MON 52276
(360 g/L glyphosate Acid)

DOCUMENT M-CP, Section 7

TOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

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Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number
22nd July 2020	CP 7.2 Addition of citrus use (under orchards)	Doc ID 110054-MCP7_GRG_Rev 1_Jul_2020 Replaces the Doc ID 110054-MCP7_GRG_Jun_2020 – Changes are given in yellow

[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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Table of Contents

CP 7 TOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCTS 5
CP 7.1 Acute Toxicity 11
CP 7.1.1 Oral toxicity 13
CP 7.1.2 Dermal toxicity 16
CP 7.1.3 Inhalation toxicity 19
CP 7.1.4 Skin irritation 23
CP 7.1.5 Eye irritation 26
CP 7.1.6 Skin sensitisation 30
CP 7.1.7 Supplementary studies on the plant protection product 38
CP 7.1.8 Supplementary studies for combinations of plant protection product 62
CP 7.2 Data on Exposure 63
CP 7.2.1 Operator exposure 64
CP 7.2.1.1 Estimation of operator exposure 65
CP 7.2.1.2 Measurement of operator exposure 67
CP 7.2.2 Bystander and resident exposure 67
CP 7.2.2.1 Estimation of resident exposure 68
CP 7.2.2.2 Estimation of bystander exposure 71
CP 7.2.2.3 Estimated recreational exposure (EFSA Guidance) 72
CP 7.2.2.4 Measurement of bystander and resident exposure 72
CP 7.2.3 Worker exposure 72
CP 7.2.3.1 Estimation of worker exposure 72
CP 7.2.3.2 Measurement of worker exposure 75
CP 7.3 Dermal Absorption 76
CP 7.3.1 Dermal absorption study 76
CP 7.4 Available Toxicological Data Relating to Co-Formulants 89
Appendix 1 – Detailed exposure calculations 89
A 1.1 Operator exposure calculations 89
A 1.2 Resident exposure calculations 107
A 1.3 Worker exposure calculations 115

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CP 7 TOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCTS

Introduction

Commission Directive 2001/99/EC included glyphosate as an active substance in Annex I to Council Directive 91/414/EEC. Following a peer review organised by the European Commission, glyphosate was included in Annex I of Council Directive 91/414/EEC with Commission Directive 2001/99/EC, entering into force on 01st July 2002. According to Regulation (EU) No 540/2011, glyphosate was deemed for approval under Regulation (EC) No 1107/2009 as well.

In agreement with Article 4 of Regulation (EC) No 1141/2010 Monsanto Europe S.A./N.V. (now Bayer Agriculture BV) on behalf of the then European Glyphosate Task Force submitted an application to Germany as RMS and Slovakia as Co-RMS notifying the intention to renew the existing approval of glyphosate on 24th March 2011 during the AIR 2 process. A collective supplementary dossier from the Glyphosate Task Force comprising 24 applicants was submitted on 25th May 2012.

On 12th November 2015, the European Food Safety Authority (EFSA) published its conclusions on the peer review of the pesticide risk assessment of the active substance glyphosate in the framework of the renewal of the approval under Commission Regulation (EU) No 1141/2010 (EFSA Journal 2015;13(11):4302)[1].

EFSA was requested by the European Commission (EC) to consider available information on the potential endocrine activity of the pesticide active substance glyphosate in accordance with Article 31 of Regulation (EC) No 178/2002. The assessment concluded that the weight of evidence indicates glyphosate does not possess endocrine disrupting properties via oestrogen, androgen, thyroid or steroidogenesis modes of action based on a comprehensive database available in the toxicology area.

On 17th March 2016, the rapporteur Member State, Germany, submitted a dossier to the European Chemical Agency for harmonised classification and labelling of the substance glyphosate. The proposal document was prepared in accordance with Article 37 of Regulation (EC) No 1272/2008 of the European Parliament and of the Council.

The Committee for Risk Assessment (RAC) assessed the hazards presented by glyphosate against the criteria in the Classification, Labelling and Packaging Regulation[2]. The RAC concluded that the available scientific evidence did not meet the criteria in the CLP Regulation and that glyphosate would not be classified as possessing STOT (specific target organ toxicity), carcinogenicity, mutagenicity or reproductive toxicity.

The AIR 2 process at EU level, concluded that it has been established with respect to one or more representative uses of at least one plant protection product containing the active substance glyphosate that the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 are satisfied. Thus, the approval criteria of demonstrating a safe use were deemed to be satisfied. It was therefore appropriate to renew the active substance glyphosate[3]. Glyphosate was renewed (date of approval) on 16th December 2017 with the expiration of approval set up for 15th December 2022.

[1] Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate in the framework of the renewal of the approval under Commission Regulation (EU) No 1141/2010; EFSA Journal 2015;13(11):4302, 107 pp; doi:10.2903/j.efsa.2015.4302.
[2] RAC Opinion proposing harmonised classification and labelling at EU level of glyphosate (ISO); N (phosphono-methyl)glycine. CLH-O-0000001412-86-149/F. Adopted 15 Mar 2017.
[3] COMMISSION IMPLEMENTING REGULATION (EU) 2017/2324.

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Bayer Agriculture BVBA[4] submits the dossier on behalf of the Glyphosate Renewal Group (GRG) for the AIR 5 process.

In the frame of the pre-submission meeting held between the GRG and the Assessment Group on Glyphosate (AGG) on 27th September 2019, the AGG provided a reference document to GRG on the process to be considered when summarizing studies from past submissions in the June 2020 renewal dossier[5].

In 1995, glyphosate active substance dossiers were submitted by both task force and individual companies comprising a total of 19 applicants. The majority of applicants of the 1995 submissions did not join the 2012 Glyphosate Task Force (GTF) nor the GRG submitting the AIR 5 dossier in 2020. The GRG was not able to get access to a total of 46 study reports from three companies that were part of the submissions in 1995 (for details please refer to the Document B, Doc ID: 110054-B-GRG_Jun_2020), because some of the companies involved in the submissions in 1995 have subsequently been acquired by/merged with other companies or have since exited the market. Therefore, the GRG contacted Germany as the former RMS for glyphosate to discuss options available in order for AGG to get access to all said 46 study reports. A list of all these studies was sent to BVL (letter from 03rd March 2020). BVL replied to this request on 24th March 2020, advising the AGG to send a "request for administrative assistance (Art. 39 of Regulation (EC) No. 1107/2009)" to the BVL. Then, BVL will forward the respective studies directly to the AGG. In the present AIR 5 Dossier, information on those inaccessible studies has been summarised based on the 2000 monograph documents[6] and are identified (as Category 4a and 4b) in the present AIR 5 dossier[7]. In these cases, GRG was unable to provide updated Appendix E summaries due to lack of access to these studies.

A number of new regulatory studies, generated after the previous EU renewal process and/or not previously submitted at EU level, are presented as part of the data package of this AIR 5 dossier. To date, those new studies have not been peer-reviewed at EU level (please refer to the Application document Rev 2 Dated May 2020 – Document F, Doc ID: 110054-F-GRG_Jun_2020).

A literature search for the active substance glyphosate and metabolites was performed in accordance with the provisions of the EFSA Guidance "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) 1107/2009" and according to the updated Appendix to this Guidance document[8]. The scientific literature review was performed for the period of 01st January 2010 until 31st December 2019, please refer to M-CA Section Toxicology (Doc ID: 110054-MCA7_GRG_Jun_2020. The identified relevant and reliable articles are presented as appendix E summaries in the M-CA Section Toxicology. For further detailed information on the Literature Review Report (LRR) and the corresponding evaluation, please refer to M-CA Section 9 "Literature". In the frame of the pre-submission meeting held on 27th September 2019, the AGG provided a reference document to GRG on the process to be considered when presenting literature in the June 2020 submission dossier[9].

During the former EU processes, public literature data was evaluated, listed and reported by the RMS. An appendix, containing information about all previously submitted and/or included public literature articles from the former EU process is presented, for sake of completeness, as Annex to the M-CA section 7 (see doc 110054-MCA7_GRG_Jun_2020).

[4] Due to the Bayer-Monsanto acquisition in 2018, the legal entity name Monsanto Europe S.A. / N.V. has been changed to Bayer Agriculture BV.
[5] AGG_Advice to GTF2_Literature search_Final Oct 2019 "HOW TO SUMMARISE STUDIES IN DOSSIERS FROM 1998 AND 2012 IN THE DOSSIER TO BE SUBMITTED JUNE 2020"
[6] Monograph and Addendum to the monograph EU 2001: Glyphosate monograph
[7] In the AIR 5 dossier, in each M document, a category has been assigned to each regulatory study included in the AIR 5 dossier (for details please refer to the Doc ID: 110054-B-GRG_Jun_2020).
[8] Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances approved 27 March 2019 (doi: 10.2903/sp.efsa.2019.EN-1612)
[9] AGG_Advice to GTF2_Literature search_Final Oct 2019 "ADVICE TO GTF2: HOW TO PRESENT THE LITERATURE SEARCH IN THE DOSSIER TO BE SUBMITTED JUNE 2020"

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Table 7-1: Information on MON 52279

Product name and code	MON 52279
Formulation type	Soluble concentrate [Code: SL]
Active substance(s) (incl. content)	Glyphosate; 360 g/L
Function	Herbicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	Yes
Product previously evaluated in another MS according to Uniform Principles	Yes

* Information on the detailed composition of MON 52276 can be found in the Confidential Section (See: Doc J CP: Doc ID: 110054-JCP_GRG_Jun_2020)

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No. 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 7-2: Justified proposals for classification and labelling for MON 52276 according to Regulation (EC) No. 1272/2008

Hazard class(es), categories	None
Hazard pictograms or Code(s) for hazard pictogram(s)	None
Signal word	None
Hazard statement(s)	None
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]

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Table 7-3: Summary of risk assessment for operators, workers, bystanders and residents for MON 52276

Exposure Scenario	Result	PPE/ Risk mitigation measures
Operators	Acceptable	No specific PPE is necessary/ MON 52276 can be applied safely to operators using tractor-mounted and hand-held application techniques
Workers	Acceptable	No specific PPE is necessary
Bystanders	Acceptable	None
Residents	Acceptable	No specific PPE is necessary

No unacceptable risk for operators, workers, bystanders and residents was identified when the product is used as intended. No specific PPE is necessary.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and bystanders/ residents is presented in the following table.

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Table 7-4: Critical uses and overall conclusion of exposure assessment

1	2	3	4	5	6	7	8	9	10			
Use-No.[1]	Crops and situation (e.g. growth stage of crop)	F, Fn, Fpn G, Gn, Gpn or I [2]	Application		Application rate		PHI (d)	Remarks: (e.g. safener/synergist (L/ha)) critical gap for operator, worker, bystander or resident exposure based on [Exposure model]	Acceptability of exposure assessment			
			Method/ Kind (incl. application technique [3]	Max. number (min. interval between applications) a) per use b) per crop/ season	Max. application rate per year kg as/ha a) Glyphosate	Water L/ha min/ max			Operator	Worker	Bystander	Residents
1	Pre emergence of crops	F	Spraying, LCTM	a) 1 b) 1	1.44	100-400	NA	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874				
2-3-6-10	Vegetables	F	Spraying, LCTM	a) 1-3 b) 1-3 (28 d)	2.16	100-400	NA	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874				
4	Orchards	F	Ground directed, shielded spray, band application	a) 1-3 b) 1-3 (28 d)	2.88	100-400	7	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874				
5	Vines	F	Ground directed, shielded spray, band application	a) 1-3 b) 1-3 (28 d)	2.88	100-400	7	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874				

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Table 7-4: Critical uses and overall conclusion of exposure assessment

1	2	3	4	5	6	7	8	9	10			
7	Railroad tracks	F	Ground directed, shielded spray	a) 2 (90 d) b) 2 (90 d)	3.6	100-400	NA	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874				
8-9	Invasive species in agricultural and non-agricultural areas	F	Spot treatment (shielded)	a) 1 b) 1	1.8	5-400	NA	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874				

1 Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
2 F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
3 e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 "Acceptability of exposure assessment"

A	Exposure acceptable without PPE/ risk mitigation measures
R	Further refinement and/ or risk mitigation measures required
N	Exposure not acceptable/ Evaluation not possible

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CP 7.1 Acute Toxicity

Summary of acute toxicity

The conclusions of the 2001 EU evaluation of MON 52276 (acute toxicity profile) are still relevant to this submission. However, a new dermal skin sensitisation study was conducted under GLP conditions, following the revised OECD 406 test guideline (modified Buehler; 9 applications). The new dermal sensitisation study confirms the results of the previously submitted non-GLP study and the 2001 EU evaluation for this endpoint.
Moreover, according to 1107/2009/EC and CLP Regulation 1272/2008, product classification can be generated by calculation or estimation based on the toxicity of the active substance and co-formulants. This calculation was performed based on the details provided in Doc J-CP (Doc ID: 110054-JCP_GRG_Jun_2020), and no classification was expected. The classification by estimation confirms thus the negative outcomes of the skin sensitisation studies performed.

Regarding the acute inhalation endpoint an acute inhalation study was performed leading to a negative outcome.

Classification by calculation confirms the negative outcome of the acute inhalation study performed (see Doc J-CP).

Additionally, two genotoxicity studies were conducted on the formulation. However, as the *in vitro* micronucleus study was considered not acceptable due to a deviation in the historical control data, another *in vitro* micronucleus study is currently ongoing.

The results are summarised in the following table:

Table 7.1-1 Summary of evaluation of the studies performed on MON 52276

Annex point	Study	Study type	Substance	Status	Remark
CP 7.1.1/001	[redacted], 1991a	Acute Oral Toxicity (OECD 401)	MON 52276	Acceptable	LD_{50}, oral, rat >5000 mg/kg bw Not classified
CP 7.1.2/001	[redacted], 1991b	Acute Dermal Toxicity (OECD 402)	MON 52276	Acceptable	LD_{50}, dermal, rat >5000 mg/kg bw Not classified
CP 7.1.3/001	[redacted], 2015	Acute Inhalation Toxicity (OECD 403)	MON 52276	Acceptable	LC_{50} >5.25 mg/L Not classified
CP 7.1.4/001	[redacted], 1991c	Skin irritation (OECD 404)	MON 52276	Acceptable	Non irritant
CP 7.1.5/001	[redacted], 1992a	Eye irritation (OECD 405)	MON 52276	Acceptable	Non irritant
CP 7.1.6/001	[redacted], 2001	Skin Sensitisation (OECD 406)	MON 52276	Acceptable	Non sensitising
CP 7.1.6/002	[redacted], 1992b	Skin Sensitisation (OECD 406)	MON 52276	Not acceptable	Non sensitising
CP 7.1.7/001	[redacted], 2016	Bacterial Reverse Mutation Assay (OECD 471)	MON 52276	Acceptable	Non genotoxic

Table 7.1-1 Summary of evaluation of the studies performed on MON 52276

Annex point	Study	Study type	Substance	Status	Remark
CP 7.1.7/002	[redacted], 2016	*In Vitro* Mammalian Cell Micronucleus Assay (OECD 487)	MON 52276	Not acceptable	Non genotoxic
CP 7.3.1/001	[redacted], 2010	*In vitro* dermal penetration in human skin	MON 52276	Acceptable	Dermal absorption values to be used: Concentrate: 0.096 % Worst-case dilution: 0.69 %

MON 52276, containing glyphosate at the nominal concentration of 360 g/L, has a low toxicity in respect to acute oral and dermal application. The formulation is irritating neither to the skin nor the eyes and does not have a sensitising potential.

The genotoxicity studies demonstrate no mutagenic potential of the formulation.

Table 7.1-2 Batches of Glyphosate 360 g/L (486 g/L isopropylammonium salt) SL (MON 52276) used for toxicity studies

Formulation/ Batch (or any information stated)	Content/ Purity/ Radiochemical purity	Study type	Author, date*
MON 52276 Batch: LLN-9105-3135-F	30.57 % glyphosate acid equivalent	Acute oral toxicity	[redacted], 1991a
MON 52276 Batch: LLN-9105-3135-F	30.8 % glyphosate acid equivalent	Acute dermal toxicity	[redacted], 1991b
MON 52276 Batch: GLP-1503-23897-F	30.3 wt % glyphosate	Acute inhalation toxicity	[redacted], 2015
MON 52276 Batch: LLN-9105-3135-F	30.57 % glyphosate acid equivalent	Acute dermal irritation/ corrosion rabbit	[redacted], 1991c
MON 52276 Batch: LLN-9102-2794-F	30.39 % glyphosate acid equivalent	Acute eye irritation/ corrosion	[redacted], 1992a
MON 52276 Batch: LLN-9105-3135-F	~31 % glyphosate	Skin sensitisation	[redacted], 1992b
MON 52276 Batch: AtCt204104	30.88 % glyphosate acid equivalent	Skin sensitisation	[redacted], 2001
MON 52276 Batch: 11427995	30.3 wt % glyphosate acid	Bacterial Reverse Mutation Assay	[redacted], 2016
MON 52276 Batch: 11427995	30.3 wt % glyphosate acid	*In vitro* micronucleus assay	[redacted], 2016

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Table 7.1-2 Batches of Glyphosate 360 g/L (486 g/L isopropylammonium salt) SL (MON 52276) used for toxicity studies

Formulation/ Batch (or any information stated)	Content/ Purity/ Radiochemical purity	Study type	Author, date*
MON 52276 Batch: AZE200810A	30.8 wt % glyphosate acid	*In vitro* micronucleus assay	[redacted], 2020
[^{14}C]glyphosate (as glyphosate acid) Batch: 53463-3-23	Glyphosate-IPA: 63.81 % Glyphosate acid: 47.28 % Radiochemical purity: >97.8 %	*In vitro* dermal penetration in human skin	[redacted], 2010

CP 7.1.1 Oral toxicity

1. Information on the study

Data point:	CP 7.1.1/001
Report author	[redacted]
Report year	1991
Report title	Acute Oral Toxicity Study In Rats
Report No	6097-91
Document No	[redacted]-91-261
Guidelines followed in study	US EPA FIFRA guideline 81-1 (1984); OECD 401 (1987 – deleted in 2001) EEC directive 84/449/EEC method B.1 (1984).
Deviations from current test guideline	Some deviations according to the most updated version of this guideline but none that could jeopardise the results of this study.
Previous evaluation	Yes, accepted in RAR (2015)
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 2a

2. Full summary of the study according to OECD format

The acute oral toxicity of the test substance, MON 52276, was evaluated in Sprague-Dawley albino rats (5 per sex) by administration of 5000 mg/kg bw by gavage at a dose volume of 4.2 mL/kg bw.

No mortality occurred during the study. Clinical signs noted 24 hours after dosing were faecal staining and/ or soft stool, as well as oral and/ or nasal discharge and hypo activity. There was no effect on body weight gain. The gross necropsy conducted at termination of the study revealed no observable abnormalities.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding oral toxicity.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:	Glyphosate
Identification:	MON 52276
Description:	Amber liquid
Lot/ Batch #:	LLN-9105-3135-F
Purity:	30.57 % glyphosate acid equivalent
Stability of test compound:	Expiry date: May 1992
2. Vehicle and/ or positive control:	None
3. Test animals:	
Species:	Rat albino
Strain:	Sprague-Dawley [CD-Crl:CD (SD)BR]
Source:	[redacted]
Age:	Approx. 9-12 weeks
Sex:	Males and females
Weight at dosing:	Males: 330 - 354 g; females: 253 - 270 g
Acclimation period:	20 days
Diet/ Food:	Purina Laboratory Chow #5001, ad libitum except for approx. 18 h before dosing and 4 hours after dosing
Water:	Tap water, *ad libitum*
Housing:	Individual housing in suspended, wire bottom, stainless steel cages.
Environmental conditions:	Temperature: 19 - 24 °C Humidity: 40 - 70 % Air changes: not reported 12-hour light/ dark cycle

B. STUDY DESIGN

In life dates: 1991-07-29 to 1991-08-12

Animal assignment and treatment:

Five fasted rats per sex received the test material at a dose level of 5000 mg/kg bw by oral gavage (limit test). Observations for mortality were made twice daily. A check for clinical signs of toxicity was made at least three times on the day of dosing and once daily thereafter for 14 days. Individual body weights were recorded just prior to fasting, prior to dosing and on days 7 and 14. On day 14 all surviving animals were sacrificed, subjected to gross necropsy and all abnormalities were recorded.

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II. RESULTS AND DISCUSSION

A. MORTALITY

There were no mortalities during the study.

B. CLINICAL OBSERVATIONS

Faecal staining and/ or soft stool was noted in all animals after dosing on Day 1. A few animals also showed oral and/ or nasal discharge, as well as hypo activity.

Table 7.1-3 Clinical signs observed after acute oral exposure

Clinical sign	Males[1]	Duration	Females[1]	Duration
Dry nasal discharge	2/5	Day 1	1/5	Day 1
Oral discharge	2/5	Day 1	0/5	--
Hypoactivity	1/5	Day 1	0/5	Day 1
Faecal staining	4/5	Day 1	1/5	Day 1
Soft stool	4/5	Day 1	5/5	Day 1

1 number affected/ total number

C. BODY WEIGHT

Body weight gain was unaffected by the administration of the test substance. Individual and mean body weights are depicted in the following table.

Table 7.1-4 Body weights

Animal No.	Body Weights (g)			
	Pre-fast	Post-fast	Day 7	Day 14
8914 M	342	311	377	401
8921 M	330	292	376	423
8883 M	354	324	397	434
8890 M	340	311	387	413
8895 M	346	316	380	421
Mean males ± SD	**342.4 ± 8.76**	**310.8 ± 11.8**	**383.4 ± 8.73**	**418.4 ± 12.3**
8953 F	253	233	280	284
8927 F	262	241	279	300
8928 F	257	236	293	298
8933 F	259	238	270	288
8941 F	270	248	292	306
Mean females ± SD	**260.2 ± 6.38**	**239.2 ± 5.72**	**282.8 ± 9.68**	**295.2 ± 9.01**
Total Mean ± SD	**301.3 ± 43.9**	**275 ± 38.7**	**333.1 ± 53.7**	**356.8 ± 65.7**

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D. NECROPSY

The gross necropsy conducted at termination of the study revealed no observable abnormalities.

III. CONCLUSIONS

The oral LD_{50} of the test material (MON 52276) in rats was greater than 5000 mg/kg bw.

3. Assessment and conclusion

<u>Assessment and conclusion by applicant</u>:
The study is in concordance with the OECD guideline 401 (1987). However, this guideline was deleted in 2001. There are some deviations according to the most updated version of this guideline but none that could jeopardise the results of this study. Therefore, the outcome can be reported as valid. The acute oral LD_{50} is above 5000 mg/kg bw. According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding oral toxicity.

<u>Assessment and conclusion by RMS</u>:

CP 7.1.2 Dermal toxicity

1. Information on the study

Data point:	CP 7.1.2/001
Report author	[redacted]
Report year	1991
Report title	Acute Dermal Toxicity Study In Rats
Report No	6098-91
Document No	[redacted] 91-262
Guidelines followed in study	US EPA FIFRA guideline 81-2 (1984); OECD 402 (1987); EEC directive 84/449/EEC method B.3 (1984); JMAFF
Deviations from current test guideline	None major (the current OECD TG 402, 2017, states the necessity of *in silico* and *in vitro* approaches and weight of evidence evaluations and as last resort prefers the *in vivo* Fixed Dose Method)
Previous evaluation	Yes, accepted in RAR (2015)
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 2a

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2. Full summary of the study according to OECD format

The acute dermal toxicity of the test substance, MON 52276, was evaluated in Sprague-Dawley albino rats (5 per sex) by dermal application of 5000 mg/kg bw for 24 hours.

No mortality occurred during the study. There were no dermal effects or clinical signs of systemic toxicity. Body weight gain was not affected. The gross necropsy conducted at termination of the study revealed no observable abnormalities.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding dermal toxicity.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test material:**

Identification:	MON 52276
Description:	Amber liquid
Lot/ Batch #:	LLN-9105-3135-F
Purity:	30.8 % glyphosate acid equivalent
Stability of test compound:	Expiry date: May 1992 (estimated)

2. **Vehicle and/ or positive control:** None

3. **Test animals:**

Species:	Rat albino
Strain:	Sprague-Dawley [CD-Crl:CD (SD)BR]
Source:	[redacted]
Age:	Approx. 9-12 weeks
Sex:	Males and females
Weight at dosing:	Males: 312 - 360 g; females: 250 - 262 g
Acclimation period:	21 days
Diet/ Food:	Purina Laboratory Chow #5001, *ad libitum*
Water:	Tap water, *ad libitum*
Housing:	Individual housing in suspended, wire bottom, stainless steel cages.
Environmental conditions:	Temperature: 19 - 24 °C Humidity: 40 - 70 % Air changes: not reported 12-hour light/ dark cycle

B. STUDY DESIGN

In life dates: 1991-07-30 to 1991-08-13

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Animal assignment and treatment:

A group of five Sprague-Dawley albino rats per sex received the undiluted test material at a dose level of 5000 mg/kg bw by dermal application to the clipped dorsal skin under an occlusive dressing for 24 hours. The dosing volume was 4.2 mL/kg bw. After 24 hours the dressing was removed and the application area was wiped free of residual test substance. Observations for mortality were made twice daily. A check for clinical signs of toxicity were made at least three times on the day of dosing and once daily thereafter for 14 days. Individual body weights were recorded just prior to clipping (one day before dosing), prior to dosing and on days 7 and 14. On day 14 all surviving animals were sacrificed, subjected to gross necropsy and all abnormalities were recorded.

II. RESULTS AND DISCUSSION

A. MORTALITY

There were no mortalities during the study.

B. CLINICAL OBSERVATIONS

No severe dermal effects were seen throughout the study. Most animals were free of significant signs of systemic toxicity, although evidence of red ocular discharge was seen in two animals and evidence of red urinary staining was seen in an additional animal at 24 hours.

C. BODY WEIGHT

Body weight gain was unaffected by the administration of the test substance. Individual and mean body weights are depicted in the following table.

Table 7.1-5 Body weights

Animal No.	Body Weights (g)			
	Day 1	Pre-dose	Day 7	Day 14
8887 M	312	320	332	345
8891 M	360	369	380	409
8901 M	358	367	397	424
8909 M	356	365	401	434
8907 M	321	330	353	382
Mean males ± SD	**341.4 ± 23.0**	**350.2 ± 23.3**	**372.6 ± 29.5**	**398.8 ± 35.9**
8923 F	257	263	266	291
8930 F	260	264	261	268
8937 F	262	266	279	290
8940 F	258	263	259	268
8946 F	250	253	262	278
Mean females ± SD	**257.4 ± 4.56**	**261.8 ± 5.07**	**265.4 ± 8.02**	**279.0 ± 11.3**
Total Mean ± SD	**299.4 ± 46.9**	**306 ± 49.2**	**319 ± 60.1**	**338.9 ± 67.9**

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D. NECROPSY

The gross necropsy conducted at termination of the study revealed no observable abnormalities.

III. CONCLUSIONS

The dermal LD_{50} of the test material (MON 52276) in rats, under conditions of this study, is greater than 5000 mg/kg bw.

3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 402 (1987). Therefore, the outcome can be reported as valid. The dermal oral LD_{50} is above 5000 mg/kg bw.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding dermal toxicity.

Assessment and conclusion by RMS:

CP 7.1.3 Inhalation toxicity

1. Information on the study

Data point:	CP 7.1.3/001
Report author	[redacted]
Report year	2015
Report title	MON 52276: Acute Inhalation Toxicity in Rats
Report No	40830
Document No	[redacted]0026415
Guidelines followed in study	US EPA OPPTS 870.1300 (1998), OECD 403 (2009)
Deviations from current test guideline	No
Previous evaluation	New study for AIR5
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 1

2. Full summary of the study according to OECD format

The acute inhalation toxicity of the test substance, MON 52276, was evaluated in Sprague-Dawley albino rats (5 per sex) via inhalation after aerosolisation at a concentration of 5.25 mg/L for 4 hours.

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No mortality occurred during the study. Following exposure, all rats exhibited irregular respiration. However, all animals recovered by day 1 and appeared active and healthy for the remainder of the 14-day observation period. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding inhalation toxicity.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:

Identification:	MON 52276
Description:	Amber liquid
Lot/ Batch #:	GLP-1503-23897-F
Composition:	30.3 wt % glyphosate

2. Vehicle and/ or positive control: None

3. Test animals:

Species:	Rat
Strain:	Sprague-Dawley derived
Source:	[redacted]
Age:	Approx. 10-11 weeks
Sex:	Males (5) and females (5)
Weight at dosing:	Males: 336 – 379 g, Females: 219 – 242 g
Acclimation period:	20 days
Diet/ Food:	Harlan Teklad Global 16 % Protein Rodent Diet® #2016, *ad libitum* (except during exposure)
Water:	Filtered tap water, *ad libitum* (except during exposure)
Housing:	Individually housed in suspended, stainless steel mesh cages

4. Environmental conditions:

Temperature:	20-23 °C
Humidity:	46-59 %
Air changes:	13/hour
Photoperiod:	12-hour light/ dark cycle

B. STUDY DESIGN

In life dates: 22 April – 12 May 2015

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Animal assignment and treatment:

On the day of and prior to exposure, the rats were examined for health and weighed. Ten healthy, naive rats (five males and five females; not previously tested) were selected for test. The animals were exposed to the targeted chamber concentration for at least 4 hours. Individual body weights of the animals were recorded prior to test substance exposure (initial) and again on days 1, 3, 7, and 14 (terminal). All animals were observed for mortality during the exposure period. The animals were examined for signs of gross toxicity, and behavioural changes upon removal from the exposure tube and at least once daily thereafter for 14 days. All rats were euthanised via CO_2 inhalation on day 14. Gross necropsies were performed on all animals. Tissues and organs of the thoracic and abdominal cavities were examined.

Table 7.1-6 Nominal chamber concentrations

Exposure Concentration (mg/L)	Total Test Substance used (g)	Total Airflow (Lpm)	Total Time of Exposure (min)	Nominal Concentration (mg/L)
5.25	708.5	36.0	244	80.66

II. RESULTS AND DISCUSSION

A. TEST ATMOSPHERE

The chamber and nominal chamber concentrations were 5.25 mg/L and 80.66 mg/L, respectively. The average mass median aerodynamic diameter was estimated to be 2.16 µm based on graphic analysis of the particle size distribution as measured with a 1 ACFM Andersen Ambient Particle Sizing Sampler with an average geometric standard deviation of 1.96.

Table 7.1-7 Concentration(s) and exposure conditions

Target conc. (mg/L air)		Nominal conc. (mg/L air)	Actual conc. (mg/L air)	MMAD [1] (µm)	GSD [2] (µm)
5.0		80.66	5.25	2.16	1.96

[1] MMAD = Mass Median Aerodynamic Diameter
[2] GSD = Geometric Standard Deviation

B. MORTALITY

There were no mortalities during the study.

C. CLINICAL OBSERVATIONS

Following exposure, all rats exhibited irregular respiration. However, all animals recovered by day 1 and appeared active and healthy for the remainder of the 14-day observation period.

D. BODY WEIGHT

Animals gained weight throughout the 14-day observation period.

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Table 7.1-8 Body weights

Animal No.	Body Weights (g)			
	Day 1	Pre-dose	Day 7	Day 14
3301 M	347	328	352	375
3302 M	379	371	402	430
3303 M	342	332	362	383
3304 M	343	323	351	377
3305 M	336	321	347	370
Mean males ± SD	**349.4 ± 17.0**	**335.0 ± 20.6**	**362.8 ± 22.6**	**387.0 ± 24.5**
3306 F	219	214	226	248
3307 F	242	237	257	266
3308 F	220	214	243	248
3309 F	227	224	241	259
3310 F	221	212	236	244
Mean females ± SD	**225.8 ± 9.58**	**220.2 ± 10.5**	**240.6 ± 11.3**	**253.0 ± 9.17**
Total Mean ± SD	**287.6 ± 66.4**	**277.6 ± 62.4**	**301.7 ± 66.6**	**320.0 ± 72.7**

E. NECROPSY

No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

III. CONCLUSIONS

The acute inhalation LC_{50} of MON 52276 in male and female rats was greater than 5.25 mg/L.

3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 403 (2009). Therefore, the outcome can be reported as valid. The acute inhalation LC_{50} of MON 52276 in rats is greater than 5.25 mg/L.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding inhalation toxicity.

Assessment and conclusion by RMS:

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CP 7.1.4 Skin irritation

1. Information on the study

Data point:	CP 7.1.4/001
Report author	[redacted]
Report year	1991c
Report title	Primary dermal irritation study in rabbits
Report No	6099-91
Document No	[redacted]-91-263
Guidelines followed in study	OECD 404 (1991); Commission Directive 92/69/EEC method B.4 (1984), US EPA FIFRA guideline 81-5 (1984)
Deviations from current test guideline	None major. 6 animals used instead of the maximum recommended of 3 in the latest revision of the guideline. First response scored at 30 minutes instead of 60 minutes.
Previous evaluation	Yes, accepted in RAR (2015)
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 2a

2. Full summary of the study according to OECD format

In a primary dermal irritation study, young adult New Zealand albino rabbits (4 male, 2 females) were dermally exposed to MON 52276. Two sites of clipped, intact skin of the back were exposed to 0.5 mL of the undiluted test substance, for 4 hours under semi-occlusive conditions. The rabbits were observed for 72 hours. Skin irritation was scored using the Draize scheme 0.5, 24, 48 and 72 hours after removal of the test substance.

Very slight to slight erythema was observed in two animals. No oedemas were observed at the application site of any animal at any observation time point. The overall mean for the 24, 48 and 72-hour readings were 0.11 for erythema and 0.0 for oedema.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding skin irritation.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:

Identification:	MON 52276
Description:	Amber liquid
Lot/ Batch #:	LLN-9105-3135-F
Purity:	30.57 % glyphosate acid equivalent
Stability of test compound:	Expiry date: May 1992 (estimated)

2. Vehicle and/ or positive control: None

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3. Test animals:

Species:	Rabbit
Strain:	New Zealand White
Source:	[redacted]
Age:	At least 8 weeks
Sex:	Males (4) and females (2)
Weight at dosing:	Not available
Acclimation period:	49 days
Diet/ Food:	Lab Rabbit Chow HF (Purina #5326)
Water:	Tap water, *ad libitum*
Housing:	Individual housing in suspended, wire bottom, stainless steel cages.
Environmental conditions:	Temperature: 15 - 21 °C Humidity: 40 - 60 % Air changes: not reported 12-hour light/ dark cycle

B. STUDY DESIGN

In life dates: 1991-07-22 to 1991-07-25

Animal assignment and treatment:

The test was conducted using young adult New Zealand albino rabbits (4 male, 2 females). An amount of 0.5 mL of the undiluted test substance was applied to the intact skin on two sites of the clipped back of the rabbits on an approx. 6.25 cm^2 gauze patch. The patch was covered with a semi-occlusive dressing. After 4 hours of exposure the dressing was removed and the skin was cleaned with water.
Skin reactions were assessed approximately 0.5, 24, 48 and 72 hours after removal of the patch. The animals were observed for mortality and clinical signs twice daily.

II. RESULTS AND DISCUSSION

A. MORTALITY

No mortality occurred.

B. CLINICAL OBSERVATIONS

No clinical signs of systemic toxicity were observed during the study.

D. NECROPSY

No necropsy was performed.

E. SKIN OBSERVATIONS

All six animals exhibited very slight to slight erythema with no oedema. Five of the six animals were free of dermal irritation by 24-hours with the remaining animal free of irritation by 72-hours.

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Table 7.1-9 Skin irritation scores

Animal No.			Scores after treatment [1]				Mean scores (24-72 h)	Reversible (day)
			0.5 h	24 h	48 h	72 h		
0259M	Erythema Oedema	Right side	0 0	0 0	0 0	0 0	0 0	NA
		Left side	1 0	0 0	0 0	0 0	0 0	NA
0249M	Erythema Oedema	Right side	1 0	0 0	0 0	0 0	0 0	NA
		Left side	2 0	0 0	0 0	0 0	0 0	NA
0252F	Erythema Oedema	Right side	2 0	1 0	1 0	0 0	0.66 0	3
		Left side	1 0	1 0	1 0	0 0	0.66 0	3
0261M	Erythema Oedema	Right side	1 0	0 0	0 0	0 0	0 0	NA
		Left side	1 0	0 0	0 0	0 0	0 0	NA
0255M	Erythema Oedema	Right side	1 0	0 0	0 0	0 0	0 0	NA
		Left side	1 0	0 0	0 0	0 0	0 0	NA
0238F	Erythema Oedema	Right side	1 0	0 0	0 0	0 0	0 0	NA
		Left side	1 0	0 0	0 0	0 0	0 0	NA

[1] scores in the range of 0 to 4

III. CONCLUSIONS

MON 52276 produced mild, transient dermal irritation. The FIFRA Primary Irritation Index of MON 52276 is 0.3; therefore, this material would be classified as Essentially Non irritating.
According to the OECD Globally Harmonised System (GHS) classification criteria MON 52276 is also not classified for skin irritation.

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3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 404 (1992). Despite some deviations compared to the most updated version of this guideline, none of them could jeopardise the results of this study. Therefore, the outcome can be reported as valid.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding skin irritation.

Assessment and conclusion by RMS:

CP 7.1.5 Eye irritation

1. Information on the study

Data point:	CP 7.1.5/001
Report author	[redacted]
Report year	1992
Report title	Primary eye irritation study in rabbits
Report No	5999-91
Document No	[redacted]-91-60
Guidelines followed in study	OECD 405 (1987), EC Directive 92/69/EEC method B.5 (1987), US EPA FIFRA guideline 81-4 (1984)
Deviations from current test guideline	None major. 6 animals used instead of the maximum recommended of 3 in the latest revision of the guideline. No use of analgesics and anaesthetics
Previous evaluation	Yes, accepted in RAR (2015)
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 2a

2. Full summary of the study according to OECD format

In an eye irritation study, 0.1 mL of the undiluted test substance was instilled into the right conjunctival sac of six young adult New Zealand albino rabbits. Animals were observed for 7 days. Eye irritation was scored 1, 24, 48 and 72 hours and 7 days after test item instillation.

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Application of MON 52276 into the rabbit eye resulted in slight to moderate conjunctival irritation in all animals. Iridial changes were noted in one animal 1 hour after instillation. There were no corneal effects noted. All eye effects were reversible within 7 days after instillation. The overall mean irritation scores (24 to 72 hours) of the six rabbits were as follows:

- for corneal opacity: 0.0
- for iris lesions: 0.0
- for conjunctival redness: 1.1
- for chemosis of the conjunctiva: 0.0

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding eye irritation.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:

Identification:	MON 52276
Description:	Clear, amber liquid
Lot/ Batch #:	LLN-9102-2794-F
Purity:	30.39 % glyphosate acid equivalent
Stability of test compound:	Expiry date: May 1992 (estimated)

2. Vehicle and/ or positive control: None

3. Test animals:

Species:	Rabbit
Strain:	New Zealand White
Source:	[redacted]
Age:	At least 8 weeks
Sex:	Males (3) and females (3)
Weight at dosing:	2.6 - 2.8 kg
Acclimation period:	49 days
Diet/ Food:	Lab Rabbit Chow HF (Purina #5326)
Water:	Tap water, *ad libitum*
Housing:	Individual housing in suspended, wire bottom, stainless steel cages.
Environmental conditions:	Temperature: 15 - 21 °C Humidity: 40 - 60 % Air changes: not reported 12-hour light/ dark cycle

B. STUDY DESIGN

In life dates: 1991-01-14 to 1991-03-11

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Animal assignment and treatment:

The test was conducted using six (3 per sex) young adult New Zealand white rabbits. An amount of 0.1 mL of the undiluted test substance was applied into the conjunctival sac of the right eye of the rabbits. The treated eyes were not rinsed after instillation. The right left remained untreated and served as the reference control.
Eye reactions were assessed according to the EPA scoring system approximately 1, 24, 48 and 72 hours, and 7 days after instillation. Eye examinations using fluorescein were done one day prior to instillation, and at each examination time-point starting with the 24-hour observation until there was no stain retention for two observations. The animals were observed for mortality and clinical signs daily.

II. RESULTS AND DISCUSSION

A. MORTALITY

No mortality occurred.

B. CLINICAL OBSERVATIONS

No clinical signs of systemic toxicity were observed during the study.

C. BODY WEIGHT

All rabbits showed the expected body weight gain.

D. NECROPSY

No necropsy was performed.

E. EYE OBSERVATIONS

Slight to moderate conjunctival irritation (redness, chemosis, discharge) was noted in all rabbits. Slight iridial changes were observed in one animal at the 1-hour reading only. There were no corneal effects noted. Three of the six animals were free of all ocular irritation within 24 to 72 hours with the remaining three animals free of irritation by Day 7.
The group mean irritation scores (24 to 72 hours) were calculated to be 0.0 for corneal opacity, 0.0 for iris lesions, and 1.1 for conjunctival redness, and 0.0 for chemosis of the conjunctiva.

The individual scores for each time point, individual mean and group mean scores (24 to 72 hours) are presented in the following table.

Table 7.1-10 Eye irritation scores

Animal No.		Scores after treatment[1]				Mean scores (24-72 h)	Reversible (day)
		1 h	24 h	48 h	72 h		
9870 F	Corneal opacity	0	0	0	0	0	3
	Iritis	0	0	0	0	0	
	Redness conjunctivae	1	1	1	0	0.66	
	Chemosis conjunctivae	1	0	0	0	0	
	Discharge	2	0	0	0	0	

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Table 7.1-10 Eye irritation scores

Animal No.		Scores after treatment[1]				Mean scores (24-72 h)	Reversible (day)
		1 h	24 h	48 h	72 h		
9871 M	Corneal opacity	0	0	0	0	0	3
	Iritis	0	0	0	0	0	
	Redness conjunctivae	1	1	1	0	0.66	
	Chemosis conjunctivae	1	0	0	0	0	
	Discharge	1	0	0	0	0	
9876 F	Corneal opacity	0	0	0	0	0	NA
	Iritis	0	0	0	0	0	
	Redness conjunctivae	2	0	0	0	0	
	Chemosis conjunctivae	1	0	0	0	0	
	Discharge	1	0	0	0	0	
9879 M	Corneal opacity	0	0	0	0	0	7
	Iritis	+	0	0	0	0	
	Redness conjunctivae	2	2	2	1	1.66	
	Chemosis conjunctivae	1	0	0	0	0	
	Discharge	0	0	0	0	0	
9880 F	Corneal opacity	0	0	0	0	0	7
	Iritis	0	0	0	0	0	
	Redness conjunctivae	1	2	2	1	1.66	
	Chemosis conjunctivae	1	0	0	0	0	
	Discharge	2	0	0	0	0	
9887 M	Corneal opacity	0	0	0	0	0	7
	Iritis	0	0	0	0	0	
	Redness conjunctivae	1	2	2	2	2	
	Chemosis conjunctivae	1	0	0	0	0	
	Discharge	3	0	0	0	0	

1 Scores in the range of 0 to 4 for cornea opacity and chemosis, 0 to 3 for redness of conjunctivae and 0 to 2 for iritis
+ Slight iridial effect

III. CONCLUSIONS

MON 52276 produced mild, transient ocular irritation. This material would be considered to produce eye irritation as defined in the EPA test guidelines (see Report Section VIII). However, MON 52276 did not cause significant ocular lesions and therefore, is not classified according to Annex VI of EEC Council Directive 67/548/EEC (L 180, 91/325, 08 July 1991).

According to EU and GHS classification criteria the test substance MON 52276 is not to be classified for eye irritation.

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3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 405 (1987). Despite some deviations compared to the most updated version of this guideline, none of them could jeopardise the results of this study. Therefore, the outcome can be reported as valid.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding eye irritation.

Assessment and conclusion by RMS:

CP 7.1.6 Skin sensitisation

1. Information on the study

Data point:	CP 7.1.6/001
Report author	[redacted]
Report year	2001
Report title	Skin sensitisation test in guinea pigs (Modified Buehler test: 9 applications)
Report No	[redacted]-2001-153
Document No	Not reported
Guidelines followed in study	OECD 406 (1992); EC Directive 96/54/EEC method B.6 (1996)
Deviations from current test guideline (OECD 406, 1992)	None[1]
Previous evaluation	Yes, accepted in RAR (2015)
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 2a

[1]: The LLNA, or, if not possible, the M&K test is clearly preferred to the Buehler test according to the current state of knowledge and the expected data requirements for plant protection products for authorisation in the EU. According to REACH, the LLNA is the first choice method, too, and a justification for the use of a different test shall be provided. Test Method Guideline B.6 by the European Commission (Reg. (EC) No. 440/2008) or even by its previous version 96/54 also recommends the preferential use of an adjuvant-test (e.g. M&K test) instead of the Buehler test without adjuvant unless a justification is given for using the Buehler method. However, no justification is available. But, since the provided Buehler test is valid this is to be accepted against the background of animal welfare.

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2. Full summary of the study according to OECD format

MON 52276 was tested for its sensitizing effect on the skin of the guinea pig in the modified Buehler test with nine induction treatments. The test-substance concentrations for the main test were selected based on the results of the pre-test. Both induction and challenge applications were performed with undiluted test substance. The study was performed using one control group consisting of 10 animals, and one test group consisting of 20 animals.

None of the animals exhibited a positive skin reaction (defined as scores of ≥ 1) after the challenge treatment.
According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding skin sensitisation.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:

Identification:	Mon 52276
Description:	Yellowish liquid
Lot/ Batch #:	A1C1204104
Purity:	30.88 %
Stability of test compound:	Expiry date: May 2003

2. Vehicle and/ or positive control: Purified water/ mercaptobenzothiazole

3. Test animals:

Species:	Guinea pig
Strain:	Hartley, CRL:(HA)BR, (COBS-VAF)
Source:	[redacted], Saint-Aubin-lés-Elbeuf, France
Age:	1 – 3 months
Sex:	Males and females
Weight at dosing:	males: 366 ± 18 g; females: 348 ± 17 g
Acclimation period:	at least 5 days
Diet/ Food:	Pelleted diet (UAR, France), *ad libitum*
Water:	Filtered drinking water, *ad libitum*
Housing:	Individually in polycarbonate cages with autoclaved sawdust bedding
Environmental conditions:	Temperature: 21 ± 2 °C Humidity: 30 – 70 % Air changes: 12/hour 12 hours light/ dark cycle

B. STUDY DESIGN

In life dates: 2001-06-19 to 2001-08-01

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Animal assignment and treatment:

MON 52276 was tested for its sensitising effect on the skin of the guinea pig using the modified Buehler method with nine induction treatments. Male and female Hartley guinea pigs, young adults were used. The test substance concentrations for the main study were selected based on the results of a preliminary test using test substance concentrations of 100 % and 75 % for both induction and challenge treatments. The main study was performed in 20 test animals and 10 control animals.

In the main study the nine inductions were done on Days 1, 3, 5, 8, 10, 12, 15, 17 and 19 on the same intact flanks of the animals. 24 hours before the applications, the treatment area was clipped. All inductions were performed under occlusive conditions with 4×4 cm test patches soaked with the undiluted test substance for 6 hours each. On Day 29, the challenge applications with undiluted test substance and vehicle were done to the clipped posterior right and left flanks of the animals under the same conditions as for the inductions. The control animals were treated with purified water for the induction treatments.
Skin reactions were assessed 24 and 48 hours after each induction and challenge treatment.
Body weights were determined at the first day of treatment of the main study and at termination. Mortality and clinical signs were recorded daily during the study period.

A positive control (reliability check) with a known sensitiser was performed in June 2001 in the laboratory according to the modified Buehler method. The positive control with mercaptobenzothiazole (20 %) showed that the chosen guinea pig strain was able to detect sensitizing compounds under the laboratory conditions chosen.

Evaluation criteria for classification as a potential skin sensitiser:
At the 24-hour and/ or 48-hour reading, 15 % or more of the test animals exhibit a positive response (scores ≥ 1) in the absence of similar results in the vehicle control group.

II. RESULTS AND DISCUSSION

A. MORTALITY

No deaths occurred.

B. CLINICAL OBSERVATIONS

No signs of systemic toxicity were observed.

C. BODY WEIGHT

The body weight was not affected.

D. NECROPSY

No necropsy was performed.

E. SKIN REACTIONS

After the induction treatments discrete erythema (grade 1) were observed in a few animals. After challenge application, except for dryness of the skin at the 24-hour reading in one animal, no skin reactions were observed (see following table).

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Table 7.1-11 Summary of positive skin responses after challenge exposure

Group	Test substance concentration	Reading time (h)	Number of animals with positive skin responses[1]
Test substance	100 % MON 52276	24	0/20
		48	0/20
Negative control	Purified water	24	0/10
		48	0/10
Positive control[2]	20 % MBT[3]	48	7/10

[1] Number of animals with skin reactions/ total number of animals
[2] Study performed in June 2001
[3] MBT = mercaptobenzothiazole

III. CONCLUSIONS

Under the experimental conditions and according to the modified Buehler method, the test substance MON 52276 does not induce delayed contact hypersensitivity in guinea pigs.

According to the classification criteria laid down in Commission Directive 93/21/EEC, the test substance should not be classified, as sensitizing to the skin.

Based on the EU classification criteria, MON 52276 is not to be classified for skin sensitisation. According to the OECD Globally Harmonised System (GHS) classification criteria MON 52276 is also not classified for skin sensitisation.

3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 406 (1992). Despite the fact that the LLNA, or, if not possible, the M&K test are clearly preferred to the Buehler test, the provided Buehler test is valid and is to be accepted against the background of animal welfare.
The results of this GLP study confirm the results of the previously submitted study evaluated by the rapporteur in 2001, which followed the previous OECD 406 (1987) test guideline.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding skin sensitisation.

Assessment and conclusion by RMS:

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1. Information on the study

Data point:	CP 7.1.6/002
Report author	[redacted]
Report year	1992b
Report title	Closed-patch repeated insult dermal sensitisation study in guinea pigs (Buehler method)
Report No	6100-91
Document No	[redacted]-91-264
Guidelines followed in study	OECD 406 (1987) EC Directive 96/54/EEC method B.6 (1984)
Deviations from current test guideline	The current OECD TG recommends for the induction phase applications on day 0, on day 6-8 and again on day 13-15. For the challenge phase, applications have to be performed on day 27-29. The study does not comply with the updated version of the guideline. A minimum of 20 animals should be used in the treatment group, 10 animals were used in this study.
Previous evaluation	No, not accepted in RAR (2015)
GLP/ Officially recognised testing facilities	No
Acceptability/ Reliability:	Supportive
Category study in AIR 5 dossier (L docs)	Category 3a

2. Full summary of the study according to OECD format

This study was conducted to assess the potential of MON 52276 (Lot No. LLN-9105-31354F) to produce hypersensitivity subsequent to repeated dermal exposure. This was accomplished by repetitive dermal application of the test chemical for a defined period of time (induction phase), followed by a rest period and challenge of the animals with a non-irritating dose to test for hypersensitivity. This method is a modification of that originally described by Buehler.

A range-finding irritation screen was conducted to determine appropriate induction and challenge dose levels. For the induction phase, 0.3 mL of 100 % MON 52276 was administered dermally to the shaved backs of 5 males and 5 female Hartley guinea pigs. Induction consisted of 3 applications, once per week for 3 weeks, each of 6 hours duration. A 14-day rest period followed the third induction dose, after which, each animal was challenged on a previously untreated area of skin using the same exposure technique. The challenge dose administered was the same as for induction. An additional group of naïve animals (5/sex) received the identical challenge dose and served as irritation controls.

Body weights were recorded pre-test and at study termination. Dermal irritation was scored at 24 and 45 hours after each induction and challenge application.
Although no positive control group was included in this study, [redacted]. frequently includes animals treated with dinitrochlorobenzene (DNCB), a known sensitizer, in sensitisation studies. A file of historical control data is maintained, demonstrating the validity of this protocol for detecting known sensitisers. These data are appended to the report.

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All animals survived and exhibited normal weight gain over the course of the study. No irritation responses were seen following administration of the induction doses. Following administration of the challenge dose, no dermal irritation responses were observed in any of the ten test animals or ten naive control animals.

Under the conditions of this study, MON 52276 exhibited no potential to produce dermal sensitisation in guinea pigs.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:

Identification:	Mon 52276
Description:	Amber liquid
Lot/ Batch #:	LLN-9105-3135-F
Purity:	~31 %
Stability of test compound:	Expiry date: May 1992

2. Vehicle and/ or positive control: Purified water

3. Test animals:

Species:	Guinea pig
Strain:	Hartley, CRL:(HA)BR
Source:	[redacted], Denver, Pennsylvania
Age:	2-3 weeks at receipt, 4-5 weeks at study initiation
Sex:	Males and females
Weight at dosing:	males: 313-362 g; females: 305-370 g
Acclimation period:	8 days for the range-finding, 15 days for the sensitisation study
Diet/ Food:	Agway Prolab Guinea Pig Diet, *ad libitum*
Water:	Automatic watering system, *ad libitum*
Housing:	Individually in stainless steel cages with wire mesh bottoms
Environmental conditions:	Temperature: 19 - 24 °C Humidity: 30 - 91 % Air changes: NA 12 hours light/ dark cycle

[redacted] has a historical data base of data for animals from the same source as those used in the study demonstrating susceptibility to dermal sensitisation with a known sensitiser (dinitrochlorobenzene) when tested using procedures described in this report.

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B. STUDY DESIGN

Animal assignment and treatment:

Prior to initiation of the study, a range-finding study was performed in order to select a slightly irritating concentration for topical induction and a non-irritating concentration for the challenge application. Six animals were treated topically with undiluted test material (100 %) and with concentrations of 50 %, 25 % and 10 % v/v of the test material in distilled water (one concentration/ site).
Based on results of the range-finding study, the undiluted material was found to be non-irritating and was, therefore, administered at a 100 % concentration for both induction and challenge.

In the main study, the test material was applied to saturation (approximately 0.3 mL) beneath a Hilltop Chamber® placed directly on the test site. The test site was on the right side of the midline, as close to the midline as possible. The chamber was covered by overlapping, impermeable plastic. This was firmly secured by an elastic adhesive bandage which was wound around the torso of the animal. The chamber was left in place for six hours after which it was removed and the skin was wiped free of any excess material with gauze and water. This was performed once a week, for three weeks, for a total of three exposures.

Fourteen days after the last induction exposure, the challenge treatment was administered. The test material was administered in the same manner as in the induction phase, but at a second site, on the left side of the midline. After six hours of exposure, the chambers were removed and the skin wiped free of any excess material.
In order to differentiate dermal reactions produced by irritation from those produced by sensitisation, ten previously untreated animals (five/ sex) were subjected to the same challenge procedures as the animals which received the three induction exposures.

Table 7.1-12 Experimental design

Group	Test material	Number of animals	Concentration (%)	
			Induction	Challenge
I	MON 52276	10 (5/ sex)	100	100
II	MON 52276 (irritation control)	10 (5/ sex)	NR[1]	100

[1] The irritation control group was treated at challenge only

Dermal evaluations were made approximately 24 and 48 hours after the induction exposure to confirm that an appropriate concentration of the test material had been selected and to evaluate response for possible preliminary indication of sensitisation. For challenge, dermal evaluations were made 24 and 48 hours after dosing.

II. RESULTS AND DISCUSSION

A. MORTALITY

All animals survived throughout the study.

B. CLINICAL OBSERVATIONS

No signs of systemic toxicity were observed.

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C. BODY WEIGHT

All animals gained weight by study termination

D. NECROPSY

No necropsy was performed.

E. SKIN REACTIONS

No dermal irritation was seen during induction exposures. Animals challenged with MON 52276 (Group I) exhibited no dermal response at challenge to a non-irritating concentration, as confirmed by a lack of dermal response in irritation control animals (Group II). The Incidence Index of sensitisation to the test material was 0 %. The Severity Indices at 24 and 48 hours were 0 for both the test material-treated animals and for the irritation controls.

Table 7.1-13 Summary of positive skin responses after challenge exposure

Group	Test substance concentration	Reading time (h)	Number of animals with positive skin responses[1]
Test substance	100 % MON 52276	24	0/10
		48	0/10
Negative control	Purified water	24	0/10
		48	0/10

[1] Number of animals with skin reactions/ total number of animals

III. CONCLUSIONS

Under the conditions of this study, MON 52276 exhibited no potential to produce dermal sensitisation in guinea pigs.

3. Assessment and conclusion

Assessment and conclusion by applicant:

This study was performed following the previous OECD 406 (1987) test guideline. However, due to major deviations with the current guideline, the results cannot be interpreted and the study is not acceptable. Therefore, another skin sensitisation study ([redacted], 2001) was performed.

Assessment and conclusion by RMS:

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CP 7.1.7 Supplementary studies on the plant protection product

1. Information on the study

Data point:	CP 7.1.7/001
Report author	[redacted]
Report year	2016
Report title	MON 52276: Bacterial Reverse Mutation Assay
Report No	AE60YE-503-BTL
Document No	MSL0027853
Guidelines followed in study	OECD 471 (1997)
Deviations from current test guideline	The concentration, homogeneity, and stability of the test substance in the vehicle were not analyzed. However, it is believed that the test substance was tested to the maximum appropriate concentration based on the laboratory records of formulation preparation (weigh tapes, etc.) and the preparation of test substance formulations immediately before usage. Therefore, lack of stability, homogeneity and concentration verification had no adverse impact on the integrity of the data or the validity of the conclusion that the test substance was negative in this study.
Previous evaluation	New study for AIR5
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Yes, valid study
Category study in AIR 5 dossier (L docs)	Category 1

2. Full summary

The test substance, MON 52276, was tested to evaluate its mutagenic potential by measuring its ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* strain WP2 *uvr*A in the presence and absence of an exogenous metabolic activation system. Water was used as the vehicle.

In the initial toxicity-mutation assay, the dose levels tested were 1.50, 5.00, 15.0, 50.0, 150, 500, 1500 and 5000 µg per plate. Neither precipitate nor toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation. Based upon these results, the maximum dose tested in the confirmatory mutagenicity assay was 5000 µg per plate.

In the confirmatory mutagenicity assay, the dose levels tested were 15.0, 50.0, 150, 500, 1500 and 5000 µg per plate. Neither precipitate nor background lawn toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation.

These results indicate MON 52276 was negative for the ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* strain WP2 *uvr*A in the presence and absence of an exogenous metabolic activation system.

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I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Material:** MON 52276

Description:	Yellow-orange liquid
Lot/ Batch#:	11427995
Purity:	30.3 wt % glyphosate acid
Expiration Date:	08 February 2018

2. **Control Materials:**

Vehicle:	Deionised water
Positive:	
non-activation:	2-nitrofluorene: 1.0 µg/plate TA98 sodium azide: 1.0 µg/plate TA100, TA1535 9-aminoacridine: 75 µg/plate TA1537 methyl methanesulfonate: 1,000 µg/plate WP2 *uvr*A
activation:	2-aminoanthracene: 1.0 µg/plate TA98, TA1535; 2.0 µg/plate TA100, TA1537; 15 µg/plate WP2 *uvr*A

3. Activation

The S9 preparations were from livers of Aroclor 1254-induced rats [redacted]). The S9 mix was composed of water, phosphate buffer, glucose 6-phosphate, β-nicotinamide-adenine dinucleotide phosphate, potassium chloride/ magnesium chloride buffer, and S9 homogenate.

4. Test Concentrations:

a. Initial toxicity-mutation assay:

The initial toxicity-mutation assay was used to establish the dose-range for the confirmatory mutagenicity assay and to provide a preliminary mutagenicity evaluation. TA98, TA100, TA1535, TA1537 and WP2 *uvr*A were exposed to the vehicle alone, positive controls and eight dose levels of the test substance ranging from 1.5 to 5000 µg/plate, in duplicate, in the presence and absence of Aroclor-induced rat liver S9.

b. Confirmatory mutagenicity assay:

The confirmatory mutagenicity assay was used to evaluate and confirm the mutagenic potential of the test substance. TA98, TA100, TA1535, TA1537 and WP2 *uvr*A were exposed to the vehicle alone, positive controls and six dose levels of the test substance ranging from 15 to 5000 µg/plate, in triplicate, in the presence and absence of Aroclor-induced rat liver S9.

B. STUDY DESIGN

1. In-life dates: 17 June 2016 to 05 July 2016

2. Plate incorporation method

One-half (0.5) milliliter of S9 or Sham mix, 100 µL of tester strain (cells seeded) and 100 µL of vehicle or test substance dilution were added to 2.0 mL of molten selective top agar at 45±2 °C. When plating the positive controls, the test substance aliquot was replaced by a 50.0 µL aliquot of appropriate positive control. After vortexing, the mixture was overlaid onto the surface of 25 mL of minimal bottom agar. After

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the overlay had solidified, the plates were inverted and incubated for 48 to 72 hours at 37±2°C. The condition of the bacterial background lawn was evaluated for evidence of test substance toxicity by using a dissecting microscope. Precipitate was evaluated after the incubation period by visual examination without magnification. Toxicity and degree of precipitation were scored relative to the vehicle control plate.

3. Statistics

None.

4. Evaluation Criteria

For the test substance to be evaluated positive, it must cause a dose-related increase in the mean revertants per plate of at least one tester strain over a minimum of two increasing concentrations of test substance as specified:
strains TA1535 and TA1537: data sets were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than 3.0-times the mean vehicle control value; strains TA98, TA100 and WP2 *uvr*A: data sets were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than 2.0-times the mean vehicle control value.

An equivocal response is a biologically relevant increase in a revertant count that partially meets the criteria for evaluation as positive. This could be a dose-responsive increase that does not achieve the respective threshold cited above or a non-dose responsive increase that is equal to or greater than the respective threshold cited. A response was evaluated as negative if it was neither positive nor equivocal.

II. RESULTS AND DISCUSSION

A. Initial toxicity-mutation assay

Neither precipitate nor toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation.

B. Confirmatory mutagenicity assay

Neither precipitate nor background lawn toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation.

Results are presented in the table below:

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Table 7.1-14 Results of the mutagenicity assays

MON 52276 [µg/plate]	Strain									
	TA 98		TA 100		TA 1535		TA 1537		WP2uvrA	
S9:	-	+	-	+	-	+	-	+	-	+
acceptable range of historical control (95 % CL)	6-26	9-37	66-114	68-128	3-23	3-23	1-13	3-15	9-41	12-44
Initial toxicity – mutation assay										
Negative controls	11	19	103	92	15	21	6	12	22	28
1.50	11	23	86	82	15	20	6	10	16	36
5.00	14	22	92	84	11	11	7	11	22	25
15.0	10	17	94	77	17	18	8	11	2	18
50.0	13	15	102	85	13	16	8	15	27	29
150	12	16	110	104	11	14	6	9	21	31
500	9	15	91	92	13	21	7	13	21	28
1000	13	16	100	98	16	15	6	12	26	28
5000	7	10	115	109	15	15	6	11	26	34
Positive controls [µg/plate]										
2-aminoanthracene: 1.0		249				126				
2.0				612				46		
15										306
2-nitrofluorene: 1.0	141									
sodium azide: 1.0			640		593					
9-aminoacridine: 75							135			
methyl methanesulfonate 1000									410	
Confirmatory mutagenicity assay										
Negative controls	10	21	104	100	14	12	8	7	24	25
15	10	21	104	98	13	16	7	5	31	29
50	9	23	98	101	18	13	10	7	22	20
150	9	32	87	95	12	18	7	8	20	36
500	10	19	101	84	17	10	7	7	18	26
1000	8	21	59	88	15	10	7	5	18	24
5000	8	5	77	78	11	13	5	5	17	23
Positive controls [µg/plate]										
2-aminoanthracene: 1.0		129				63				
2.0				447				53		
15										356
2-nitrofluorene: 1.0	306									
sodium azide: 1.0			663		507					
9-aminoacridine: 75							122			
methyl methanesulfonate 1000									392	

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Historical negative and positive control values are presented in the table below:

Historical Negative and Positive Control Values
2015
Revertants per plate

Strain	Control	Activation									
		None					Rat Liver				
		Mean	SD	Min	Max	95% CL	Mean	SD	Min	Max	95% CL
TA98 (2015)	Neg	16	5	6	43	6-26	23	7	5	53	9-37
	Pos	190	191	42	2468		329	176	91	1786	
TA100 (2015)	Neg	90	12	62	233	66-114	98	15	63	157	68-128
	Pos	697	172	239	1767		671	284	138	2692	
TA1535 (2015)	Neg	13	5	2	35	3-23	13	5	3	33	3-23
	Pos	624	196	50	2509		137	110	24	1060	
TA1537 (2015)	Neg	7	3	1	20	1-13	9	3	2	23	3-15
	Pos	392	292	24	2887		73	53	19	574	
WP2 *uvr*A (2015)	Neg	25	8	7	73	9-41	28	8	10	96	12-44
	Pos	336	112	89	1026		352	117	78	1409	

SD=standard deviation; Min=minimum value; Max=maximum value; 95% CL = Mean ±2 SD (but not less than zero); Neg=negative control (including but not limited to deionized water, dimethyl sulfoxide, ethanol and acetone); Pos=positive control

III. CONCLUSIONS

Based on the results of this study, MON 52276 is considered to be negative (not mutagenic) in the Bacterial Reverse Gene Mutation Assay.

3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 471 (1997). Despite some deviations, the test was considered acceptable.
MON 52276 is considered to be negative (not mutagenic) with and without metabolic activation in this gene mutation in bacteria.

According to CLP Regulation (EC) 1272/2008, MON 52276 (Glyphosate 360 g/L SC) does not require classification regarding genotoxicity.

Assessment and conclusion by RMS:

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1. Information on the study

Data point:	CP 7.1.7/002
Report author	[redacted]
Report year	2016
Report title	*In Vitro* Mammalian Cell Micronucleus Assay in Human Peripheral Blood Lymphocytes (HPBL)
Report No	AE60YE.348.BTL
Document No	MSL0027858
Guidelines followed in study	OECD 487 (2014)
Deviations from current test guideline	The concentration, homogeneity, and stability of the test substance in the vehicle were not analyzed. However, it is believed that the test substance was tested to the maximum appropriate concentration based on the laboratory records of formulation preparation (weigh tapes, etc.) and the preparation of test substance formulations immediately before usage. Therefore, lack of stability, homogeneity and concentration verification had no adverse impact on the integrity of the data or the validity of the conclusion that the test substance was negative in this study.
Previous evaluation	New study for AIR5
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Supportive
Category study in AIR 5 dossier (L docs)	Category 1

2. Full summary

The test substance, MON 52276, was tested to evaluate the potential to induce micronuclei in human peripheral blood lymphocytes (HPBL) in both the absence and presence of an exogenous metabolic activation system. Water was used as the vehicle.

In the preliminary toxicity assay, the doses tested ranged from 0.2 to 2000 µg/mL, which was the limit dose for this assay. Cytotoxicity [defined as 55 ± 5 % cytokinesis-blocked proliferation index (CBPI) relative to the vehicle control] was not observed at any dose the non-activated and S9-activated 4-hour treatment conditions. Cytotoxicity was observed at 2000 µg/mL in the non-activated 24-hour treatment condition. Based upon these results, the doses chosen for the micronucleus assay ranged from 2 to 2000 µg/mL for the non-activated 4-hour exposure group; from 6 to 2000 µg/mL for the S9-activated 4-hour and the non-activated 24-hour exposure group.

In the micronucleus assay, cytotoxicity was not observed at any dose of the non-activated and S9-activated 4-hour treatment conditions. Cytotoxicity was observed at 2000 µg/mL in the non-activated 24-hour treatment condition. The doses selected for microscopic evaluation were 200, 600, and 2000 µg/mL for the non-activated and S9-activated 4-hour exposure groups; and 200, 1000, and 2000 µg/mL for the non-activated 24-hour exposure group.

No significant or dose-dependent increases in micronuclei induction were observed in treatment groups with or without S9 ($p > 0.05$; Fisher's Exact and Cochran-Armitage tests).

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Based on above findings MON 52276 was considered negative for the induction of micronuclei in the presence and absence of the exogenous metabolic activation system.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Material:** MON 52276
   - Description: Yellow-orange liquid
   - Lot/ Batch#: 11427995
   - Purity: 30.3 wt % glyphosate acid
   - Expiration Date: 08 February 2018

2. **Control Materials:**
   - Vehicle control: Water
   - Positive control: Cyclophosphamide (2.5, 5, and 7.5 µg/mL)
     Vinblastine (5, 7.5, and 10 ng/mL)
3. **Metabolic activation system:** Rat liver S9 mix
4. **Test organisms:** Human peripheral blood lymphocytes were obtained from a healthy non-smoking individual (32 year old male)

B. STUDY DESIGN

1. **In-life dates:** 27 June 2016 to 30 July 2016

2. Test concentrations

a. Preliminary Toxicity Test

0.2, 0.6, 2, 6, 20, 60, 200, 600, and 2000 µg/mL for non-activated, 4 hour treatment, 24 hour harvest; non-activated, 24 hour treatment, 24 hour harvest; S9-activated, 4 hour treatment, 24 hour harvest

b. Micronucleus Assay

2, 60, 200, 600, and 2000 µg/mL for the non-activated, 4 hour treatment, 24 hour harvest; 6, 60, 200, 600, and 2000 µg/mL for the S9-activated, 4 hour treatment, 24 hour harvest; 6, 200, 600, 1000, 1200, 1400, 1600, 1800, and 2000 µg/mL for non-activated, 24 hour treatment, 24 hour harvest

c. Micronucleus Evaluation

200, 600, and 2000 µg/mL for non-activated, 4 hour treatment, 24 hour harvest and S9-activated, 4 hour treatment, 24 hour harvest; 200, 1000, and 2000 for non-activated, 24 hour treatment, 24 hour harvest

3. Collection of Cells

In non-activated 24 hr treatment, cells were collected after being exposed to cytochalasin B (cyto B) for 24 hours (± 30 minutes), 1.5 to 2 normal cell cycles, to ensure identification and selective analysis of micronucleus frequency in cells that have completed one mitosis evidenced by binucleated cells. The cyto B exposure time for the 4 hour treatment in the non-activated and the S9-activated studies was 20 hours (± 30 minutes). Cell suspension slides were prepared and coded for scoring.

4. Cell Cycle Kinetics Scoring

For the preliminary toxicity test, at least 500 cells were evaluated to determine the cytokinesis-blocked proliferation index (CBPI) at each dose level and the control. For the micronucleus assay, at least 1,000 cells (500 cells per culture were evaluated to determine the CBPI at each dose level and the control.

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5. Micronucleus Scoring

A minimum of 2000 binucleated cells from each concentration (1000 binucleated cells from each culture) were examined and scored for the presence of micronuclei.

6. Statistics

Statistical analysis was performed using the Fisher's exact test ($p \leq 0.05$) for a pairwise comparison of the percentage of micronucleated cells in each treatment group with that of the vehicle control. The Cochran-Armitage trend test was used to assess dose-responsiveness.

7. Evaluation Criteria

The test substance was considered to have induced a positive response if: at least one of the test concentrations exhibited a statistically significant increase when compared with the concurrent negative control ($p \leq 0.05$), and the increase was concentration-related ($p \leq 0.05$), and results were outside the 95 % control limit of the historical negative control data. The test substance was considered to have induced a clear negative response if none of the criteria for a positive response were met.

II. RESULTS AND DISCUSSION

In the preliminary toxicity test, cytotoxicity [defined as 55 ± 5 % cytokinesis-blocked proliferation index (CBPI) relative to the vehicle control] was not observed at any dose the non-activated and S9-activated 4-hour treatment conditions. Cytotoxicity was observed at 2000 µg/mL in the non-activated 24-hour treatment condition. The test substance was soluble in the treatment medium at all doses tested at the beginning and conclusion of the treatment period.

In the micronucleus assays, the test substance was soluble in the treatment medium at all doses tested at the beginning and conclusion of the treatment period. Cytotoxicity was not observed at any dose the non-activated and S9-activated 4-hour treatment conditions; cytotoxicity was observed at 2000 µg/mL in the non-activated 24-hour treatment condition. No significant or dose-dependent increases in micronuclei induction were observed in treatment groups with or without S9.

Results are presented in the table below:

Table 7.1-15 Results of the micronucleus assay

Concentration (µg/mL)	CBPI	Cytotoxicity	Micronucleated binucleated cells (%)	95 % Control Limits	Range [min-max]
4h treatment without S9					
Water	1.725	-	0.4	0.00-0.82	0.05-1.43
MON 52276, 200	1.679	6 %	0.3		
MON 52276, 600	1.613	15 %	0.3		
MON 52276, 2000	1.616	15 %	0.4		
4h treatment with S9					
Water	1.553	-	0.3	0.00-0.78	0.10-1.50
MON 52276, 200	1.621	-12 %	0.4		
MON 52276, 600	1.615	-11 %	0.4		
MON 52276, 2000	1.545	1 %	0.3		
CP, 5	1.301	46 %	1.4**	0.50-2.51	0.40-3.30
24h treatment without S9					
Water	1.814	-	0.4	0.00-1.01	0.10-2.00
MON 52276, 200	1.805	1 %	0.4		

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Table 7.1-15 Results of the micronucleus assay

Concentration (µg/mL)	CBPI	Cytotoxicity	Micronucleated binucleated cells (%)	95 % Control Limits	Range [min-max]
MON 52276, 1000	1.605	26 %	0.3		
MON 52276, 2000	1.394	52 %	0.6		
VB, 10	1.141	83 %	1.6**	0.04-3.48	0.50-5.70

CBPI: Cytokinesis-blocked proliferation index
CP: Cyclophosphamide
VB: Vinblastine

Historical negative and positive control values are presented below:

HISTORICAL CONTROL VALUES
MICRONUCLEUS INDUCTION
2013-2015

NON-ACTIVATED TEST SYSTEM

Historical Values	Micronucleated Binucleated Cells (%)			
	Negative Control[1]		Positive Controls	
	4-hour	24-hour	4-hour [2]	24-hour [3]
Mean	0.36	0.39	3.77	1.76
Standard Deviation	±0.23	±0.31	±1.66	±0.86
95% Control Limits	0.00-0.82	0.00-1.01	0.46-7.08	0.04-3.48
Range [5]	0.05-1.43	0.10-2.00	1.00-10.10	0.50-5.70

S9-ACTIVATED TEST SYSTEM

Historical Values	Micronucleated Binucleated Cells (%)	
	Negative Control[1]	Positive Control [4]
Mean	0.33	1.51
Standard Deviation	±0.23	±0.50
95% Control Limits	0.00-0.78	0.50-2.51
Range [5]	0.10-1.50	0.40-3.30

1. Solvents include water, saline, DMSO, ethanol, acetone, and other non-standard and Sponsor supplied vehicles.
2. Positive control for non-activated 4 hour studies, Mitomycin C (MMC).
3. Positive control for non-activated 24 hour studies, Vinblastine (VB).
4. Positive control for S9-activated studies, Cyclophosphamide (CP).
5. Range from minimum to maximum.

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III. CONCLUSIONS

Based on these results, MON 52276 was considered to be negative for the induction of micronuclei in the non-activated and S9-activated test systems in the *in vitro* mammalian micronucleus test using human peripheral blood lymphocytes.

3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 487 (2014). Under the experimental conditions reported, the test item did not induce micronuclei as determined by the *in vitro* micronucleus test in human lymphocytes. Therefore, MON 52276 is considered to be non-mutagenic in this *in vitro* micronucleus test when tested up to cytotoxic concentrations.
However, considering the deviations identified in the study, the study is considered supportive only.

Assessment and conclusion by RMS:

1. Information on the study

Data point:	CP 7.1.7/003
Report author	[redacted]
Report year	2020
Report title	MON 52276: Micronucleus Test in Human Lymphocytes *in vitro*
Report No	WC22PQ
Document No	CV-2019-0628
Guidelines followed in study	OECD 487 (2016)
Deviations from current test guideline	None
Previous evaluation	New study for AIR5
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 1

2. Full summary

The test substance, MON 52276, was tested to evaluate the potential to induce micronuclei in human peripheral blood lymphocytes (HPBL) in both the absence and presence of an exogenous metabolic activation system. Minimal Essential Medium was used as the vehicle.

The doses tested in the Preliminary Toxicity Test ranged from 19.53 to 5000 µg/mL. No precipitate of the test item was observed in the parallel blood-free cultures at the end of the exposure in the 4-hour exposure groups or in the 24-hour continuous exposure group. Microscopic assessment of the slides prepared from the exposed cultures showed that binucleate cells were present at up to 5000 µg/mL in all three exposure

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groups. The test item induced some evidence of toxicity in the 4-hour exposure group in the absence of S9 and in the 24-hour exposure group. There was no marked toxicity demonstrated in the 4-hour exposure group in the presence of S9. The maximum dose level selected for the Main Experiment was the maximum recommended dose level and was 5000 µg/mL for all three exposure groups.

The dose levels used in the Main Experiment were selected using data from the Preliminary Toxicity Test where the results indicated that the maximum concentration should be limited by toxicity. The doses selected for the Main Experiment ranged from 321.5 to 5000 µg/mL for the 4-hour treatment without S9, 4-hour treatment in the presence of S9, and 24-hour treatment in the absence of S9.

Duplicate cultures of human lymphocytes, treated with the test item, were evaluated for micronuclei in binucleate cells at up to four dose levels, together with vehicle (quadruplicate cultures) and positive controls (duplicate cultures). Three exposure conditions in a single experiment were used for the study using a 4-hour exposure in the presence and absence of a standard metabolizing system (S9) at a 2 % final concentration and a 24-hour exposure in the absence of metabolic activation. At the end of the exposure period, the cell cultures were washed and then incubated for a further 24 hours in the presence of Cytochalasin B.

The test item demonstrated some modest toxicity in the 4-hour exposure in the absence of S9 and achieved near optimum toxicity at the maximum recommended dose level in the 24-hour exposure. There was no marked toxicity demonstrated in the 4-hour exposure group in the presence of S9 up to the maximum recommended dose level.

The test item did not induce any statistically significant increases in the frequency of binucleate cells containing micronuclei in the 4-hour exposure group in the presence of S9 or in the 24-hour continuous exposure group where the maximum dose was the maximum recommended dose level.

The 4-hour group in the absence of S9 included a dose level (1250 µg/mL) which induced a small but statistically significant increase in binucleate cells containing micronuclei. However, since this increase was well within the laboratory historical control range (within 95 % control limits) for a vehicle and was not part of a dose related response it was considered to be of no toxicological significance.

The dose formulation analysis performed for the Main Experiment demonstrated that the test item formulations were accurate and within acceptable limits.

The test item, MON 52276 was considered to be non-clastogenic and non-aneugenic to human lymphocytes *in vitro*.

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I. MATERIALS AND METHODS

A. MATERIALS

5. **Test Material:** MON 52276

Description:	Yellow liquid
Lot/ Batch#:	AZE200810A
Purity:	30.8 % w/w glyphosate acid (41.5% w/w isopropylamine glyphosate); tested as received, with no correction for purity
Expiration Date:	2023-05-20

6. **Control Materials:**

Vehicle control:	Minimal Essential Medium (MEM) (Batch No. 2091547)
Positive control:	Mitomycin C (MMC) (Batch No. SLBR6518V): 0.2 µg/mL for 4-hour/-S9 exposure Demecolcine (DC) (Batch No. BCBV3422): 0.075 µg/mL for 24-hour/-S9 exposure Cyclophosphamide (CP) (Batch No. A0389648): 8 µg/mL for 4-hour/+S9 exposure

7. **Metabolic activation system:** Rat liver S9 mix
8. **Test organisms:** Human peripheral blood lymphocytes were obtained from healthy non-smoking individuals: 25 year old female for Preliminary Toxicity Test and 35 year old female for Main Experiment

Demecolcine (DC) is not one of the suggested positive control substances listed in the OECD 487 guideline but the substances are recommendations only, and DC is a derivative of Colchicine, one of the recommended substances. There is sufficient laboratory historical control data to demonstrate its effectiveness and suitability as an aneugen.

B. METHODS

1. In-life dates: 2020-01-31 to 2020-03-25

2. Test concentrations

a. Preliminary Toxicity Test
0, 19.53, 39.06, 78.13, 156.25, 312.5, 625, 1250, 2500 and 5000 µL/mL for 4-hour treatment without S9, 4-hour treatment with S9, and 24-hour treatment without S9.

b. Micronucleus Assay
0, 312.5, 625, 1250, 2500, 3750, 5000 µg/mL for the 4-hour treatment without S9, 4-hour treatment with S9, and 24-hour treatment without S9.

c. Micronucleus Evaluation
0, 1250, 2500, 3750, 5000 µg/mL for the 4-hour treatment without S9, 4-hour treatment with S9, and the 24-hour treatment without S9.

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3. Collection and Treatment of Cells

For each experiment, sufficient whole blood was drawn from the peripheral circulation of a non smoking volunteer (18-35) who had been previously screened for suitability. The volunteer had not knowingly been exposed to high levels of radiation or hazardous chemicals and had not knowingly recently suffered from a viral infection.

Cells (whole blood cultures) were grown in Eagle's minimal essential medium with HEPES buffer (MEM), supplemented “in-house” with L-glutamine, penicillin/streptomycin, amphotericin B and 10 % fetal bovine serum (FBS), at approximately 37 ºC with 5 % CO_2 in humidified air. The lymphocytes of fresh heparinised whole blood were stimulated to divide by the addition of phytohaemagglutinin (PHA).

The Preliminary Toxicity Test was performed using the exposure conditions as described for the Main Experiment but using single cultures for the test item dose levels and duplicate cultures for the vehicle controls, whereas the Main Experiment used duplicate cultures for the test item and quadruplicate cultures for the vehicle controls. Parallel flasks, containing culture medium without whole blood, were established for the three exposure conditions so that test item precipitate observations could be made. Precipitate observations were recorded at the beginning and end of the exposure periods.

a. 4-Hour Exposure With Metabolic Activation (S9)

After approximately 48 hours incubation at approximately 37 ºC, 5 % CO_2 in humidified air, the cultures were transferred to tubes and centrifuged. Approximately 9 mL of the culture medium was removed, reserved, and replaced with the required volume of MEM (including serum) and 1.0 mL of the appropriate solution of vehicle control or test item was added to each culture. For the positive control, 0.1 mL of the appropriate solution was added to the cultures. 1.0 mL of 20 % S9-mix (i.e. 2 % final concentration of S9 in standard co factors) was added to the cultures of the Preliminary Toxicity Test and the Main Experiment. All cultures were then returned to the incubator. The nominal total volume of each culture was 10 mL.

After 4 hours at approximately 37 ºC, the cultures were centrifuged, the treatment medium removed by suction and replaced with an 8 mL wash of MEM culture medium. After a further centrifugation the wash medium was removed by suction and replaced with the reserved original culture medium, supplemented with Cytochalasin B at a final concentration of 4.5 µg/mL, and then incubated for a further 24 hours.

b. 4-Hour Exposure Without Metabolic Activation (S9)

After approximately 48 hours incubation at approximately 37 ºC with 5 % CO_2 in humidified air, the cultures were decanted into tubes and centrifuged. Approximately 9 mL of the culture medium was removed and reserved. The cells were then resuspended in the required volume of fresh MEM (including serum) and dosed with 1.0 mL of the appropriate vehicle control, test item solution or 0.1 mL of positive control solution. The nominal total volume for each culture was 10 mL.

After 4 hours at approximately 37 ºC, the cultures were centrifuged, the treatment medium was removed by suction and replaced with an 8 mL wash of MEM culture medium. After a further centrifugation the wash medium was removed by suction and replaced with the reserved original culture medium, supplemented with Cytochalasin B, at a final concentration of 4.5 µg/mL, and then incubated for a further 24 hours.

c. 24-Hour Exposure Without Metabolic Activation (S9)

The exposure was continuous for 24 hours in the absence of metabolic activation. Therefore, when the cultures were established the culture volume was a nominal 9 mL. After approximately 48 hours incubation, the cultures were removed from the incubator and dosed with 1.0 mL of vehicle control, test item dose solution or 0.1 mL of positive control solution. The nominal total volume of each culture was 10 mL. The cultures were then incubated for 24 hours, the tubes and the cells washed in MEM before resuspension in fresh MEM with serum. At this point Cytochalasin B was added at a final concentration of 4.5 µg/mL, and then the cells were incubated for a further 24 hours.

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The extended exposure detailed above does not follow the suggested cell treatment schedule in the Guideline. This is because it avoids any potential interaction between Cytochalasin B and the test item during exposure to the cells and any effect this may have on the activity or response. Additionally, as the stability or reactivity of the test item is unknown prior to the start of the study this modification of the schedule is considered more effective and reproducible due to the in-house observations on human lymphocytes and their particular growth characteristics in this study type and also the significant laboratory historical control data using the above format.

At the end of the Cytochalasin B treatment period the cells were centrifuged, the culture medium was drawn off and discarded, and the cells resuspended in MEM. The cells were then treated with a mild hypotonic solution (0.0375M KCl) before being fixed with fresh methanol/glacial acetic acid (19:1 v/v). The fixative was changed at least three times and the cells stored at approximately 4 ºC prior to slide making.

The lymphocytes were re-suspended in several mL of fresh fixative before centrifugation and re suspension in a small amount of fixative. Several drops of this suspension were dropped onto clean, wet microscope slides and left to air dry with gentle warming. Each slide was permanently labeled with the appropriate identification data. When the slides were dry they were stained in 5 % Giemsa for 5 minutes, rinsed, dried and a cover slip applied using mounting medium.

4. Cell Cycle Kinetics Scoring

A minimum of approximately 500 cells per culture were scored for the incidence of mononucleate, binucleate and multinucleate cells and the cytokinesis block proliferation index (CBPI) value expressed as a percentage of the vehicle controls. The CBPI indicates the number of cell cycles per cell during the period of exposure to Cytochalasin B.

5. Micronucleus Scoring

The micronucleus frequency in 1000 binucleated cells was analyzed per culture (2000 binucleated cells per concentration for the test item and positive control and 4000 binucleated cells for the vehicle controls). Cells with 1, 2 or more micronuclei were recorded and included in the total.

The criteria for identifying micronuclei were that they were round or oval in shape, non refractile, not linked to the main nuclei and with a diameter that was approximately less than a third of the mean diameter of the main nuclei. Binucleate cells were selected for scoring if they had two nuclei of similar size with intact nuclear membranes situated in the same cytoplasmic boundary. The two nuclei could be attached by a fine nucleoplasmic bridge which was approximately no greater than one quarter of the nuclear diameter.

6. Statistics

The frequency of binucleate cells with micronuclei was compared, where necessary, with the concurrent vehicle control value using the Chi-squared Test on observed numbers of cells with micronuclei. A toxicologically significant response was recorded when the p value calculated from the statistical analysis of the frequency of binucleate cells with micronuclei was less than 0.05 and there was a dose-related increase in the frequency of binucleate cells with micronuclei.

The dose-relationship (trend-test) was assessed using a linear regression model. An arcsine square-root transformation was applied to the percentage of binucleated cells containing micronuclei (excluding positive controls). A linear regression model was then applied to these transformed values with dose values fitted as the explanatory variable. The F-value from the model was assessed at the 5 % statistical significance level.

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7. Evaluation Criteria

Providing that all of the acceptability criteria are fulfilled, a test item is considered to be clearly negative if, in all of the experimental conditions examined:

1. None of the test concentrations exhibits a statistically significant increase compared with the concurrent negative control.
2. There is no dose-related increase when evaluated with an appropriate trend test.
3. The results in all evaluated dose groups are within the range of the laboratory historical control data.

The test system is then considered to be unable to induce chromosome breaks and/or gain or loss.

Providing that all of the acceptability criteria are fulfilled, a test item may be considered to be clearly positive, if in any of the experimental conditions examined, there is one or more of the following applicable:

1. At least one of the test concentrations exhibits a statistically significant increase compared with the concurrent negative control.
2. The increase is dose-related in at least one experimental condition when evaluated with an appropriate trend test.
3. The results are substantially outside the range of the laboratory historical negative control data.

When all the criteria are met, the test item is considered able to induce chromosome breaks and/or gain or loss in this test system.

There is no requirement for verification of a clear positive or negative response.

In case the response is neither clearly negative nor clearly positive as described above or in order to assist in establishing the biological relevance of a result, the data should be evaluated by expert judgement and/or further investigations. The Study Director may make a judgement based on experience and the biological relevance of the data and any justification for acceptance of the data will be included in the report. Scoring additional cells (where appropriate) or performing a repeat experiment possibly using modified experimental conditions (e.g. concentration spacing, other metabolic activation conditions (i.e. S9 concentration or S9 origin)) could be useful.

II. RESULTS AND DISCUSSION

The dose range for the Preliminary Toxicity Test was 0, 19.53, 39.06, 78.13, 156.25, 312.5, 625, 1250, 2500 and 5000 µg/mL. The maximum dose was the maximum recommended dose level.

No precipitate of the test item was observed in the parallel blood-free cultures at the end of the exposure in the 4-hour exposure groups or in the 24-hour continuous exposure group. Microscopic assessment of the slides prepared from the exposed cultures showed that binucleate cells were present at up to 5000 µg/mL in all three exposure groups.

The test item induced some evidence of toxicity in the 4-hour exposure group in the absence of S9 and in the 24-hour exposure group. There was no marked toxicity demonstrated in the 4-hour exposure group in the presence of S9.

The maximum dose level selected for the Main Experiment was the maximum recommended dose level and was 5000 µg/mL for all three exposure groups.

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Table 7.1-16: CBPI Data: Preliminary Toxicity Test, 4-hour exposure without metabolic activation

Treatment/ Concentration (µg/mL)	Mononucleate Cells	Binucleate Cells	Multinucleate Cells	CBPI[c]	Cytostasis (%)
Vehicle (MEM)	137	319	44	1,81	0
	139	317	44		
19,53	-	-	-	-	-
39,06	-	-	-	-	-
78,13	-	-	-	-	-
156,25	-	-	-	-	-
312,5	-	-	-	-	-
625	168	286	46	1,76	6
1250	179	291	30	1,70	14
2500	169	295	36	1,73	10
5000	216	271	13	1,59	27

[c] Mean value for vehicle
- Not selected for scoring
MEM Minimal Essential Medium

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Table 7.1-17: CBPI Data: Preliminary Toxicity Test, 4-hour exposure with metabolic activation

Treatment / Concentration (µg/mL)	Mononucleate Cells	Binucleate Cells	Multinucleate Cells	CBPI[c]	Cytostasis (%)
Vehicle (MEM)	177	285	38	1.73	0
	184	262	54		
19.53	-	-	-	-	-
39.06	-	-	-	-	-
78.13	-	-	-	-	-
156.25	-	-	-	-	-
312.5	-	-	-	-	-
625	223	242	35	1.62	15
1250	204	259	37	1.67	8
2500	154	303	43	1.78	0‡
5000	187	277	36	1.70	4

[c] Mean value for vehicle
- Not selected for scoring
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control
MEM Minimal Essential Medium

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Table 7.1-18: CBPI Data: Preliminary Toxicity Test, 24-hour exposure without metabolic activation

Treatment / Concentration (µg/mL)	Mononucleate Cells	Binucleate Cells	Multinucleate Cells	CBPI[c]	Cytostasis (%)
Vehicle (MEM)	104	339	57	1,86	0
	132	332	36		
19,53	-	-	-	-	-
39,06	-	-	-	-	-
78,13	-	-	-	-	-
156,25	-	-	-	-	-
312,5	-	-	-	-	-
625	148	320	32	1,77	10
1250	137	348	15	1,76	12
2500	218	280	2	1,57	34
5000	285	215	0	1,43	50

c Mean value for vehicle
\- Not selected for scoring
MEM Minimal Essential Medium

In the micronucleus test, the qualitative assessment of the slides determined that the toxicity was similar to that observed in the Preliminary Toxicity Test, and that there were binucleate cells suitable for scoring at the maximum dose level of test item, 5000 µg/mL, in all three exposure groups.

The CBPI data confirm the qualitative observations in that a dose-related toxicity was observed in the 4-hour exposure group in the absence of S9 and in the 24-hour exposure group and no marked toxicity was observed in the 4-hour exposure group in the presence of S9.

The vehicle control cultures had frequencies of cells with micronuclei within the expected range and were considered acceptable for addition to the laboratory historical negative control data range.

The positive control items induced statistically significant increases in the frequency of cells with micronuclei with responses that were compatible with those in the laboratory historical positive control data range. Thus, the sensitivity of the assay and the efficacy of the S9-mix were validated.

The test item demonstrated some modest toxicity in the 4-hour exposure in the absence of S9 at the maximum dose level and achieved near optimum toxicity at the maximum recommended dose level in the 24-hour exposure. There was no marked toxicity demonstrated in the 4-hour exposure group in the presence of S9 up to the maximum recommended dose level.

The test item did not induce any statistically significant increases in the frequency of binucleate cells containing micronuclei in the 4-hour exposure group in the presence of S9 or in the 24-hour continuous exposure group where the maximum dose was the maximum recommended dose level.

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The 4-hour group in the absence of S9 included a dose level (1250 µg/mL) which induced a small but statistically significant increase in binucleate cells containing micronuclei. However, since this increase was well within the laboratory historical control range (within 95 % control limits) for a vehicle and was not part of a dose related response, it was considered to be of no toxicological significance.

Cytostasis and micronucleus data are presented in the tables below.

Table 7.1-19: CBPI Data: Main Experiment, 4-hour exposure without metabolic activation

Treatment/ Concentration (µg/mL)	Replicate	Mononucleate Cells	Binucleate Cells	Multinucleate Cells	CBPI	Mean CBPI	Mean Cytostasis (%)
Vehicle (MEM)	A_1	193	262	45	1,70	1,66	0
	A_2	189	273	38	1,70		
	B_1	220	251	29	1,62		
	B_2	234	220	46	1,62		
312,5	A	-	-	-	-	-	-
	B	-	-	-	-		
625	A	-	-	-	-	-	-
	B	-	-	-	-		
1250	A	180	288	32	1,70	1,71	0‡
	B	196	253	51	1,71		
2500	A	180	302	18	1,68	1,68	0‡
	B	193	275	32	1,68		
3750	A	238	240	22	1,57	1,52	22
	B	283	206	11	1,46		
5000	A	299	190	11	1,42	1,41	39
	B	311	181	8	1,39		
MMC 0.2	A	267	227	6	1,48	1,48	27
	B	266	230	4	1,48		

MMC Mitomycin C
- Not selected for scoring
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control
MEM Minimal Essential Medium

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Table 7.1-20: CBPI Data: Main Experiment, 4-hour exposure with metabolic activation

Treatment/ Concentration (µg/mL)	Replicate	Mononucleate Cells	Binucleate Cells	Multinucleate Cells	CBPI	Mean CBPI	Mean Cytostasis (%)
Vehicle (MEM)	A_1	139	300	61	1.84	1.77	0
	A_2	165	282	53	1.78		
	B_1	162	294	44	1.76		
	B_2	192	273	35	1.69		
312.5	A	-	-	-	-	-	-
	B	-	-	-	-		
625	A	-	-	-	-	-	-
	B	-	-	-	-		
1250	A	203	255	42	1.68	1.74	4
	B	149	305	46	1.79		
2500	A	199	268	33	1.67	1.73	6
	B	161	288	51	1.78		
3750	A	180	275	45	1.73	1.77	0‡
	B	147	300	53	1.81		
5000	A	163	295	42	1.76	1.76	1
	B	163	294	43	1.76		
CP 6	A	267	229	4	1.47	1.47	39
	B	279	214	7	1.46		

CP Cyclophosphamide
\- Not selected for scoring
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control
MEM Minimal Essential Medium

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Table 7.1-21: CBPI Data: Main Experiment, 24-hour exposure without metabolic activation

Treatment/ Concentration (µg/mL)	Replicate	Mononucleate Cells	Binucleate Cells	Multinucleate Cells	CBPI	Mean CBPI	Mean Cytostasis (%)
Vehicle (MEM)	A_1	120	377	3	1.77	1.69	0
	A_2	171	321	8	1.67		
	B_1	180	314	6	1.65		
	B_2	175	321	4	1.66		
312.5	A	-	-	-	-	-	-
	B	-	-	-	-		
625	A	-	-	-	-	-	-
	B	-	-	-	-		
1250	A	141	359	0	1.72	1.70	0‡
	B	164	333	3	1.68		
2500	A	220	280	0	1.56	1.60	13
	B	184	315	1	1.63		
3750	A	303	196	1	1.40	1.44	36
	B	261	239	0	1.48		
5000	A	385	115	0	1.23	1.27	61
	B	346	154	0	1.31		
DC 0.075	A	354	111	35	1.36	1.36	48
	B	360	106	34	1.35		

DC Demecolcine
- Not selected for scoring
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control
MEM Minimal Essential Medium

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Table 7.1-22: Cytostasis and Micronucleus Data: Main Experiment, 4-hour exposure without metabolic activation

Treatment/ Concentration (µg/mL)	Replicate	Mean Cytostasis (%)	Binucleated cells containing micronuclei			
			%	Mean %	*p* -value[b]	Trend test *p* -value[d]
Vehicle (MEM)	A_1	0	0,40	0,43	-	0,059
	A_2		0,30			
	B_1		0,50			
	B_2		0,50			
1250	A	0‡	0,90	0,90	0.0228*	
	B		0,90			
2500	A	0‡	0,60	0,55	-	
	B		0,50			
3750	A	22	0,60	0,80	0,0641	
	B		1,00			
5000	A	39	0,80	0,75	-	
	B		0,70			
MMC 0.2	A	27	4,50	4,05	1.58E-25***	-
	B		3,60			

[b] *p*-values are for comparison with the control using Chi-square test
[d] Trend test *p*-values using Linear regression model applied to control and test item concentrations
MMC Mitomycin C
MEM Minimal Essential Medium
* P<0.05
*** P<0.001
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control

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Table 7.1-23: Cytostasis and Micronucleus Data: Main Experiment, 4-hour exposure with metabolic activation

Treatment/ Concentration (µg/mL)	Replicate	Mean Cytostasis (%)	Binucleated cells containing micronuclei			
			%	Mean %	*p* -value[b]	Trend test *p* -value[d]
Vehicle (MEM)	A_1	0	0.10	0.50	-	0.365
	A_2		0.30			
	B_1		0.60			
	B_2		1.00			
1250	A	4	0.90	0.65	0.4589	
	B		0.40			
2500	A	6	0.30	0.40	-	
	B		0.50			
3750	A	0‡	0.20	0.25	-	
	B		0.30			
5000	A	1	0.30	0.35	-	
	B		0.40			
CP 6	A	39	2.60	2.50	1.04E-11***	-
	B		2.40			

[b] *p*-values are for comparison with the control using Chi-square test
[d] Trend test *p*-values using Linear regression model applied to control and test item concentrations
CP Cyclophosphamide
MEM Minimal Essential Medium
*** P<0.001
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control

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Table 7.1-24: Cytostasis and Micronucleus Data: Main Experiment, 24-hour exposure without metabolic activation

Treatment/ Concentration (µg/mL)	Replicate	Mean Cytostasis (%)	Binucleated cells containing micronuclei			
			%	Mean %	*p* -value[b]	Trend test *p* -value[d]
Vehicle (MEM)	A_1	0	0.00	0.03	-	0.588
	A_2		0.10			
	B_1		0.00			
	B_2		0.00			
1250	A	0‡	0.20	0.20	-	
	B		0.20			
2500	A	13	0.30	0.30	-	
	B		0.30			
3750	A	36	0.00	0.05	-	
	B		0.10			
5000	A	61	0.20	0.10	-	
	B		0.00			
DC 0.075	A	48	4.30	4.70	1.43E-42***	-
	B		5.10			

[b] *p*-values are for comparison with the control using Chi-square test
[d] Trend test *p*-values using Linear regression model applied to control and test item concentrations
DC Demecolcine
MEM Minimal Essential Medium
*** P<0.001
‡ Cytostasis reported as 0 as the CBPI value is equal to or higher than the solvent control

The test item was formulated within two hours of it being applied to the test system. Stability and homogeneity was evaluated, and the test item formulations were shown to be stable for up to 24 hours. Dose formulation analysis was performed on the dose formulations of the Main Experiment, which demonstrated that the test item formulations were accurate and within acceptable limits; the results are presented in the table below.

Table 7.1-25: Results of Formulation Analysis

Nominal Concentration (mg/mL)	Analytically Determined Concentration	
	mg/mL	Percent of Nominal
0	None detected	-
3.13	2.71	86
6.25	5.19	83
12.5	11.9	95
25.0	24.3	97
37.5	37.2	99
50	48.8	98

Historical Control Data

Many experiments with human lymphocytes have established a range of micronucleus frequencies for control cultures. The current in-house historical ranges (July 2016 to May 2018) are presented below.

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Table 7.1-26: Historical range for vehicle control cultures

	4 hour exposure without S9	4 hour exposure with S9	24 hour exposure without S9
	% binucleate cells with micronuclei	% binucleate cells with micronuclei	% binucleate cells with micronuclei
Minimum	0.05	0.05	0.15
Maximum	1.20	1.30	0.90
Mean	0.56	0.51	0.47
Standard Deviation	0.29	0.29	0.19
95 % Control Limits	0 – 1.43	0 – 1.38	0 – 1.04
Number of Experiments	50	50	50

Table 7.1-27: Historical range for positive control cultures

	4 hour exposure without S9 (MMC)	4 hour exposure with S9 (CP)	24 hour exposure without S9 (DC)
	% binucleate cells with micronuclei	% binucleate cells with micronuclei	% binucleate cells with micronuclei
Minimum	1.33	1.75	1.80
Maximum	11.80	8.15	6.70
Mean	5.51	3.79	3.41
Standard Deviation	2.43	1.39	1.04
95 % Control Limits	0 – 12.8	0 – 7.96	0.29 – 6.53
Number of Experiments	50	50	50

III. CONCLUSIONS

MON 52276 did not induce any toxicologically significant increases in the frequency of binucleate cells with micronuclei in either the absence or presence of a metabolizing system. MON 52276 was therefore considered to be non-clastogenic and non-aneugenic to human lymphocytes *in vitro*.

3. Assessment and conclusion

Assessment and conclusion by applicant:

MON 52276 was tested in a guideline study on its clastogenic and aneugenic potential in human lymphocytes *in vitro*. MON 52276 did not induce any toxicologically significant increases in the frequency of binucleate cells with micronuclei in either the absence or presence of a metabolizing system. MON 52276 was therefore considered to be non-clastogenic and non-aneugenic to human lymphocytes *in vitro*.

Assessment and conclusion by RMS:

CP 7.1.8 Supplementary studies for combinations of plant protection product

None

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CP 7.2 Data on Exposure

Table 7.2-1 Summary of representative uses (risk envelope approach)

Crop	Application method	Water volume [L/ha]	Number of applications	kg, L product / ha	Maximum total application rate per year [kg a.s./ha]	Minimum application interval [days]	Application timing [e.g. BBCH]
All crops (pre-sowing, pre-planting)	Field spraying, tractor-mounted	100-400	1	4	1.44	Not applicable	Pre-emergence
Vegetables	Field spraying, tractor-mounted	100-400	2[1]	6	2.16	28	Post-harvest, pre-sowing, pre-planting
Orchards	Ground directed, shielded spray, band application[2]	100-400	2[1]	8	2.88	28	Post-emergence of weeds
Vines	Ground directed, shielded spray, band application[3]	100-400	2[1]	8	2.88	28	Post-emergence of weeds
Railroad tracks	Ground directed, spray	100-400	2	10	3.6	90	Post-emergence of weeds
Invasive species in agricultural and non-agricultural areas	Spot treatment (shielded)	5 - 400	1	5	1.8	Not applicable	Post-emergence of weeds

[1] 2 applications at higher rates are considered worst case compared to 3 application at a lower dose rate, hence the selection of the GAP with 2 applications for a risk envelope approach.
[2] Band application in the rows below the trees or as spot treatments. The treated area represents not more than 50 % of the total orchard area. The application rate with reference to the total orchard surface area is not more than 50 % of the stated dose rate.
[3] Band application in the rows below the vine stock or as spot treatments. The treated area represents not more than 50 % of the total vineyard area. The application rate with reference to the total vineyard surface area is not more than 50 % of the stated dose rate.

The worst-case uses are presented to cover the different scenarios in the GAPs (risk envelope). Moreover, the calculations were performed considering that the total area is treated which is also a worst case compared to the real conditions for band and spot application.

The following table provides the endpoints used in the evaluation:

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Table 7.2-2 Endpoints used for risk assessment

Endpoint	Endpoints used for risk assessment
Dermal penetration[1]	Concentrate: 0.096 % Dilution (1:150): 0.69 %
AOEL	0.1 mg/kg bw/day
Oral bioavailability	20 %

[1] Dermal penetration data – please refer to Section CP 7.3 for further details.

CP 7.2.1 Operator exposure

Risk assessment for operator

MON 52276 is formulated as a soluble liquid (SL) containing nominal 360 g glyphosate acid/L as the active substance. The product is used as herbicide for the control of annual, perennial and biennial weeds.

Applications are made pre-sowing, pre-planting and post-harvest of the crops, as well as post-emergence of weeds.

The formulation MON 52276 is commercialised in 1 L bottle, 5 – 20 L container, 60 – 120 – 200 – 640 and 1000 L for agricultural and amenities uses.

With respect to the intended use on railway tracks, the product is applied using special designed spray trains releasing the product as a coarse spray and with a very low risk of spray drift.
For this use the maximum recommended application rate amounts to 1.8 kg a.s./ha twice a year. Recommended spray volumes are in the range of 100 – 400 L/ha.

Concerning the application with a spray train, it has to be noted that for loading of the formulation tank of the spray train only 1000 L bulk containers (IBCs) are used. The transfer of the product to the formulation tank is performed in a closed system via a hose connecting the product container to the formulation tank. For this purpose, both the product containers as well as the formulation tank of the spray train are equipped with a fast couple system, using dry-break couplings. With this system, the transfer/loading process is a vacuum operation (not pumped): if there is any break in a hose, only air gets sucked in rather than chemical being pumped out. Therefore, operator exposure during loading is very unlikely to occur. Furthermore, the spray train protects the operator from exposure to the spray. Thus it can reasonably be concluded that with the use of a train-multi-purpose-vehicle significant operator exposure to MON 52276 is unlikely to occur.

In this respect, the intended use with vehicle mounted ground boom spray equipment obviously represents a worst case as for this type of application the mixing and loading is done manually by the operator. In addition, with regard to the model approach used for the assessment, i.e. the EFSA model, it has to be noted that large scale spray conditions in the field are assumed (= boom sizes >24 m) which obviously represents a worst case as compared to an application with a spray train (treatment width about 5 m). Furthermore, with that use the maximum application rate relevant for the railway use is covered. Considering the maximum application rate relevant for the railway use as worst case also no adaptation of the dermal absorption values to account for a lower in use concentration is triggered. Therefore, it is concluded that the assessment being conducted regarding the intended vehicle mounted ground boom spray application in the field covers the intended application on railway ballast with a spray train.

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Regarding the application of the product with a knapsack, it is obvious to consider that the situation is not different as compared to the situation when the product is applied with knapsack type application equipment. Here as well it has to be noted that the maximum application rate relevant for the railway use is covered and furthermore as far as the maximum application rate is concerned - as worst case - an adaptation of the dermal absorption values is not required. Therefore, it is concluded that the intended application to railway ballast using knapsack type application equipment is covered by the assessment being conducted regarding the intended hand held uses.

A summary of the representative uses for MON 52276 is presented in Table 7.2-3.

CP 7.2.1.1 Estimation of operator exposure

The estimated operator exposure to Glyphosate according to the EFSA OPEX is summarised in the table below.

As guidance on the derivation of acute endpoints for non-dietary human exposure has not yet been published, it is not possible to carry out an acute risk assessment for operators at this time.

Table 7.2-4 Estimated operator exposure to Glyphosate

		Glyphosate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Pre-emergence of crops (bare soil) Tractor mounted boom spray application outdoors (downward spraying)			
Application rate		1.44 kg a.s./ha (4 L MON 52276/ha)	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0056187	5.62
	Work wear – arms, body and legs covered (no gloves)	0.0038142	3.81
Vegetables Including: Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet) Tractor mounted boom spray application outdoors (downward spraying)			
Application rate		2 x 1.08 kg a.s./ha (6 L MON 52276/ha)	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0044526	4.45
	Work wear – arms, body and legs covered (no gloves)	0.0030224	3.02
Orchard crops Including: stone and pome fruits, kiwi, tree nuts, banana, and table olives, citrus Outdoor, downward spraying, vehicle-mounted			
Application rate		2 x 1.44 kg a.s./ha (8 L MON 52276/ha)	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0078501	7.85
	Work wear – arms, body and legs covered (no gloves)	0.0038465	3.85
Outdoor, downward spraying, manual hand-held			
Spray application	Potential exposure	0.0421985	42.2

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Table 7.2-4 Estimated operator exposure to Glyphosate

		Glyphosate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
(AOEM; 75th percentile) Body weight: 60 kg	Work wear – arms, body and legs covered (no gloves)	0.0066923	6.69
Outdoor, downward spraying, manual knapsack			
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0114136	11.4
	Work wear – arms, body and legs covered (no gloves)	0.0022052	2.21
Vines Ground directed, shielded spray Outdoor, downward spraying, vehicle-mounted			
Application rate		2 x 1.44 kg a.s./ha (8 L MON 52276/ha)	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0078501	7.85
	Work wear – arms, body and legs covered (no gloves)	0.0038465	3.85
Outdoor, downward spraying, manual hand-held			
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0421985	42.2
	Work wear – arms, body and legs covered (no gloves)	0.0066923	6.69
Outdoor, downward spraying, manual knapsack			
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0114136	11.4
	Work wear – arms, body and legs covered (no gloves)	0.0022052	2.21
Railroad tracks (bare soil) Ground directed, spray – application by spray train			
Application rate		2 x 1.8 kg a.s./ha (10 L MON 52276/ha)	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0067407	6.74
	Work wear – arms, body and legs covered (no gloves)	0.0045770	4.58
Invasive species in agricultural and non-agricultural areas Spot treatment (shielded)/spray application – manual knapsack			
Application rate		1.8 kg a.s./ha (5 L MON 52276/ha)	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0030263	3.03
	Work wear – arms, body and legs covered (no gloves)	0.0014121	1.41

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Conclusion

Based on the EFSA model predictions for tractor-mounted and hand-held application techniques, the operator exposure is predicted to be within acceptable limits and below 7 % of the AOEL for glyphosate for an operator that applies the product without using PPE.

Thus, according to the EFSA Guidance calculations, a safe use could be demonstrated for operators using MON 52276 for proposed uses, even if no PPE is worn.

CP 7.2.1.2 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and consideration of the above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

CP 7.2.2 Bystander and resident exposure

Risk assessment for bystander and resident

The estimation of bystander and resident exposure was performed according to the EFSA Guidance on "the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products" (EFSA Journal 2014;12(10):3874).

Regarding the spray train application, spray drift (direct drift and drift deposition in adjacent areas) can be regarded as the most relevant source for exposure for resident/ bystander. In this context, it has to be taken into consideration that spray trains are specifically designed to release the spray as a very coarse spray with an accordingly very low risk of spray drift. Hence, it is concluded that in terms of spray drift and subsequently drift deposition in adjacent areas, the application with a tractor mounted ground boom field crop sprayer represents a worst-case surrogate and accordingly covers the application with a spray train.
With regard to the intended applications of MON 52276 using vehicle mounted ground boom spray equipment, resident/ bystander exposure was assessed using the EFSA model. Beside exposure via spray drift, the model also considers the possibility of re-entry into treated crops which can reasonably be excluded as far as applications on railway tracks are concerned. Furthermore, the model assumes exposure via vapour whereby the exposure values proposed by the model refer to large scale applications performed in the field. This obviously covers worst-case conditions with regard to a railway ballast treatment which can be characterised as a band treatment.

Accordingly, it is concluded that the intended application to railway ballast using a spray train or other vehicle mounted boom equipment is covered by the assessment conducted regarding spray applications in the field using vehicle mounted ground boom spray equipment. For this conclusion, it is also taken into account that, as far as applications performed on railway ballast are concerned, maximum application rates as well as maximum in-use concentrations are covered. Furthermore, no adaptation of the dermal absorption values is required.

Concerning applications performed with hand held spray equipment, the EFSA guidance indicates: "It is noted that no data are available for manual application. Therefore, the WoG proposes that the same data be used for manual application as for vehicle application as a first tier assessment (i.e. deposition values for broadcast air-assisted sprayers for upwards manual application, and field crop sprayer values for downwards manual application)". Hence, with the assessment conducted to assess the vehicle mounted application, the application with knapsack type application equipment is covered as well.

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Regarding the use in invasive species, the scenario "golf course, turf or other sports lawns" was selected for non-agricultural areas as it is the appropriate model to evaluate recreational exposure for non-agricultural areas according to the EFSA model. The application is made by spot treatment with a knapsack sprayer.
For agricultural areas, scenarios for cereals, low berries and small fruits, etc. were selected to cover this use.

The outcome of the estimations is presented in Table 7.2-4. Detailed calculations are in Appendix I.

CP 7.2.2.1 Estimation of resident exposure

The estimated resident exposure to Glyphosate is summarised in the following table.

Table 7.2-5 Estimated resident exposure to Glyphosate

		Glyphosate	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Pre-emergence of crops (bare soil) Tractor mounted boom spray application outdoors Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		1.44 kg a.s./ha (4 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0029810	2.98
	Vapour (75th perc.)	0.0010700	1.07
	Deposits (75th perc.)	0.0003785	0.38
	Re-entry (75th perc.)	0.0016767	1.68
	Sum (mean)	0.0043954	4.40
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0006622	0.66
	Vapour (75th perc.)	0.0002300	0.23
	Deposits (75th perc.)	0.0000677	0.07
	Re-entry (75th perc.)	0.0009315	0.93
	Sum (mean)	0.0013469	1.35
Vegetables Including: Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet) Tractor mounted boom spray application outdoors Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		2 x 1.08 kg a.s./ha (6 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0022358	2.24
	Vapour (75th perc.)	0.0010700	1.07

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Table 7.2-5 Estimated resident exposure to Glyphosate

		Glyphosate	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
	Deposits (75th perc.)	0.0004326	0.43
	Re-entry (75th perc.)	0.0019160	1.92
	Sum (mean)	0.0041979	4.20
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0004967	0.50
	Vapour (75th perc.)	0.0002300	0.23
	Deposits (75th perc.)	0.0000774	0.08
	Re-entry (75th perc.)	0.0010645	1.06
	Sum (mean)	0.0013789	1.38
Orchard crops Including: stone and pome fruits, kiwi, tree nuts, banana, and table olives, citrus Ground directed, shielded spray, band application Buffer zone: 2-3(m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		2 x 1.44 kg a.s./ha (8 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0029810	2.98
	Vapour (75th perc.)	0.0010700	1.07
	Deposits (75th perc.)	0.0024676	2.47
	Re-entry (75th perc.)	0.0025547	2.55
	Sum (mean)	0.0067710	6.77
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0006622	0.66
	Vapour (75th perc.)	0.0002300	0.23
	Deposits (75th perc.)	0.0004413	0.44
	Re-entry (75th perc.)	0.0014193	1.42
	Sum (mean)	0.0020355	2.04
Vines Ground directed, shielded spray Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		2 x 1.44 kg a.s./ha (8 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0029810	2.98
	Vapour (75th perc.)	0.0010700	1.07
	Deposits (75th perc.)	0.0007106	0.71
	Re-entry (75th perc.)	0.0025547	2.55

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Table 7.2-5 Estimated resident exposure to Glyphosate

		Glyphosate	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
	Sum (mean)	0.0053590	5.36
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0006622	0.66
	Vapour (75th perc.)	0.0002300	0.23
	Deposits (75th perc.)	0.0001271	0.13
	Re-entry (75th perc.)	0.0014193	1.42
	Sum (mean)	0.0017830	1.78
Railroad tracks (bare soil) Ground directed, spray Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		2 x 1.8 kg a.s./ha (10 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0037263	3.73
	Vapour (75th perc.)	0.0010700	1.07
	Deposits (75th perc.)	0.0005323	0.53
	Re-entry (75th perc.)	0.0023579	2.36
	Sum (mean)	0.0054789	5.48
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0008278	0.83
	Vapour (75th perc.)	0.0002300	0.23
	Deposits (75th perc.)	0.0000952	0.10
	Re-entry (75th perc.)	0.0013099	1.31
	Sum (mean)	0.0017500	1.75
Invasive species in non-agricultural areas Spot treatment (shielded)/spray application Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		1.8 kg a.s./ha (5 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0175730	17.6
	Vapour (75th perc.)	0.0010700	1.07
	Deposits (75th perc.)	0.0003185	0.32
	Re-entry (75th perc.)	0.0022860	2.29
	Sum (mean)	0.0127953	12.8
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0029124	2.91
	Vapour (75th perc.)	0.0002300	0.23

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Table 7.2-5 Estimated resident exposure to Glyphosate

		Glyphosate	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
	Deposits (75th perc.)	0.0000123	0.01
	Re-entry (75th perc.)	0.0000274	0.03
	Sum (mean)	0.0019044	1.90
Invasive species in agricultural areas Spot treatment (shielded)/spray application Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		1.8 kg a.s./ha (5 L MON 52276/ha)	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0175730	17.6
	Vapour (75th perc.)	0.0010700	1.07
	Deposits (75th perc.)	0.0003185	0.32
	Re-entry (75th perc.)	0.0003038	0.30
	Sum (mean)	0.0129790	13.0
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0029124	2.91
	Vapour (75th perc.)	0.0002300	0.23
	Deposits (75th perc.)	0.0000123	0.01
	Re-entry (75th perc.)	0.0001688	0.17
	Sum (mean)	0.0020116	2.01

Results

According to the EFSA Guidance, the total estimated systemic resident exposure of children and adults to glyphosate, after application on the intended crops, is much lower than 100 % the AOEL. The highest exposure for the resident child is expected for invasive species in agricultural and non-agricultural areas and is lower than 50 % of the AOEL (44.6 %).

Therefore, it is concluded that resident exposure to MON 52276 is acceptable in all crops for adults and children.

CP 7.2.2.2 Estimation of bystander exposure

The product MON 52276 contains the active substance glyphosate that has acute toxicity and/ or the potential to exert effects after a single dose and hence in this instance according to the EFSA guidance, repeat exposure estimates (using 75th percentile values) and acute exposure estimates (using 95th percentile values) are required.
Since no AAOEL has been agreed for glyphosate, only estimates of resident exposures (using 75th percentile values) which consider the long-term risk are presented.

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CP 7.2.2.3 Estimated recreational exposure (EFSA Guidance)

Table 7.2-6 Estimated recreational exposure to Glyphosate

		Glyphosate	
Model data		**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Knapsack sprayer application outdoors to low crops[1]			
Application rate:		1.8 kg a.s./ha (5 L MON 52276/ha)	
Child Body weight: 10 kg	Recreational exposure	0.0056880	5.69
Adult Body weight: 60 kg	Recreational exposure	0.0002190	0.22

[1] As a worst case, in the EFSA Guidance calculator the crop type "golf course, turf and other sports lawns" was chosen in order to present the corresponding recreational exposure scenario.

Results

According to the EFSA Guidance, the total estimated systemic residential exposure after application on non-crop areas (recreation area) of children and adults to glyphosate amounts to 0.0084492 mg/kg bw/day and 0.0015111 mg/kg bw/day, respectively. These values correspond to 8.45 % and 1.51 % of the AOEL of glyphosate, respectively.

Conclusion

Therefore, it is concluded that there is no undue risk to any bystander and resident, child and adult, after exposure to MON 52276. This has no labelling implications.

CP 7.2.2.4 Measurement of bystander and resident exposure

Since the resident and/ or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for Glyphosate will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of resident/ bystander exposure was not necessary and was therefore not performed

CP 7.2.3 Worker exposure

Risk assessment for worker

The estimation of worker exposure was performed according to the EFSA Guidance on "the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products" (EFSA Journal 2014;12(10):3874).

CP 7.2.3.1 Estimation of worker exposure

For most of the intended uses of MON 52276 there are no foreseen re-entry activities. The only reasonable re-entry scenario for orchards and grapes is inspection of the crops and it normally requires no dermal contact to the foliage, but rather consists of a visual inspection. However, the AOEM model does not take into account worker tasks such as inspection and irrigation for these crops.

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Therefore, in accordance with the transfer coefficients proposed in the EFSA Guidance and the default value of 2 hours for inspection activities, the worker exposure was calculated with the following formula:

Systemic exposure [mg a.s/kg bw/day] = (AR (kg sa/ha) x DFR [µg/cm²] × TC [cm²/h] × T [h/day]) × MAF/ 1 000 × DA [%]/ BW

Where:
Dislodgeable foliar residue (DFR): 3 µg/cm² of foliage/kg a.s. applied/ha × application rate [kg a.s/ha]
Transfer coefficient (TC): 12500 cm²/h (total potential exposure) and 1400 cm²/h (arms, body and legs covered). No gloves for this scenario.
Work rate (T): 2 hours
Multiple application factor (MAF): 1.52 (2 applications, 28 days interval, DT_{50} = 30 days)
Dermal absorption (DA): 0.096 % concentrate and 0.69 % dilution
Body weight (BW): 60 kg

The estimation of worker exposure after entry into a previously treated area or handling a crop treated with MON 52276 according to the critical uses is summarised in **Table 7.2-7**. Detailed calculations are in Appendix 1.

Table 7.2-7 Estimated worker exposure to Glyphosate

		Glyphosate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Pre-emergence of crops (bare soil) No worker's tasks			
Vegetables Including: Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet) Reaching, picking Outdoor Work rate: 8 hours/day, DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			
Number of applications and application rate		2 x 1.08 kg a.s./ha (6 L MON 52276/ha)	
Body weight: 60 kg	Potential TC: 5800 cm²/person/h	0.0263418	26.3
	Work wear (arms, body and legs covered) TC: 2500 cm²/person/h	0.0113542	11.4
	Work wear (arms, body and legs covered) and gloves TC: 580 cm²/person/h	0.0026342	2.63
Orchards Including: stone and pome fruits, kiwi, tree nuts, banana, and table olives, citrus **Inspection, irrigation** Outdoor Work rate: **2 hours/day** DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha			

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Table 7.2-7 Estimated worker exposure to Glyphosate

		Glyphosate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Number of applications and application rate		2 x 1.44 kg a.s./ha (8 L MON 52276/ha)	
Body weight: 60 kg	Potential TC: **12500** cm^2/person/h	0.0189237	18.9
	Work wear (arms, body and legs covered) TC: **1400** cm^2/person/h	0.0021194	2.12
	Work wear (arms, body and legs covered) and gloves TC: **NA** cm^2/person/h	NA	NA
Vines **Inspection, irrigation** Outdoor Work rate: **2 hours/day** DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha			
Number of applications and application rate		2 x 1.44 kg a.s./ha (8 L MON 52276/ha)	
Body weight: 60 kg	Potential TC: **12500** cm^2/person/h	0.0189237	18.9
	Work wear (arms, body and legs covered) TC: **1400** cm^2/person/h	0.0021194	2.12
	Work wear (arms, body and legs covered) and gloves TC: NA cm^2/person/h	NA	NA
Railroad tracks (bare soil) No worker's tasks			
Invasive species in non-agricultural areas Maintenance Outdoor Work rate: 8 hours/day, DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha			
Number of applications and application rate		1.8 kg a.s./ha (5 L MON 52276/ha)	
Body weight: 60 kg	Potential TC: 5800 cm^2/person/h	0.0041760	4.18
	Work wear (arms, body and legs covered) TC: 2500 cm^2/person/h	0.0018000	1.80
	Work wear (arms, body and legs covered) and gloves TC: 580	0.0004176	0.42
Invasive species in agricultural areas			

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Table 7.2-7 Estimated worker exposure to Glyphosate

		Glyphosate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Inspection, irrigation Outdoor Work rate: 2 hours/day, DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha			
Number of applications and application rate		1.8 kg a.s./ha (5 L MON 52276/ha)	
Body weight: 60 kg	Potential TC: 12500 cm^2/person/h	0.0022500	2.25
	Work wear (arms, body and legs covered) TC: 1400 cm^2/person/h	0.0002520	0.25
	Work wear (arms, body and legs covered) and gloves TC: NA	NA	NA

Conclusion

According to the EFSA Guidance, for a professional worker wearing adequate work clothing, but no PPE, when performing re-entry activities, the estimated systemic exposure to glyphosate is much lower than 100 % the AOEL.

With respect to the intended use of MON 52276 on pre emergence crops and railway tracks, it is concluded that worker exposure is not relevant. Indeed, no re-entry and worker's tasks are expected.

Therefore, it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing (but no PPE), when re-entering crops treated with MON 52276. As a standard rule, it should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried.

CP 7.2.3.2 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

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CP 7.3 Dermal Absorption

The percentage absorptions used in the exposure assessment are in Table CP 7.3-1.

Table 7.3-1 Dermal absorption end-points for the risk assessment

	Test results	Adapted values used in calculations for risk assessment (%)	Reference
Concentrate	0.086	0.096	[redacted], 2010 EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873)
Dilution (1:12.5)	0.17	0.23	[redacted], 2010 EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873)
Dilution (1:150)	0.34	0.69	[redacted], 2010 EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873)

CP 7.3.1 Dermal absorption study

1. Information on the study

Data point:	CP 7.3.1/001
Report author	[redacted]
Report year	2010
Report title	*In Vitro* Absorption of Glyphosate through Human Epidermis
Report No	JV2084-REG
Document No	DTL-09-094
Guidelines followed in study	OECD 428 (2004); OECD (Guidance Document No. 28 (2004). The Conduct of Skin Absorption Studies; European Commission Guidance Document on Dermal Absorption (2004)
Deviations from current test guideline	None
Previous evaluation	Yes, accepted in RAR (2015)
GLP/ Officially recognised testing facilities	Yes
Acceptability/ Reliability:	Valid
Category study in AIR 5 dossier (L docs)	Category 2a

2. Full summary of the study according to OECD format

The objective of this study was to evaluate the potential dermal absorption of glyphosate from a 360 g/L SL formulation concentrate, as well as from two representative in-use dilutions prepared as 1:12.5 (v/v) and 1:150 (v/v) aqueous dilutions.

^{14}C-glyphosate was incorporated into the concentrate formulation and dilutions prior to application. The doses were applied to human epidermal membranes at a rate of 10 µL/cm^2 and left unoccluded for an

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exposure period of 24 hours. The absorption process was followed by taking samples of the receptor fluid (physiological saline) at recorded intervals throughout the exposure period. The distribution of glyphosate within the test system and a 24-hour absorption profile were determined. All samples were analysed by liquid scintillation counting (LSC).

For the formulation concentrate and both aqueous dilutions, the vast majority of the applied glyphosate was removed from the surface of the epidermis during the washing procedure at the end of the 24 hour exposure period (mean 97.4-99.0 %).

The mean total amount of glyphosate recovered from the epidermis was 0.120 %, 0.235 % and 0.505 % of the applied dose (concentrate, 1/12.5 v/v dilution and 1/150 v/v dilution, respectively). The amount of potentially biologically available glyphosate (absorbed + epidermis after tape striping) for the concentrate, 1/12.5 and 1/150 dilutions were 0.064 %, 0.134 % and 0.277 %, respectively.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test materials:

a) Non radio-labelled test substance:

Identification:	Isopropylamine salt of glyphosate technical material (glyphosate-IPA)
Description:	Clear, water white to amber viscous liquid (solution in water)
Lot/ Batch #:	A8B60170S0
Chemical purity:	Glyphosate-IPA: 63.81 % Glyphosate acid: 47.28 %
Stability of test compound:	Stable under ambient conditions Expiry date: 2012-01-25

b) Analytical reference standard:

Identification:	Glyphosate acid
Description:	White solid
Lot/ Batch #:	GLP-0810-19515-A
Chemical purity:	99.8 %
Stability of test compound:	Expiry date: 2011-01-31

c) Radio-labelled test substance

Identification:	^{14}C-glyphosate (as glyphosate acid)
Lot/ Batch #:	53463-3-23
Chemical purity:	99.8 %
Radiochemical purity:	97.8 % (confirmed by analysis)
Specific activity:	47 mCi/mmol; 1739 MBq/mmol; 277.9 µCi/mg; 10.28 MBq/mg
Stability of test compound:	Stable under deep freeze (-20 °C)

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A. MATERIALS

c) Blank formulation

Identification:	Proprietary surfactant blend (MON 8153)
Concentration of a.s.:	0 %
Description:	Not reported
Lot/ Batch #:	Not reported
Stability of test compound:	Not reported

d) Formulated test substance

Identification:	MON 52276
	The formulation concentrate used was not supplied as complete formulation, but had to be prepared from the ingredients a) and c) described above, to allow the incorporation of the radiolabel.
	The test substance concentration in the prepared formulation was confirmed by analysis.

2. Test skin source:

Species:	Human excised skin
Source:	Tissue bank (not further specified)

3. Test system: Glass diffusion cells
Physiological saline

B. STUDY DESIGN

1. In life dates: 9 June to 26 August 2009

2. Test apparatus and treatment

a) Assembly of diffusion cells
The type of glass diffusion cell used in this study had an exposed membrane area of 2.54 cm^2. Discs of approximately 3.3 cm diameter of prepared skin membrane from several different skin samples were mounted, dermal side down, in diffusion cells held together with individually numbered clamps. The total volume of the receptor fluid chamber was approximately 4.5 mL.

b) Assessment of membrane integrity
Membrane integrity was assessed by measurement of electrical resistance across the membrane. Membranes with a resistance <10 kΩ were discarded. After the completion of the integrity assessment, the contents of the donor and receptor chambers were discarded.

c) Selection of cells and dosing
Each dose (concentrate, 1:12.5 dilution and 1:150 dilution) was represented by six diffusion cells with intact membranes from at least three different donors. The receptor chambers of the cells containing small magnetic stirrer bars were filled with a recorded volume of receptor fluid (physiological saline) and placed in a water bath maintained at a temperature of 32 ºC ± 1 ºC. The physiological saline receptor fluid was chosen to ensure that the test substance could freely partition into the receptor fluid from the skin membrane and never reached a concentration that would limit its diffusion. The receptor fluid (saline) provided adequate solubility because glyphosate has high aqueous solubility (water solubility of glyphosate acid = 10.5 g/L at 20° C, The Pesticides Manual, 2006). The area of epidermis exposed to the test formulation in each cell was 2.54 cm^2, with 10 µL/cm^2 applied to each diffusion cell. Glyphosate concentrations for each

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dose were 3693 µg a.s./cm^2 (formulation concentrate), 296 µg a.s./cm^2 (1:12.5 dilution) and 25.2 µg a.s./cm^2 (1:150 dilution). After dosing, the cells were replaced in a water bath maintained at 32 °C ± 1 °C. The formulation was applied to the skin membranes and left unoccluded for the duration of the exposure period (24 hours).

d) Sampling of receptor fluid

Samples of the receptor fluid (500 µL) were taken from the receptor chambers at 0.5, 1, 2, 3, 4, 6, 8, 10, 12, 16, 20 and 24 hours after application. The receptor chambers were stirred continuously and the volume of fluid in the receptor chamber maintained by the replacement of a volume of fresh receptor fluid, equal to the sample volume, after each sample was taken.

e) Measurement of mass balance

All apparatus and epidermis upper surface were washed with deionised water and Teepol® L and sponged thoroughly until decontamination appeared complete or until it was apparent that radiolabel may be being extracted from the epidermis using a Geiger counter. All sponges were digested in Soluene 350®. The digests made up to a recorded volume and a sample taken for analysis.

To assess penetration through human *stratum corneum*/ epidermis, a tape stripping technique was employed. The surface of the skin was allowed to dry naturally, prior to the removal of successively deeper layers of the *stratum corneum* by the repeated application of adhesive tape (Scotch 3M Magic Tape, 1.9 cm wide) up to a maximum of 5 strips. The strips were extracted individually for approximately 20 hours in a solution of 30 % v/v methanol in water. The extracts were sequentially numbered and analysed by liquid scintillation counting (LSC). If the epidermis started to tear and/ or pieces came away during the tape stripping procedure, the process was terminated as soon as noticed. In such cases, the last strip taken was digested with the remaining epidermis to avoid underestimating residual penetrant in the epidermis. The total number of tape strips was recorded for each epidermis sample. The remaining epidermis was then carefully removed from the receptor chamber and digested in Soluene 350®, together with the final tape strip taken if tearing had occurred, and analysed by LSC.

3. Statistics

The data did not warrant statistical analysis, other than group means and standard deviations.

II. RESULTS AND DISCUSSION

In order to add all the data for the cells that had been excluded in the study report for the neat formulation and the 1 in 150 dilution it was necessary to reconstruct the results from the raw data files. The following tables and figures are derived from this work and may differ slightly from previously presented tables due to rounding differences. The data have been evaluated according to the EFSA 2017 guidance.

Table 7.3 2 presents the data from all the cells used for the neat or concentrate formulation test expressed in terms of percentage of radioactivity or dose applied.

Table 7.3 5 presents the data from the high dose group cells excluding the two cells considered to be outliers for the neat or concentrate formulation test expressed in terms of percentage of radioactivity or dose applied. Cells 20 and 27, which were from the same human donor, showed up to 100x higher diffusion into the receptor fluid compared with the other cells of that treatment group, which indicated either fragility of that donor specimen or membrane damage during dose application. Further support for the exclusion of these cells is provided by the spray dilution results which also presented much lower proportions of radioactivity in the receptor fluid than observed for cells 20 and 27 when the trend would have been expected to be in the opposite direction i.e. higher proportional absorption from the spray dilutions.

Table 7.3 6 presents the data from all the cells used for the 28.8 g/L (1 in 12.5 dilution) representative spray dilution expressed in terms of percentage of radioactivity or dose applied. No cells required exclusion from this test group.

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Table 7.3 7 presents the data from all the cells used for the 2.4 g/L (1 in 150 dilution) representative spray dilution expressed in terms of percentage of radioactivity or dose applied.

Table 7.3 10 presents the data from the low (2.4 g/L) dose group cells excluding the two cells considered to be outliers expressed in terms of percentage of radioactivity or dose applied. Cell numbers 25 and 28 required exclusion from this test group as the receptor fluid profiles clearly showed immediate break-through of radioactivity (see figure A 1.3) implying that the membrane had been damaged during application. The duplicate cells (16 and 30) displayed much lower levels of absorption and normal absorption profiles.

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Table 7.3-2 Distribution of radioactivity at 24 hours after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the rate of 360 g/L to human skin samples (All cells)

% dose applied	Group Human HD	Group Human HD	Group Human HD	Group Human HD	Group Human HD	Group Human HD	Group Human HD N = 6 K N° = 1	
Donor N°	1124L	1124L	1115B	1105	1110E	1105		
Sex	Female	Female	Female	Female	Female	Female		
Cell N°	Cell 2	Cell 3	Cell 13	Cell 20	Cell 23	Cell 27	MEAN	SD
Skin wash 24h	92.94	102.81	103.12	92.26	97.12	100.84	98.18	4.83
SC 1	0.013	0.062	0.023	0.005	0.023	0.011	0.023	0.021
SC 2	0.005	0.016	0.008	0.006	0.020	0.009	0.011	0.006
SURFACE DOSE	0.018	0.078	0.031	0.010	0.043	0.020	0.033	0.025
Donor chamber	9.030	n.d.	n.d.	n.d.	n.d.	n.d.	1.505	3.686
TOTAL NON ABSORBED	**101.98**	**102.88**	**103.15**	**92.27**	**97.17**	**100.86**	**99.72**	**4.248**
Skin	0.032	0.074	0.073	0.027	0.039	0.122	0.061	0.036
SC3	0.003	0.005	0.008	n.d.	0.004	0.017	0.006	0.006
SC4	n.d.	0.004	0.006	n.d.	0.010	n.d.	0.003	0.004
SC5	0.043	0.004	n.d.	n.d.	0.002	n.d.	0.008	0.017
TOTAL SC 3+ [1]	0.046	0.012	0.014	n.d.	0.016	0.017	0.018	0.015
TOTAL Stratum Corneum	0.064	0.091	0.045	0.010	0.060	0.037	0.051	0.027
TOTAL DOSE SITE	**0.078**	**0.087**	**0.087**	**0.027**	**0.056**	**0.139**	**0.079**	**0.037**
Receptor fluid (12h)	0.0033	0.0021	0.0022	7.2786	0.0127	0.9353	1.3724	2.9173
Receptor fluid (24h)	0.0057	0.0032	0.0038	9.4377	0.0215	0.9953	1.7445	3.7895
POTENTIAL (dose site+ receptor)	**0.084**	**0.090**	**0.091**	**9.465**	**0.077**	**1.135**	**1.824**	**3.767**
POTENTIAL (skin+ receptor)	0.116	0.164	0.164	9.492	0.116	1.257	1.885	3.753
TOTAL RECOVERY	**102.07**	**102.97**	**103.24**	**101.73**	**97.24**	**101.99**	**101.54**	**2.188**
% Ratio receptor 12h/24h	57.13	65.26	57.26	77.12	59.00	93.97	68.29	14.69
Evaluation according to EFSA Guidance								
Absorption >75 % within half of study duration?					No. (include SC values except SC1 & SC2)			
Recovery <95 %?					No correction needed			
Total % Potentially Absorbable adjusted according to EFSA (2017)					**Mean (% dose site +% receptor) + (SD*1) = 5.6 %**			

[1]: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
SD: standard deviation
n.d.: below limit of detection.
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

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Figure 7.3-3 Cumulative Absorption Profile after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the nominal rate of 360 g/L to human skin (All cells)

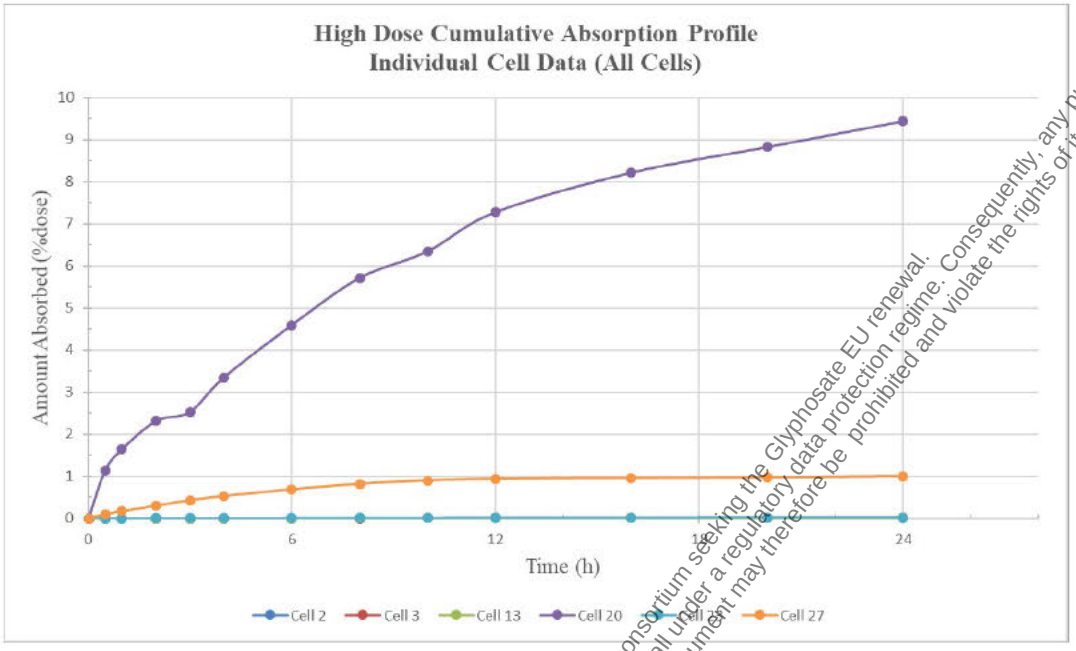

Figure 7.3-4 Cumulative Absorption Profile after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the nominal rate of 360 g/L to human skin (Reported cells)

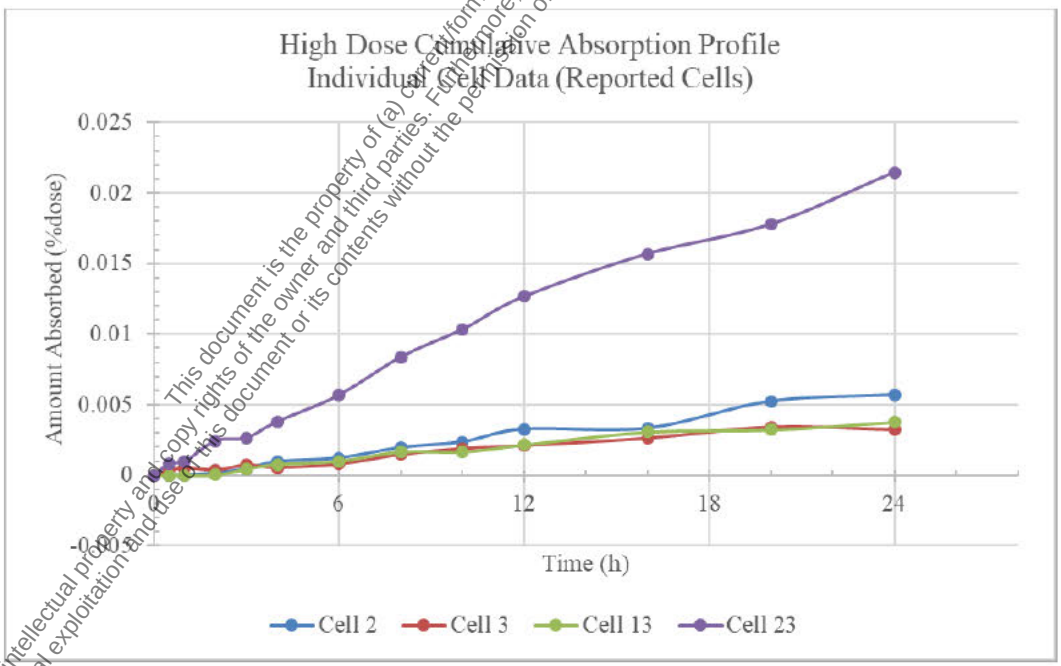

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Table 7.3-5 Distribution of radioactivity at 24 hours after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the rate of 360 g/L to human skin samples (reported cells).

% dose applied	Group Human HD	Group Human HD	Group Human HD	Group Human HD	Group Human HD N = 4 K N° = 1.6	
Donor N°	1124L	1124L	1115B	1110E		
Sex	Female	Female	Female	Female		
Cell N°	Cell 2	Cell 3	Cell 13	Cell 23	MEAN	SD
Skin wash 24h	92.94	102.81	103.12	97.12	98.99	4.890
SC 1	0.013	0.062	0.023	0.023	0.030	0.022
SC 2	0.005	0.016	0.008	0.020	0.012	0.007
SURFACE DOSE	0.018	0.078	0.031	0.043	0.043	0.026
Donor chamber	9.030	n.d.	n.d.	n.d.	2.257	4.515
TOTAL NON ABSORBED	**101.98**	**102.88**	**103.15**	**97.17**	**101.29**	**2.798**
Skin	0.032	0.074	0.073	0.039	0.055	0.022
SC3	0.003	0.005	0.008	0.004	0.005	0.002
SC4	n.d.	0.004	0.006	0.010	0.005	0.004
SC5	0.043	0.004	n.d.	0.002	0.012	0.021
TOTAL SC 3+ [a]	0.046	0.012	0.014	0.016	0.022	0.016
TOTAL Stratum Corneum	0.064	0.091	0.045	0.060	0.065	0.019
TOTAL DOSE SITE	**0.078**	**0.087**	**0.087**	**0.056**	**0.077**	**0.015**
Receptor fluid (12h)	0.0033	0.0021	0.0022	0.0127	0.005	0.005
Receptor fluid (24h)	0.0057	0.0032	0.0038	0.0215	0.009	0.009
POTENTIAL (dose site+ receptor)	**0.084**	**0.090**	**0.091**	**0.077**	**0.085**	**0.006**
POTENTIAL (skin+ receptor)	0.116	0.164	0.164	0.116	0.140	0.028
TOTAL RECOVERY	**102.07**	**102.97**	**103.24**	**97.24**	**101.38**	**2.804**
% Ratio receptor 12h/24h	57.13	65.26	57.26	59.00	59.66	3.831
Evaluation according to EFSA Guidance						
Absorption >75 % within half of study duration?					No. (include SC values except SC1 & SC2)	
Recovery <95 %?					No correction needed	
Total % Potentially Absorbable adjusted according to EFSA					**Mean (% dose site +% receptor) + (SD*1.6) = 0.096 %**	

[a]: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
SD: standard deviation
n.d.: below limit of detection.
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

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Table 7.3-6 Distribution of radioactivity at 24 hours after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the nominal rate of 28.8 g/L to human skin (All cells)

% dose applied	Group Human ID	Group Human ID	Group Human ID	Group Human ID	Group Human ID	Group Human ID	Group Human ID N = 6 K N° N - 1	
Donor N°	11242A	1124A	1115B	1105	1110E	1110E		
Sex	Female	Female	Female	Female	Female	Female		
Cell N°	Cell 4	Cell 5	Cell 14	Cell 21	Cell 24	Cell 29	MEAN	SD
Skin wash 24h	100.42	98.15	97.48	97.41	96.42	94.77	97.44	1.87
SC 1	0.028	0.005	0.040	0.002	0.181	0.112	0.061	0.071
SC 2	0.024	0.005	0.013	0.006	0.091	0.066	0.034	0.036
SURFACE DOSE	0.052	0.010	0.054	0.009	0.272	0.178	0.096	0.106
Donor chamber	n.d.	1.837	4.439	0.008	2.503	4.749	2.256	2.067
TOTAL NON ABSORBED	**100.47**	**99.99**	**101.97**	**97.43**	**99.20**	**99.70**	**99.79**	**1.50**
Skin	0.136	0.119	0.062	0.028	0.146	0.138	0.105	0.048
SC3	0.009	0.007	0.012	n.d.	0.031	0.029	0.014	0.013
SC4	0.016	0.009	0.010	n.d.	0.016	0.015	0.011	0.006
SC5	0.002	0.020	0.005	n.d.	0.010	0.018	0.009	0.008
TOTAL SC 3+ [a]	0.027	0.035	0.026	n.d.	0.057	0.063	0.035	0.023
TOTAL Stratum Corneum	0.079	0.045	0.080	0.009	0.329	0.240	0.130	0.125
TOTAL DOSE SITE	**0.162**	**0.154**	**0.088**	**0.028**	**0.202**	**0.200**	**0.139**	**0.069**
Receptor fluid (12h)	0.012	0.010	0.016	0.014	0.026	0.011	0.015	0.006
Receptor fluid (24h)	**0.019**	**0.020**	**0.025**	**0.054**	**0.034**	**0.021**	**0.029**	**0.014**
POTENTIAL (dose site+ receptor)	**0.181**	**0.175**	**0.113**	**0.082**	**0.236**	**0.221**	**0.168**	**0.060**
POTENTIAL (skin+ receptor)	0.155	0.139	0.087	0.082	0.179	0.158	0.133	0.040
TOTAL RECOVERY	**100.65**	**100.17**	**102.08**	**97.51**	**99.43**	**99.92**	**99.96**	**1.50**
% Ratio receptor 12h/24h	64.00	50.79	62.90	26.29	77.55	54.57	56.01	17.25

Evaluation according to EFSA Guidance	
Absorption >75 % within half of study duration?	No. (include SC values except SC1 & SC2)
Recovery <95 %?	No correction needed
Total % Potentially Absorbable adjusted according to EFSA (2017)	**Mean (% dose site +% receptor) + (SD*1) = 0.23 %**

[a]: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
SD: standard deviation
n.d.: below limit of detection.
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

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Table 7.3-7 Distribution of radioactivity at 24 hours after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the nominal rate of 2.4 g/L to human skin (All cells)

% dose applied	Group Human LD	Group Human LD	Group Human LD	Group Human LD	Group Human LD	Group Human LD	Group Human LD N = 6 K N° = 1	
Donor N°	1124A	1115B	1105	1110E	1105	1110E		
Sex	Female	Female	Female	Female	Female	Female		
Cell N°	Cell 6	Cell 15	Cell 16	Cell 25	Cell 28	Cell 30	MEAN	SD
Skin wash 24h	99.49	100.46	95.99	84.40	83.58	97.78	93.62	7.62
SC 1	0.483	0.166	0.032	0.017	0.507	0.086	0.215	0.223
SC 2	0.174	0.042	0.010	0.069	0.000	0.030	0.054	0.064
SURFACE DOSE	0.657	0.208	0.042	0.087	0.507	0.116	0.269	0.253
Donor chamber	n.d.	n.d.	0.029	n.d.	0.414	0.005	0.075	0.167
TOTAL NON ABSORBED	**100.15**	**100.66**	**96.06**	**84.48**	**84.50**	**97.90**	**93.96**	**7.52**
Skin	0.414	0.027	0.134	0.174	1.057	0.165	0.328	0.379
SC3	0.056	0.024	0.010	n.d.	n.d.	0.024	0.019	0.021
SC4	0.049	0.018	n.d.	n.d.	n.d.	0.025	0.015	0.020
SC5	0.030	0.005	n.d.	n.d.	n.d.	0.019	0.009	0.013
TOTAL SC 3+ [a]	0.135	0.046	0.010	n.d.	n.d.	0.068	0.043	0.053
TOTAL Stratum Corneum	0.792	0.254	0.051	0.087	0.507	0.184	0.313	0.285
TOTAL DOSE SITE	**0.549**	**0.073**	**0.143**	**0.174**	**1.057**	**0.233**	**0.372**	**0.374**
Receptor fluid (12h)	0.054	0.031	0.131	12.62	11.52	0.038	4.06	6.21
Receptor fluid (24h)	0.082	0.039	0.179	12.54	11.47	0.050	4.06	6.16
POTENTIAL (dose site+ receptor)	0.632	0.112	0.322	12.71	12.53	0.283	4.431	6.344
POTENTIAL (skin+ receptor)	**0.497**	**0.066**	**0.313**	**12.71**	**12.53**	**0.22**	**4.39**	**6.38**
TOTAL RECOVERY	**100.78**	**100.78**	**96.38**	**97.19**	**97.03**	**98.19**	**98.39**	**1.94**
% Ratio receptor 12h/24h	65.81	78.24	73.22	100.65	100.41	76.58	82.48	14.61

Evaluation according to EFSA Guidance	
Absorption >75 % within half of study duration?	Yes. (exclude SC values)
Recovery <95 %?	No correction needed
Total % Potentially Absorbable adjusted according to EFSA (2017)	**Mean (% dose site +% receptor) + (SD*1) = 10 %**

[a]: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
SD: standard deviation
n.d.: below limit of detection.
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

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Figure 7.3-8 Cumulative Absorption Profile after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the nominal rate of 2.4 g/L to human skin (All cells)

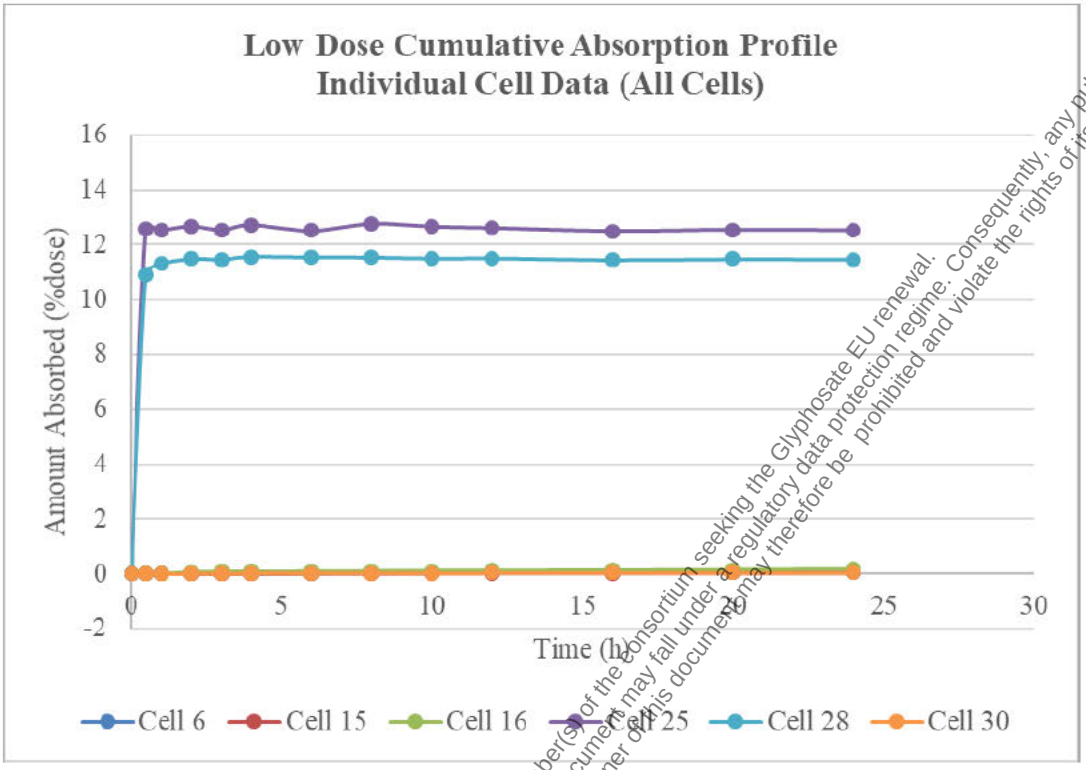

Figure 7.3-9 Cumulative Absorption Profile after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the nominal rate of 2.4 g/L to human skin (Reported cells)

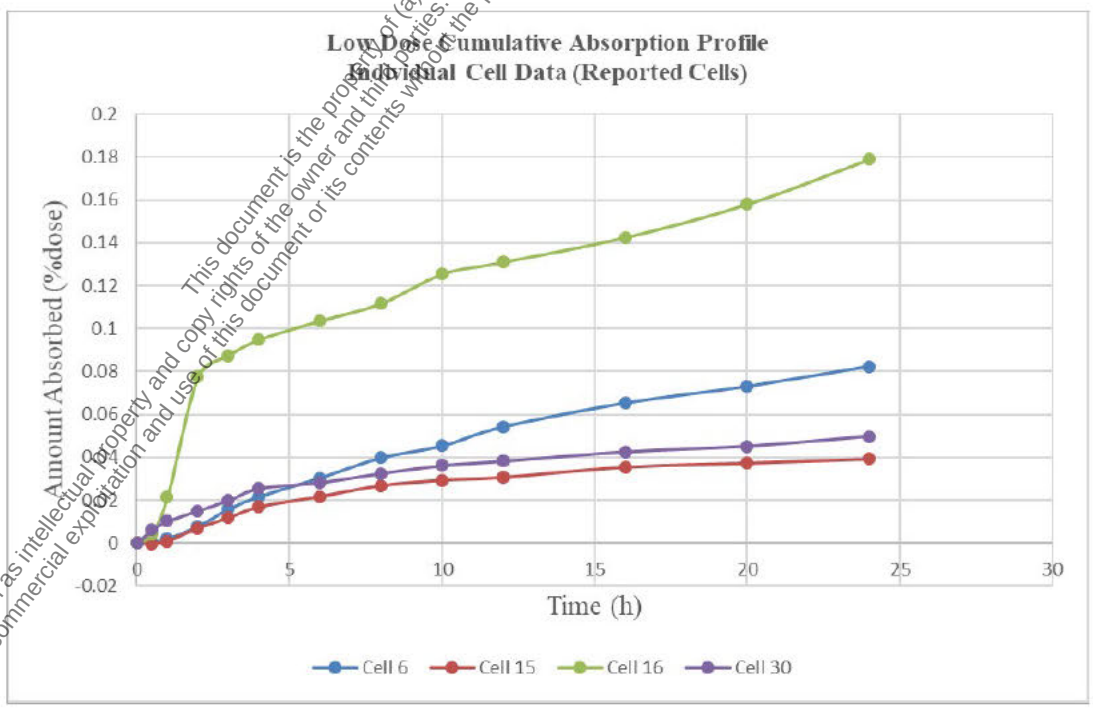

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Table 7.3-10 Distribution of radioactivity at 24 hours after dose application of [^{14}C]-glyphosate in a SL 360 formulation at the rate of 2.4 g/L to human skin (reported cells)

% dose applied	Group Human LD	Group Human LD	Group Human LD	Group Human LD	Group Human LD N = 4 K N° = 1.6	
Donor N°	1124A	1115B	1105	1110E		
Sex	Female	Female	Female	Female		
Cell N°	Cell 6	Cell 15	Cell 16	Cell 30	MEAN	SD
Skin wash 24h	99.49	100.46	95.99	97.78	98.43	1.97
SC 1	0.483	0.166	0.032	0.086	0.19	0.20
SC 2	0.174	0.042	0.010	0.030	0.06	0.07
SURFACE DOSE	0.657	0.208	0.042	0.116	0.26	0.28
Donor chamber	n.d.	n.d.	0.029	0.005	0.01	0.01
TOTAL NON ABSORBED	100.15	100.66	96.06	97.90	98.69	2.13
Skin	0.414	0.027	0.134	0.165	0.18	0.16
SC3	0.056	0.024	0.010	0.024	0.03	0.02
SC4	0.049	0.018	n.d.	0.025	0.02	0.02
SC5	0.030	0.005	n.d.	0.019	0.01	0.01
TOTAL SC 3+ [a]	0.135	0.046	0.010	0.068	0.06	0.05
TOTAL Stratum Corneum	0.792	0.254	0.051	0.184	0.32	0.33
TOTAL DOSE SITE	0.549	0.073	0.143	0.233	0.25	0.21
Receptor fluid (12h)	0.045	0.029	0.125	0.036	0.06	0.04
Receptor fluid (24h)	0.082	0.039	0.179	0.050	0.09	0.06
POTENTIAL (dose site+ receptor)	**0.632**	**0.112**	**0.322**	**0.283**	**0.34**	**0.22**
POTENTIAL (skin+ receptor)	0.497	0.066	0.313	0.215	0.27	0.18
TOTAL RECOVERY	100.78	100.78	96.38	98.19	99.03	2.15
% Ratio receptor 12h/24h	65.81	78.24	73.22	76.58	73.46	5.51

Evaluation according to EFSA Guidance	
Absorption >75 % within half of study duration?	No. (include SC values except SC1 & SC2)
Recovery <95 %?	No correction needed
Total % Potentially Absorbable adjusted according to EFSA	**Mean (% dose site +% receptor) + (SD*1.6) = 0.69 %**

[a]: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
SD: standard deviation
n.d.: below limit of detection.
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III. CONCLUSIONS

The dermal penetration through human dermatomed skin of [^{14}C]-glyphosate in the SL 360 formulation was investigated at three nominal concentrations corresponding to the neat product (360 g/L) and to two representative spray dilutions of 28.8 g/L and 2.4 g/L, respectively.

Concentrate

The mean percentage of glyphosate in the SL 360 formulation that was considered to be potentially absorbable *(directly absorbed plus total remaining at dose site)* over a period of 24 hours for the neat formulation was 0.085 % for the human skin. Applying the EFSA guidance (2017) this value adjusts to 0.096 %.

Intermediate Dose level (28.8 g/L, Spray dilution)

The mean percentage of glyphosate in the SL 360 formulation that was considered to be potentially absorbable *(directly absorbed plus total remaining at dose site)* over a period of 24 hours for the intermediate dose rate was 0.168 % for human skin. Applying the EFSA guidance (2017) this value adjusts to 0.23 %.

Low Dose level (Spray dilution)

The mean percentage of glyphosate in the SL 360 formulation that was considered to be potentially absorbable *(directly absorbed plus total remaining at dose site)* over a period of 24 hours for the low dose rate was 0.34 % for human skin. Applying the EFSA guidance (2017) this value adjusts to 0.69 %.

Therefore, the following dermal absorption value can be proposed for use in the non-dietary risk assessments for [^{14}C]-glyphosate in the glyphosate SL 360 formulation:

- 0.096 % for the neat formulation (360 g/L)
- 0.23 % for the intermediate dose (28.8 g/L)
- 0.69 % for the low dose (2.4 g/L).

3. Assessment and conclusion

Assessment and conclusion by applicant:

The study is in concordance with the OECD guideline 428 (2004) and GLP compliant. Therefore, the study is considered acceptable.
According to the EFSA Guidance on Dermal Absorption (2017), the dermal absorption estimates to be used for risk assessment are set at 0.096 % for the concentrate, 0.23 % for the intermediate dose and 0.69 % for the low dose in human skin.

Assessment and conclusion by RMS:

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CP 7.4 Available Toxicological Data Relating to Co-Formulants

CONFIDENTIAL information - data provided separately (Document J)

Appendix 1 – Detailed exposure calculations

A 1.1 Operator exposure calculations

Table A 1-1: Input parameters considered for the estimation of operator exposure in bare soil (EFSA Model)

Substance name	Glyphosate	
Product name	MON 52276	
Reference value non acutely toxic active substance (RVNAS)	0.1	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	2	mg/kg bw/day
Crop type	Bare soil	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	100	L/ha
Maximum application rate of active substance	1.44	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.10%	
Dermal absorption of in-use dilution	0.69%	
Oral absorption of active substance	20.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	1	
Interval between multiple applications	365	days
Season (upward spraying orchards only)	not relevant	

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Table A 2-2: Estimation of longer term operator exposure towards Glyphosate in bare soil (EFSA model)

Operator exposure for MON 52276 outdoor spray applications

Application rate of active substance	1.44	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	72	kg a.s./day	*i_AmountAS*
Dermal absorption of the product	0.10%		*i_AbscpProduct*
Dermal absorption of in-use dilution	0.69%		*i_Abscinuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	130674	497229	AOEM	
	Body	72095	249504	AOEM	
	Head	3736	20488	AOEM	
	Protected hands (gloves)	557	14261	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	1053	10530	AOEM	
	Protected head (hood and face shield)	60	1160	AOEM	
	Inhalation	13	32	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear - arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	19679	52541	AOEM	
	Body	5371	30781	AOEM	
	Head	280	851	AOEM	
	Protected hands (gloves)	432	5488	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	164	402	AOEM	
	Inhalation	9	34	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear - arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted	

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Table A 3-3: Estimation of longer term operator exposure towards Glyphosate in bare soil (EFSA model), cont'd

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.3371223	0.2288509	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0056187	0.0038142	
% of RVNAS	5.62%	3.81%	

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	125.4473550	2.0907892	D15*_AbsorpProduct
Body	69.2111340	1.1535189	D16*_AbsorpProduct
Head	3.5861936	0.0597699	D17*_AbsorpProduct
Inhalation	13.2172818	0.2202880	D21*_AbsorpInhalation
Sum	211.4619644	3.5243661	
With RPE/PPE (as selected above)			
Hands	125.4473550	2.0907892	D18*_AbsorpProduct
Body	1.0105203	0.0168420	D19*_AbsorpProduct or D16*_AbsorpProduct*F24
Head	3.5861936	0.0597699	D20*_AbsorpProduct or D17*_AbsorpProduct*F25
Inhalation	13.2172818	0.2202880	D21*_AbsorpInhalation*G25
Sum	143.2613507	2.3876892	
Water soluble	143.2613507	2.3876892	C70*F26

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	73.6870551	1.2281176	D30*_AbsorpInuse
Body	41.2009511	0.6866825	D31*_AbsorpInuse
Head	1.9472981	0.0324550	D32*_AbsorpInuse
Inhalation	8.8250050	0.1470834	D35*_AbsorpInhalation
Sum	125.6603094	2.0943385	
With RPE/PPE (as selected above)			
Hands	73.6870551	1.2281176	D33*_AbsorpInuse
Body	1.1302116	0.0188369	D34*_AbsorpInuse or D31*_AbsorpInuse*F38
Head	1.9472981	0.0324550	D32*_AbsorpInuse*F39
Inhalation	8.8250050	0.1470834	D35*_AbsorpInuse*G39
Sum	85.5895699	1.4264928	

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Table A 4-4: Input parameters considered for the estimation of operator exposure in vegetables (EFSA Model)

Substance name	Glyphosate	
Product name	MON 52276	
Reference value non acutely toxic active substance (RVNAS)	0.1	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)		mg/kg bw/day
Crop type	Fruiting vegetables	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	100	L/ha
Maximum application rate of active substance	1.08	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.10%	
Dermal absorption of in-use dilution	0.69%	
Oral absorption of active substance	20.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	2	
Interval between multiple applications	28	days
Season (upward spraying orchards only)	not relevant	

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Table A 5-5: Estimation of longer term operator exposure towards Glyphosate in vegetables (EFSA model)

Operator exposure for MON 52276 outdoor spray applications

Application rate of active substance	1.08	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	54	kg a.s./day	*i_AmountAS*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	0.69%		*i_Absorbuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	104715	397440	AOEM	
	Body	58895	229499	AOEM	
	Head	2802	15366	AOEM	
	Protected hands (gloves)	462	10696	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	816	7898	AOEM	
	Protected head (hood and face shield)	45	870	AOEM	
	Inhalation	12	32	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	8009	42559	AOEM	
	Body	4478	23086	AOEM	
	Head	202	638	AOEM	
	Protected hands (gloves)	370	5307	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	123	301	AOEM	
	Inhalation	8	29	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted	

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Table A 6-6: Estimation of longer term operator exposure towards Glyphosate in vegetables (EFSA model), cont'd

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.2671553	0.1813458
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0044526	0.0030224
% of AVNAS	4.45%	3.02%

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	100.5263516	1.6754392	*D[5']_AbsorpProduct*
Body	56.5396061	0.9423268	*D[6']_AbsorpProduct*
Head	2.6896452	0.0448274	*D[7']_AbsorpProduct*
Inhalation	12.1327817	0.2022130	*D[2']_AbsorpInhalation*
Sum	171.8883846	2.8648064	
With RPE/PPE (as selected above)			
Hands	100.5263516	1.6754392	*D[8']_AbsorpProduct*
Body	0.7830745	0.0130512	*D[9']_AbsorpProduct or D[5']_AbsorpProduct'F24*
Head	2.6896452	0.0448274	*D[20']_AbsorpProduct or D[7']_AbsorpProduct'F25*
Inhalation	12.1327817	0.2022130	*D[21']_AbsorpInhalation'G25*
Sum	116.1318530	1.9355309	
Water soluble	116.1318530	1.9355309	*C30'F26*

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	55.2652914	0.9210882	*D30']_Absorpinuse*
Body	30.9007134	0.5150119	*D31']_Absorpinuse*
Head	1.4604736	0.0243412	*D32']_Absorpinuse*
Inhalation	7.6404802	0.1273413	*D35']_AbsorpInhalation*
Sum	95.2669585	1.5877826	
With RPE/PPE (as selected above)			
Hands	55.2652914	0.9210882	*D33']_Absorpinuse*
Body	0.8476587	0.0141276	*D34']_Absorpinuse or D31']_Absorpinuse'F38*
Head	1.4604736	0.0243412	*D32']_Absorpinuse'F39*
Inhalation	7.6404802	0.1273413	*D35']_Absorpinuse'G39*
Sum	65.2139038	1.0868984	

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Table A 7-7: Input parameters considered for the estimation of operator exposure in orchards (EFSA Model)

Substance name	Glyphosate	
Product name	MON 52276	
Reference value non acutely toxic active substance (RVNAS)	0.1	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)		mg/kg bw/day
Crop type	Pome fruit	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	100	L/ha
Maximum application rate of active substance	1.44	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.10%	
Dermal absorption of in-use dilution	0.69%	
Oral absorption of active substance	20.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	2	
Interval between multiple applications	28	days
Season (upward spraying orchards only)	not relevant	

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Table A 8-8: Estimation of longer term operator exposure towards Glyphosate in orchards (EFSA model)

Operator exposure for MON 52276 outdoor spray applications

Application rate of active substance	1.44	kg a.s./ha	*i_AppRate*
Assumed area treated	10	ha/day	*d_AreaTreated*
Amount of active substance applied	14.4	kg a.s./day	*i_AmountAS*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	0.69%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Mixing and loading

Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Hands	37853	142003	AOEM	
Body	23258	156319	AOEM	
Head	747	4098	AOEM	
Protected hands (gloves)	195	2852	AOEM	
Protected body (workwear or protective garment and sturdy footwear)	253	2106	AOEM	
Protected head (hood and face shield)	12	232	AOEM	
Inhalation	8	31	AOEM	
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
Gloves	No			
Clothing	rk wear - arms, body and legs covered		cl. in AOEM model	
Head and respiratory PPE	None		1	1
Water soluble bag	No		1	

Application

Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Hands	23333	26437	AOEM	This scenario assumes that small area equipment is used
Body	32813	40565	AOEM	
Head	192	2250	AOEM	
Protected hands (gloves)	93	29	AOEM	
Protected body (workwear or protective garment and sturdy footwear)	400	473	AOEM	
Inhalation	20	188	AOEM	
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
Gloves	No			
Clothing	rk wear - arms, body and legs covered		cl. in AOEM model	
Head and respiratory PPE	None		1	1
Closed cab	No		vehicle mounted	

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Table A 9-9: Estimation of longer term operator exposure towards Glyphosate in orchards (EFSA model), cont'd

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.4710069	0.2307929	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0078501	0.0038465	
% of RVNAS	7.85%	3.85%	

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	36.3390384	0.6056506	D15*_AbsorpProduct
Body	22.3279566	0.3721326	D16*_AbsorpProduct
Head	0.7172387	0.0119540	D17*_AbsorpProduct
Inhalation	8.1870733	0.1364512	D21*_AbsorpInhalation
Sum	67.5713070	1.1261884	
With RPE/PPE (as selected above)			
Hands	36.3390384	0.6056506	D18*_AbsorpProduct
Body	0.2426604	0.0040443	D19*_AbsorpProduct or D15*_AbsorpProduct*F24
Head	0.7172387	0.0119540	D20*_AbsorpProduct or D17*_AbsorpProduct*F25
Inhalation	8.1870733	0.1364512	D21*_AbsorpInhalation*G25
Sum	45.4860108	0.7581002	
Water soluble	45.4860108	0.7581002	C30*F26

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	160.9956611	2.6832610	D30*_AbsorpInuse
Body	220.8911190	3.6815186	D31*_AbsorpInuse
Head	1.3225249	0.0220421	D32*_AbsorpInuse
Inhalation	20.2262733	0.3371046	D35*_AbsorpInhalation
Sum	403.4355783	6.7239263	
With RPE/PPE (as selected above)			
Hands	160.9956611	2.6832610	D33*_AbsorpInuse
Body	2.7623945	0.0460399	D34*_AbsorpInuse or D31*_AbsorpInuse*F38
Head	1.3225249	0.0220421	D32*_AbsorpInuse*F39
Inhalation	20.2262733	0.3371046	D35*_AbsorpInuse*G39
Sum	185.3068538	3.0884476	

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Table A 10-10: Input parameters considered for the estimation of operator exposure in vines (EFSA Model)

Substance name	Glyphosate	
Product name	MON 52276	
Reference value non acutely toxic active substance (RVNAS)	0.1	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)		mg/kg bw/day
Crop type	Grapes	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	100	L/ha
Maximum application rate of active substance	1.44	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.10%	
Dermal absorption of in-use dilution	0.69%	
Oral absorption of active substance	20.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3 m	
Number of applications		
Interval between multiple applications	28	days
Season (upward spraying orchards only)	not relevant	

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Table A 11-11: Estimation of longer term operator exposure towards Glyphosate in vines (EFSA model)

Operator exposure for MON 52276 outdoor spray applications

Application rate of active substance	1.44	kg a.s./ha	*i_AppRate*
Assumed area treated	10	ha/day	*d_AreaTreated*
Amount of active substance applied	14.4	kg a.s./day	*i_AmountAS*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	0.69%		*i_Absoinuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

OutdoorSoluble concentrates, emulsifiable concentrate, etc.DownwardVehicle-mou

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	37853	142003	AOEM	
	Body	23258	156319	AOEM	
	Head	747	4098	AOEM	
	Protected hands (gloves)	195	2852	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	253	2106	AOEM	
	Protected head (hood and face shield)	12	232	AOEM	
	Inhalation	8	31	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	23338	26437	AOEM	This scenario assumes that small area equipment is used
	Body	32012	40565	AOEM	
	Head	152	2250	AOEM	
	Protected hands (gloves)	93	29	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	400	473	AOEM	
	Inhalation	20	188	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted	

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Table A 12-12: Estimation of longer term operator exposure towards Glyphosate in vines (EFSA model), cont'd

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.4710069	0.2307929	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0078501	0.0038465	
% of RVNAS	7.85%	3.85%	

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	36.3390384	0.6056506	D15*I_AbsorpProduct
Body	22.3279566	0.3721326	D16*I_AbsorpProduct
Head	0.7172387	0.0119540	D17*I_AbsorpProduct
Inhalation	8.1870733	0.1364512	D21*I_AbsorpInhalation
Sum	67.5713070	1.1261884	
With RPE/PPE (as selected above)			
Hands	36.3390384	0.6056506	D18*I_AbsorpProduct
Body	0.2426604	0.0040443	D19*I_AbsorpProduct or D15*I_AbsorpProduct*F24
Head	0.7172387	0.0119540	D20*I_AbsorpProduct or D17*I_AbsorpProduct*F25
Inhalation	8.1870733	0.1364512	D21*I_AbsorpInhalation*G25
Sum	45.4860108	0.7581002	
Water soluble	45.4860108	0.7581002	C70*F26

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	160.9956611	2.6832610	D30*I_AbsorpInuse
Body	220.8911190	3.6815186	D31*I_AbsorpInuse
Head	1.3225249	0.0220421	D32*I_AbsorpInuse
Inhalation	20.2262733	0.3371046	D35*I_AbsorpInhalation
Sum	403.4355783	6.7239263	
With RPE/PPE (as selected above)			
Hands	160.9956611	2.6832610	D33*I_AbsorpInuse
Body	2.7623945	0.0460399	D34*I_AbsorpInuse or D31*I_AbsorpInuse*F38
Head	1.3225249	0.0220421	D32*I_AbsorpInuse*F39
Inhalation	20.2262733	0.3371046	D35*I_AbsorpInuse*G39
Sum	185.3068538	3.0884476	

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Table A 13-13: Input parameters considered for the estimation of operator exposure in railroad tracks (EFSA Model)

Substance name	Glyphosate	
Product name	MON 52276	
Reference value non acutely toxic active substance (RVNAS)	0.1	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)		mg/kg bw/day
Crop type	Bare soil	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	100	L/ha
Maximum application rate of active substance	1.8	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/ kg a.s. applied/ha
Dermal absorption of product	0.10%	
Dermal absorption of in-use dilution	0.69%	
Oral absorption of active substance	20.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	2	
Interval between multiple applications	90	days
Season (upward spraying orchards only)	not relevant	

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Table A 14-14: Estimation of longer term operator exposure towards Glyphosate in railroad tracks (EFSA model)

Operator exposure for MON 52276 outdoor spray applications

Application rate of active substance	1.8	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	90	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	0.69%		*i_Absoinuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

OutdoorSoluble concentrates, emulsifiable concentrate, etc.Downward spraying Vehicle-mounted

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	155165	591584	AOEM	
	Body	84338	266215	AOEM	
	Head	4670	25610	AOEM	
	Protected hands (gloves)	644	17826	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	1283	13163	AOEM	
	Protected head (hood and face shield)	75	1450	AOEM	
	Inhalation	14	32	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	13349	61869	AOEM	
	Body	7464	38476	AOEM	
	Head	353	1064	AOEM	
	Protected hands (gloves)	486	5633	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	205	502	AOEM	
	Inhalation	10	39	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted	

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Table A 15-15: Estimation of longer term operator exposure towards Glyphosate in railroad tracks (EFSA model), cont'd

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.4044441	0.2746223	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0067407	0.0045770	
% of RVNAS	6.74%	4.58%	

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	148.9586556	2.4826443	*D15*_AbsorpProduct*
Body	80.9649254	1.3494154	*D16*_AbsorpProduct*
Head	4.4827420	0.0747124	*D17*_AbsorpProduct*
Inhalation	14.1248086	0.2354135	*D21*_AbsorpInhalation*
Sum	248.5311316	4.1421855	
With RPE/PPE (as selected above)			
Hands	148.9586556	2.4826443	*D18*_AbsorpProduct*
Body	1.2315248	0.0205254	*D19*_AbsorpProduct or D15*_AbsorpProduct*F24*
Head	4.4827420	0.0747124	*D20*_AbsorpProduct or D17*_AbsorpProduct*F25*
Inhalation	14.1248086	0.2354135	*D21*_AbsorpInhalation*G25*
Sum	168.7977310	2.8132955	
Water soluble	168.7977310	2.8132955	*C70*F26*

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	92.1088189	1.5351470	*D30*_AbsorpInuse*
Body	51.5011889	0.8583531	*D31*_AbsorpInuse*
Head	2.4341226	0.0405687	*D32*_AbsorpInuse*
Inhalation	9.8688575	0.1644810	*D35*_AbsorpInhalation*
Sum	155.9129880	2.5985498	
With RPE/PPE (as selected above)			
Hands	92.1088189	1.5351470	*D33*_AbsorpInuse*
Body	1.4127645	0.0235461	*D34*_AbsorpInuse or D31*_AbsorpInuse*F33*
Head	2.4341226	0.0405687	*D32*_AbsorpInuse*F33*
Inhalation	9.8688575	0.1644810	*D35*_AbsorpInuse*G33*
Sum	105.8245636	1.7637427	

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Table A 16-16: Input parameters considered for the estimation of operator exposure for invasive species in agricultural/ non-agricultural areas (EFSA Model)

Substance name	Glyphosate	
Product name	MON 52276	
Reference value non acutely toxic active substance (RVNAS)	0.1	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)		mg/kg bw/day
Crop type	Golf course, turf or other sports lawns	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	5	L/ha
Maximum application rate of active substance	1.8	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.10%	
Dermal absorption of in-use dilution	0.10%	
Oral absorption of active substance	20.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Manual Knapsack	
Buffer strip	2-3	m
Number of applications	1	
Interval between multiple applications	365	days
Season (upward spraying orchards only)	notrelevant	

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Table A 17-17: Estimation of longer term operator exposure towards Glyphosate for invasive species in agricultural/ non-agricultural areas (EFSA model)

Operator exposure for MON 52276 outdoor spray applications

Application rate of active substance	1.8	kg a.s./ha	*i_AppRate*
Assumed area treated	1	ha/day	*d_AreaTreated*
Amount of active substance applied	1.8	kg a.s./day	*i_AmountAS*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	0.10%		*i_Absorbuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Manual-Knapsack		
Season	not relevant		

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	11394	30578	AOEM	
	Body	964	3344	AOEM	
	Head	6	13	AOEM	
	Protected hands (gloves)	22	197	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	30	124	AOEM	
	Protected head (hood and face shield)	6	13	AOEM	
	Inhalation	30	31	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	1853	5056	AOEM	
	Body	106642	164408	AOEM	
	Head	34	102	AOEM	
	Protected hands (gloves)	8	26	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	10684	75156	AOEM	
	Inhalation	31	31	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	rk wear – arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted	

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Table A 18-18: Estimation of longer term operator exposure towards Glyphosate for invasive species in agricultural/ non-agricultural areas (EFSA model), cont'd

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.1815779	0.0847236	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0030263	0.0014121	
% of RVNAS	3.03%	1.41%	

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	10.9382400	0.1823040	D15*_AbsorpProduct
Body	0.9250560	0.0154176	D16*_AbsorpProduct
Head	0.0057600	0.0000960	D17*_AbsorpProduct
Inhalation	30.0000000	0.5000000	D21*_AbsorpInhalation
Sum	41.8690560	0.6978176	
With RPE/PPE (as selected above)			
Hands	10.9382400	0.1823040	D18*_AbsorpProduct
Body	0.0288000	0.0004800	D19*_AbsorpProduct or D15*_AbsorpProduct*F24
Head	0.0057600	0.0000960	D20*_AbsorpProduct or D17*_AbsorpProduct*F25
Inhalation	30.0000000	0.5000000	D21*_AbsorpInhalation*G25
Sum	40.9728000	0.6828800	
Water soluble	40.9728000	0.6828800	C20*F26

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg	Formula
Without RPE/PPE			
Hands	1.8528000	0.0308800	D30*_AbsorpInuse
Body	106.6416000	1.7773600	D31*_AbsorpInuse
Head	0.0144000	0.0002400	D32*_AbsorpInuse
Inhalation	31.2000000	0.5200000	D35*_AbsorpInhalation
Sum	139.7088000	2.3284800	
With RPE/PPE (as selected above)			
Hands	1.8528000	0.0308800	D33*_AbsorpInuse
Body	10.6836000	0.1780600	D34*_AbsorpInuse or D31*_AbsorpInuse*F38
Head	0.0144000	0.0002400	D32*_AbsorpInuse*F39
Inhalation	31.2000000	0.5200000	D35*_AbsorpInuse*G39
Sum	43.7508000	0.7291800	

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A 1.2 Resident exposure calculations

Table A 192-1: Input parameters considered for the estimation of resident exposure in bare soil

Resident exposure for MON 52276			
Croptype	Bare soil		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.44	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	14.4	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorpProduct
Dermal absorption of in-use dilution	0.69%		i_AbsorpInuse
Oral absorption	20.00%		i_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	4.32	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 202-2: Estimation of resident exposure towards Glyphosate in bare soil (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0298104	0.0107000	0.0037852	0.0167670	0.0439538
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0029810	0.0010700	0.0003785	0.0016767	0.0043954
% of RVNAS	2.98%	1.07%	0.38%	1.68%	4.40%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0397333	0.0138000	0.0040618	0.0558900	0.0808164
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0006622	0.0002300	0.0000677	0.0009315	0.0013469
% of RVNAS	0.66%	0.23%	0.07%	0.93%	1.35%

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Table A 212-3: Input parameters considered for the estimation of resident exposure in vegetables

Resident exposure for MON 52276			
Croptype	Fruiting vegetables		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.08	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	10.8	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorpProduct
Dermal absorption of in-use dilution	0.69%		i_AbsorpInuse
Oral absorption	20.00%		i_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	3.24	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Vpair
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 222-4: Estimation of resident exposure towards Glyphosate in vegetables (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0223578	0.0107000	0.0043255	0.0191602	0.0419792
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0022358	0.0010700	0.0004326	0.0019160	0.0041979
% of RVNAS	2.24%	1.07%	0.43%	1.92%	4.20%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0298000	0.0138000	0.0046416	0.0638675	0.0827317
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0004967	0.0002300	0.0000774	0.0010645	0.0013789
% of RVNAS	0.50%	0.23%	0.08%	1.06%	1.38%

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Table A 232-5: Input parameters considered for the estimation of resident exposure in orchards

Resident exposure for MON 52276			
Croptype	Pome fruit		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.44	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	14.4	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorbProduct
Dermal absorption of in-use dilution	0.69%		i_Absorbinuse
Oral absorption	20.00%		i_AbsorbOralinuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	4.32	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	23.96%		
Drift percentage on surface (mean)	18.96%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 242-6: Estimation of resident exposure towards Glyphosate in orchards (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0238104	0.0107000	0.0246761	0.0255470	0.0677097
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0029810	0.0010700	0.0024676	0.0025547	0.0067710
% of RVNAS	2.98%	1.07%	2.47%	2.55%	6.77%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0397333	0.0138000	0.0264792	0.0851566	0.1221314
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0006622	0.0002300	0.0004413	0.0014193	0.0020355
% of RVNAS	0.66%	0.23%	0.44%	1.42%	2.04%

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Table A 252-7: Input parameters considered for the estimation of resident exposure in vines

Resident exposure for MON 52276			
Croptype	Grapes		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.44	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	14.4	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorpProduct
Dermal absorption of in-use dilution	0.69%		i_Absorpinuse
Oral absorption	20.00%		i_AbsorpOralinuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	4.32	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Vpair
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	6.90%		
Drift percentage on surface (mean)	5.25%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 262-8: Estimation of resident exposure towards Glyphosate in vines (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0238104	0.0107000	0.0071062	0.0255470	0.0535899
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0023810	0.0010700	0.0007106	0.0025547	0.0053590
% of RVNAS	2.98%	1.07%	0.71%	2.55%	5.36%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0397333	0.0138000	0.0076255	0.0851566	0.1069799
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0006622	0.0002300	0.0001271	0.0014193	0.0017830
% of RVNAS	0.66%	0.23%	0.13%	1.42%	1.78%

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Table A 272-9: Input parameters considered for the estimation of resident exposure in railroad tracks

Resident exposure for MON 52276			
Croptype	Bare soil		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.8	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	18	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorpProduct
Dermal absorption of in-use dilution	0.69%		i_Absorpinuse
Oral absorption	20.00%		d_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.0%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 282-10: Estimation of resident exposure towards Glyphosate in railroad tracks (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0372630	0.0107000	0.0053230	0.0235786	0.0547891
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0037263	0.0010700	0.0005323	0.0023579	0.0054789
% of RVNAS	3.73%	1.07%	0.53%	2.36%	5.48%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0496667	0.0138000	0.0057120	0.0785953	0.1049982
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0008278	0.0002300	0.0000952	0.0013099	0.0017500
% of RVNAS	0.83%	0.23%	0.10%	1.31%	1.75%

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Table A 292-11: Input parameters considered for the estimation of resident exposure for invasive species in non-agricultural areas

Resident exposure for MON 52276			
Croptype	Golf course, turf or other sports lawns		
Application method	Downward spraying		
Application equipment	Manual-Knapsack		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.8	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	360	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorpProduct
Dermal absorption of in-use dilution	0.10%		i_AbsorpInuse
Oral absorption	20.00%		d_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 302-12: Estimation of resident exposure towards Glyphosate for invasive species in non-agricultural areas (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1757304	0.0107000	0.0031853	0.0228600	0.1279531
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0175730	0.0010700	0.0003185	0.0022860	0.0127953
% of RVNAS	17.57%	1.07%	0.32%	2.29%	12.80%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1747440	0.0138000	0.0007358	0.0016425	0.1142640
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0029124	0.0002300	0.0000123	0.0000274	0.0019044
% of RVNAS	2.91%	0.23%	0.01%	0.03%	1.90%

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Table A 312-13: Input parameters considered for the estimation of resident exposure for invasive species in agricultural

Resident exposure for MON 52276			
Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Manual-Knapsack		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	1.8	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	360	g a.s./l	d_ConcAS
Dermal absorption of product	0.10%		i_AbsorbProduct
Dermal absorption of in-use dilution	0.10%		i_Absorbinuse
Oral absorption	20.00%		d_AbsorbOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m³/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m³/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.0%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h	d_TcEntryCh

Table A 322-14: Estimation of resident exposure towards Glyphosate for invasive species in agricultural (EFSA Model)

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1757304	0.0107000	0.0031853	0.0030375	0.1297900
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0175730	0.0010700	0.0003185	0.0003038	0.0129790
% of RVNAS	17.57%	1.07%	0.32%	0.30%	12.98%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1747440	0.0138000	0.0007358	0.0101250	0.1206945
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0029124	0.0002300	0.0000123	0.0001688	0.0020116
% of RVNAS	2.91%	0.23%	0.01%	0.17%	2.01%

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Table A 332-15: Input parameters considered for the estimation of recreational exposure for invasive species in non-agricultural areas

Recreational exposure for MON 52276			
Croptype	Golf course, turf or other sports lawns		
Application method	Downward spraying		
Application equipment	Manual-Knapsack		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Application rate of the product	1.8	kg a.s./ha	i_AppRate
Dermal absorption of product	0.10%		i_AbsorpProduct
Dermal absorption of in-use dilution	0.10%		i_AbsorpInuse
Oral absorption	20.00%		i_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm²	d_DFR
Exposure duration dermal	2	hours	d_ReExpDur
Light clothing adjustment factor Adult resident	18.0%		d_ClothAF
Drift percentage on surface	100.00%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm²/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm²	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm²	d_MouthGrass

Table A 342-16: Estimation of recreational exposure for invasive species in non-agricultural areas (EFSA Model)

2. Details

	Systemic exposure [mg a.s./day]	Systemic exposure [mg a.s./kg bw/day]	Formula	Comments
1-3 year old child				
Surface deposits				
Dermal	0.0046800	0.0004680	(i_AppRate/100)*C13*d_Turf*d_ReTCCh*d_ReExpDur*MAX(i_AbsorpProduct,i_AbsorpInuse)*d_MAF)	
Hand to mouth	0.0342000	0.0034200	(i_AppRate/100)*C13*d_Turf*d_SalExt*d_AreaHM*d_ReFreqHM*d_ReExpDur*i_AbsorpOralInuse*d_MAF	
Object to mouth	0.0180000	0.0018000	(i_AppRate/100)*C13*d_DRP*d_MouthGrass*i_AbsorpOralInuse*d_MAF	
Total systemic exposure	0.0568800	0.0056880		
% of RVNAS		5.69%		
Adult				
Surface deposits (dermal)	0.0131400	0.0002190	(i_AppRate/100)*C13*d_Turf*d_ReTCAd*d_ReExpDur*MAX(i_AbsorpProduct,i_AbsorpInuse)*d_MAF	
% of RVNAS		0.22%		

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A 1.3 Worker exposure calculations

Table A 353-1: Input parameters considered for the estimation of worker exposure in bare soil

Worker exposure from residues on foliage for MON 52276			
Crop type	Bare soil		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	NA		
Main body parts in contact with foliage	NA		
Application rate of active substance	1.44	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	0.69%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	4.32	µg a.s./cm²	*d_DFR*
Working hours	NA	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	NA	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	NA	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	NA	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

Table A 363-2: Estimation of worker exposure towards Glyphosate in bare soil (EFSA Model)

Not relevant

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)				NA for treatment of bare soil
Total systemic exposure per kg body weight (mg/kg bw/day)				
% of RVNAS				

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Table A 373-3: Input parameters considered for the estimation of worker exposure in vegetables

Worker exposure from residues on foliage for MON 52276

Crop type	Fruiting vegetables		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Reaching, picking		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	1.08	kg a.s./ha	i_AppRate
Number of applications	2		i_AppNo
Interval between multiple applications	28	days	i_AppInt
Half-life of active substance	30	days	d_HalflifeAS
Multiple application factor	1.5		d_MAF
Dermal absorption of the product	0.10%		i_AbsorpProduct
Dermal absorption of the in-use dilution	0.69%		i_AbsorpInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	3.24	µg a.s./cm^2	d_DFR
Working hours	8	hr	d_WorkHr
Dermal transfer coefficient - Total potential exposure	5800	cm^2/hr	d_DermTcUCV
Dermal transfer coefficient - arms, body and legs covered	2500	cm^2/hr	d_DermTcCV1
Dermal transfer coefficient - hands, arms, body and legs covered	580	cm^2/hr	d_DermTcCV2
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	d_InhalTcAut
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	d_InhalTcCut
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	d_InhalTcSort

Table A 383-4: Estimation of worker exposure towards Glyphosate in vegetables (EFSA Model)

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	1.5805071	0.6812531	0.1580507	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0263418	0.0113542	0.0026342	
% of RVNAS	26.34%	11.35%	2.63%	

2. Details

	Systemic exposure [mg a.s. /day]	Systemic exposure [mg a.s./kg bw/day]	Formula	Comments
Dermal - Potential	1.5805071	0.0263418	d_DermTcUCV*d_WorkHr*i_DFR*i_MAF/1000*i_AbsorpInuse	
Dermal - Work wear - arms, body and legs covered	0.6812531	0.0113542	d_DermTcCV1*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse	
Dermal - Working wear and gloves	0.1580507	0.0026342	d_DermTcCV2*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse	
Inhalation				Na for outdoor activities

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Table A 393-5: Estimation of worker exposure towards Glyphosate in orchards (EFSA Model)

Worker exposure - Glyphosate		
Orchards/Grapes		
AOEL	mg/kg bw/d	0.1
Application rate	kg as/ha	1.44
DFR	µg/cm2	3
MAF		1.523647
Dermal absorption	%	1%
Time	h	2
Body weight	kg	60
TC (potential exposure)	cm2/h	12500
TC (work wear)	cm2/h	1400
TC (work wear + gloves)	cm2/h	NA
t1/2	d	30
λ		0.023105

Potential exposure	
SDE	**%AOEL**
0.018923697	18.92

Work wear	
SDE	**%AOEL**
0.002119454	2.12

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Table A 403-6: Estimation of worker exposure towards Glyphosate in vines (EFSA Model)

Worker exposure - Glyphosate		
Orchards/Grapes		
AOEL	mg/kg bw/d	0.1
Application rate	kg as/ha	1.44
DFR	µg/cm2	3
MAF		1.523647
Dermal absorption	%	1%
Time	h	2
Body weight	kg	60
TC (potential exposure)	cm2/h	12500
TC (work wear)	cm2/h	1400
TC (work wear + gloves)	cm2/h	NA
t1/2	d	30
λ		0.023105

Potential exposure	
SDE	**%AOEL**
0.018923697	18.92

Work wear	
SDE	**%AOEL**
0.002119454	2.12

Table A 413-7: Input parameters considered for the estimation of worker exposure in railroad tracks

Worker exposure from residues on foliage for MON 52276			
Crop type	Bare soil		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	NA		
Main body parts in contact with foliage	NA		
Application rate of active substance	1.8	kg a.s./ha	*i_AppRate*
Number of applications	2		*i_AppNo*
Interval between multiple applications	90	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.1		*d_MAF*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	0.69%		*i_Absorpinuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm^2	*d_DFR*
Working hours	NA	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	NA	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	NA	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	NA	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

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Table A 423-8: Estimation of worker exposure towards Glyphosate in railroad tracks (EFSA Model)

Not relevant

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)				NA for treatment of bare soil
Total systemic exposure per kg body weight (mg/kg bw/day)				
% of RVNAS				

2. Details

	Systemic exposure [mg a.s. /day]	[mg a.s./kg bw/day]	Formula	Comments
Dermal - Potential	#VALUE!		*d_DermTcUCV*d_WorkHr*d_DFR*i_MAF/1000*i_AbsorpInuse*	
Dermal - Work wear - arms, body and legs covered	#VALUE!		*d_DermTcCV1*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse*	
Dermal - Working wear and gloves	NA		*d_DermTcCV2*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse*	
Inhalation				Na for outdoor activities

Table A 433-9: Input parameters considered for the estimation of worker exposure for invasive species in non-agricultural areas

Worker exposure from residues on foliage for MON 52276			
Crop type	Golf course turf or other sports lawns		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Manual-Knapsack		
Worker's task	Maintenance		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	1.8	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	0.10%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm^2	*d_DFR*
Working hours	8	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	5800	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	2500	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	580	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

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Table A 443-10: Estimation of worker exposure towards Glyphosate for invasive species in non-agricultural areas (EFSA Model)

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0.2505600	0.1080000	0.0250560	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0041760	0.0018000	0.0004176	
% of RVNAS	4.18%	1.80%	0.42%	

2. Details

	Systemic exposure [mg a.s. /day]	Systemic exposure [mg a.s./kg bw/day]	Formula	Comments
Dermal - Potential	0.2505600	0.0041760	*d_DermTcUCV*d_WorkHr*i_DFR*i_MAF/1000*i_AbsorpInuse*	
Dermal - Work wear - arms, body and legs covered	0.1080000	0.0018000	*d_DermTcCV1*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse*	
Dermal - Working wear and gloves	0.0250560	0.0004176	*d_DermTcCV2*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse*	
Inhalation				Na for outdoor activities

Table A 453-9: Input parameters considered for the estimation of worker exposure for invasive species in agricultural areas

Worker exposure from residues on foliage for MON 52276			
Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Manual-Knapsack		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	1.8	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	0.10%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	0.10%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	5.4	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting, bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

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Table A 463-10: Estimation of worker exposure towards Glyphosate for invasive species in agricultural areas (EFSA Model)

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0.1350000	0.0151200	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0022500	0.0002520		
% of RVNAS	2.25%	0.25%		

2. Details

	Systemic exposure [mg a.s. /day]	Systemic exposure [mg a.s./kg bw/day]	Formula	Comments
Dermal - Potential	0.1350000	0.0022500	*d_DermTcUCV*d_WorkHr*i_DFR*i_MAF/1 000*i_AbsorpInuse*	
Dermal - Work wear - arms, body and legs covered	0.0151200	0.0002520	*d_DermTcCV1*d_WorkHr*d_DFR*d_MAF/ 1000*i_AbsorpInuse*	
Dermal - Working wear and gloves	no TC available for this assessment		*d_DermTcCV2*d_WorkHr*d_DFR*d_MAF/ 1000*i_AbsorpInuse*	
Inhalation				Na for outdoor activities

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