrit. 2 - H315 and needs to be labelled with the statement EUH208, gloves, respiratory protective equipment (RPE) and coverall are required when handling the product.

**B.6.4.1.2. Estimation of operator exposure assuming personal protective equipment is used**

Exposure to the product for operators wearing personal protective equipment was not calculated because it had already been shown that the estimated exposure of Equip during mixing/loading and application is well below the systemic AOEL even if personal protective equipment is not worn.

**B.6.4.1.3. Measurement of operator exposure**

Since the risk assessment carried out indicated that the health-based limit value (AOEL<sub>systemic</sub>) for the active substance foramsulfuron will not be exceeded under practical conditions of use, a study to provide a measure of operator exposure to the formulated product Equip under field conditions was not necessary and therefore was not carried out.

**B.6.4.2. Bystander and resident exposure**

The worst-case situation of a bystander is a person standing at the edge of the area being treated during a full working day. Dermal and inhalation exposure due to drift of spray material are considered to be far lower than the exposure of an operator who is always nearer to the source of drift material. The results of the operator exposure estimation have shown that operators are not exposed to critical levels when handling the product under the recommended conditions of use. There is thus no reason to anticipate unacceptably high exposure of bystanders present for only a short period of time during the spraying operation.

**B.6.4.3. Worker exposure**



Equip is applied in corn, where entering of crops shortly after spraying is not necessary. Therefore estimations of worker exposure are not needed. In any case, the results of the operator exposure estimation have shown that operators are not exposed to critical levels when handling the product under the recommended conditions of use. There is thus no reason to anticipate an unacceptably high exposure, if a worker nevertheless enters the field after the spraying operation.

#### B.6.5. EXPOSURE AND RISK ASSESSMENT

Operator exposure to the product Equip was modelled with German model and UK-POEM. Systemic exposure was estimated to be under the AOEL of 0.1 mg/kg bw/day even if no personal protective equipment (PPE) is used. As the product is classified as Skin Irrit. 2 - H315 and needs to be labelled with the statement EUH208, gloves, respiratory protective equipment (RPE) and coverall are required during mixing and loading. The product presents an aspiration hazard (Asp. Tox. 1 - H304) and needs to be stored locked up. Re-entry activities after spraying of Equip on the representative use on corn are not necessary. Bystander and resident are not anticipated to be exposed for unacceptably high levels of foramsulfuron.

Exposure of operator, worker, bystander and resident is estimated to be on acceptable level and no risk for health is anticipated when the product Equip is used according to the instructions under the recommended conditions of use.

#### B.6.6. REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
B.6.1.1		1999	Rat acute oral toxicity - AE F130360 + AE F122006, 22.5 + 22.5 g/l oil flowable code AE F130360 01 1K05 A3. AGV248/9939 35/AC ! TOX/99/262- 57!C005915 GLP, unpublished TOX2000- 1065	Y	N		Bayer Crop Science	In DAR 2001

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
B.6.1.2		2000	Rat acute dermal toxicity - AE F130360 + AE F122006, 22.5 + 22.5 g/l oil flowable code AE F130360 01 1K05 A3. AGV246/9939 52/AC ! TOX/00/262- 58!C005916 GLP, unpublished TOX2000- 1066	Y	N		Bayer Crop Science	In DAR 2001
B.6.1.3		1999	Rat acute inhalation toxicity - AE F130360 + AE F122006, 22.5 + 22.5 g/l oil flowable code AE F130360 01 1K05 A3. 374/078 ! TOX/99/262- 54 ! C005786 GLP, unpublished TOX2000- 1067	Y	N		Bayer Crop Science	In DAR 2001

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B.6.1.4		1999	Rabbit skin irritancy - AE F130360 + AE F122006, 22.5 + 22.5 g/l oil flowable code AE F130360 01 1K05 A3. AGV247/9936 43/SE ! TOX/99/262- 59!C005917 GLP, unpublished TOX2000- 1068	Y	N		Bayer Crop Science	In DAR 2001
B.6.1.5		2000	Rabbit eye irritancy - AE F130360 + AE F122006, 22.5 + 22.5 g/l oil flowable code AE F130360 01 1K05 A3. AGV245/9939 33/SE ! TOX/00/262- 60!C005918 GLP, unpublished TOX2000- 1069	Y	N		Bayer Crop Science	In DAR 2001

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B.6.1.6.1		1999	Guinea-pig sensitisation (3 induction Buehler test) - AE F130360 + AE F122006 22.5 + 22.5 g/l oil flowable code AE F130360 01 1K05 A3. AGV225/9937 44/SS ! TOX/99/262-69!C005974 GLP, unpublished TOX2000-1070	Y	N		Bayer Crop Science	In DAR 2001
B.6.1.6.2		2001	EQUIP (AE F130360 01 1K05 A3xx) - Sensitising potential in the guinea-pig - Modified Buehler Test (9 induction application Study No. 198/131 GLP, unpublished	Y	Y		Bayer Crop Science	Submitted for the purpose of renewal

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B.6.1.6.3		2004	AEF 130360 - Evaluation of potential dermal sensitization in the local lymph node assay (LLNA) Report No: C039527 Study No: SA 03305 GLP, unpublished	Y	Y		Bayer Crop Science	Submitted for the purpose of renewal
B.6.2.1		1999	In vivo dermal absorption study in the male rat. Code [14C]-AE F130360. AGV224/9941 56 ! TOX/99/262- 46 ! C006428 GLP, unpublished TOX2000- 1071	Y	N		Bayer Crop Science	In DAR 2001