Renewal Assessment Report
under Regulation (EU) No 1107/2009

TRINEXAPAC-ETHYL
Trinexapac-ethyl 250 g/L ME

Volume 3 – B.6 (PPP)
Toxicology and metabolism data and assessment of risks for humans

Rapporteur Member State: Lithuania
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B.6. TOXICOLOGY AND METABOLISM DATA AND ASSESSMENT OF RISKS FOR HUMANS

B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT

Trinexapac-ethyl 250 g/L ME (A8587F) is a micro-emulsion (ME) containing 250 g/L trinexapac-ethyl for use as a plant growth regulator in field crops. A8587F was not a representative product during the previous EU review process of trinexapac-ethyl resulting in the Annex I to Directive 91/414/EEC inclusion of this active substance. The representative formulation of the 91/414/EEC review was MODDUS 250 EC (A-7225M), a 250 g/L emulsifiable concentrate of trinexapac-ethyl.

The toxicological studies (i.e., acute oral and dermal toxicity, skin and eye irritation studies) have been performed with the formulation A8587B (also named as CGA163935 ME 250). The acute inhalation and skin sensitisation studies have been conducted on A8587F.

An assessment of the similarity of the formulations has been provided by the notifier. Information on the detailed composition of the precursor formulation A8587B and the representative formulation A8587F can be found in the volume 4. It is concluded by RMS that these formulations could be considered similar with regards to acute toxicity and irritation. The results from the acute oral and dermal toxicity, skin and eye irritation studies with A8587B can be bridged to the formulation A8587F.

B.6.1.1. Oral toxicity

Previous evaluation	**A new study submitted for the purpose of renewal.**

Report:	Hartmann H, 1991, CGA163935 ME 250 (A8587B): Acute Oral Toxicity In The Rat. Experimental Toxicology, CIBA-GEIGY Ltd., 4332 Stein, Switzerland. Laboratory Report No. 901522, issue date 14 February 1991. Unpublished. (Syngenta File No. CGA16935/0107)

GUIDELINES: Acute Oral Toxicity (rat) OECD 401 (1987): OPPTS 870.1100 (2002).

NB. Acute oral OECD 401 was deleted 17th December 2002 and replaced by either 420 'Fixed Dose Method' or 425 'Up-and-Down Procedure'

GLP: Signed and dated GLP and Quality Assurance statements were provided.

There were no deviations from the regulatory guideline considered to compromise the scientific validity of the study.

EXECUTIVE SUMMARY

In an acute oral toxicity study, groups of fasted, 6-8 week old, Tif: RAI f (SPF) rats *(*5/sex*)* were given a single oral dose of CGA163935 ME 250 (A8587B) in distilled water at a dose of 3000 mg/kg bw and observed for 14 days.

Piloerection, abnormal body positions, exophthalmos, and dyspnea were seen, being common symptoms in acute tests. Additionally, reduced locomotor activity and respiratory sounds were noticed in all animals. Ataxia was seen in the males one hour after administration.

The animals recovered within 5 to 6 days.

At autopsy, no deviations from normal morphology were found.

The acute oral LD_{50} to males and females is in excess of 3000 mg/kg bw (limit dose, no mortalities), therefore no classification is required for acute oral toxicity of A8587F according to Regulation (EC) No 1272/2008 as amended.

MATERIALS AND METHODS

Materials:

Test Material:	CGA163935 ME 250 (A8587B)
Description:	Formulation, liquid
Lot/Batch number:	P.010001
Purity:	Not reported
CAS#:	Not reported
Stability of test compound:	Reanalysis date: October 1992

Vehicle and/or positive control: Distilled water.

Test Animals:	
Species	Rat
Strain	Tif: RAI f (SPF)
Age/weight at dosing	6-8 weeks / 178-236 g
Source	CIBA-GEIGY Limited, Animal Production, 4332 Stein, Switzerland
Housing	5 per cage (sexes separately) in Macrolon cages type 4
Acclimatisation period	At least 5 days
Diet	NAFAG 890 Tox *ad libitum* (except overnight prior to dosing)
Water	Water *ad libitum*
Environmental conditions	Temperature: 22 ± 2°C Humidity: 55 ± 10% Air changes: approximately 15 per hour Photoperiod: 12 hours light / 12 hours dark

Study Design and Methods:

In-life dates: Start: 8 January 1991 End: 5 February 1991

Animal assignment and treatment: In an acute oral toxicity study, 5 male and 5 female fasted 6-8 week old Tif: RAI f (SPF) rats were given a single oral dose of 3000 mg/kg of CGA163935 ME 250 (A8587B) by gavage. The test substance was diluted in vehicle (distilled water) and dosed at a volume of 10 ml/kg bodyweight.

All animals were examined for mortality twice daily on working days and once daily at weekends. Clinical signs were recorded once daily for 14 days. Body weights were recorded on day 1 (immediately prior to administration) and on days 7 and 14. All animals were necropsied and examined macroscopically.

Statistics: The acute oral LD_{50} was estimated (limit dose, no mortalities).

RESULTS AND DISCUSSION

Mortality: There were no mortalities.

Clinical observations: Piloerection, abnormal body positions, exophthalmos, and dyspnea were seen, being common symptoms in acute tests. Additionally, reduced locomotor activity and respiratory sounds were noticed in all animals. Ataxia was seen in the males one hour after administration. The animals recovered within 5 to 6 days.

Bodyweight: There was no effect on bodyweight.

Necropsy: At autopsy, no deviations from normal morphology were found.

CONCLUSION: The acute oral LD_{50} (to males and females) of CGA163935 ME 250 (A8587B) is in excess of 3000 mg/kg bw (limit dose, no mortalities), therefore no classification is required for acute oral toxicity of A8587F according to Regulation (EC) No 1272/2008 as amended.

(Hartmann H, 1991)

RMS comments:

The study follows the OECD TG 401 (1987) Limit Test conditions. The Certificate of Analysis corresponding of tested A8587B Bach No P.010001 was submitted on request.

The study is acceptable.

RMS conclusion:

The acute oral LD_{50} of the test substance CGA163935 ME 250 (A8587B) in rats of both sexes was > 3000 mg/kg bw (limit dose). No classification is required for acute oral toxicity of A8587B according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No.1272/2008 on the basis of this test result.

B.6.1.2. Dermal toxicity

Previous evaluation	**A new study submitted for the purpose of renewal.**

Report:	Hartmann H, 1991a. CGA163935 ME 250 (A8587B): Acute Dermal Toxicity In The Rat. Experimental Toxicology, CIBA-GEIGY Ltd., 4332 Stein, Switzerland. Laboratory Report No. 901525, issue date 11 February 1991. Unpublished. (Syngenta File No.CGA16935/0106)

GUIDELINES: Acute Dermal Toxicity (rat) OECD 402 (1987): OPPTS 870.1200 (1998): 92/69/EEC B.3 (1992)

GLP: Signed and dated GLP and Quality Assurance statements were provided.

There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

EXECUTIVE SUMMARY

In an acute dermal toxicity study, groups of 7-8 week old, Tif: RAI f (SPF) rats *(*5/sex*)* were given a single dermal application of undiluted CGA163935 ME 250 (A8587B) at a dose of 4000 mg/kg bw and observed for 14 days.

Piloerection, abnormal body positions, and dyspnea were seen, being common symptoms in acute dermal tests. Additionally, reduced locomotor activity and trismus was observed during the application day. The animals recovered within 5 days.

At autopsy, no deviations from normal morphology were found.

The acute dermal LD_{50} to males and females is in excess of 4000 mg/kg bw (limit dose, no mortalities), therefore no classification is required for acute dermal toxicity of A8587B according to Regulation (EC) No 1272/2008 as amended.

MATERIALS AND METHODS

Materials:

Test Material:	CGA163935 ME 250 (A8587B)
Description:	Formulation, liquid
Lot/Batch number:	P.010001
Purity:	Not reported
CAS#:	Not reported
Stability of test compound:	Reanalysis date: October 1992

Vehicle and/or positive control: None

Test Animals:	
Species	Rat
Strain	Tif: RAI f (SPF)
Age/weight at dosing	7-8 weeks / 207-231 g
Source	CIBA-GEIGY Limited, Animal Production, 4332 Stein, Switzerland
Housing	Individually in Macrolon cages type 3
Acclimatisation period	At least 5 days
Diet	NAFAG 890 Tox *ad libitum* (except overnight prior to dosing)
Water	Water *ad libitum*
Environmental conditions	Temperature: 22 ± 2°C Humidity: 55 ± 10% Air changes: approximately 15 per hour Photoperiod: 12 hours light / 12 hours dark

Study Design and Methods:

In-life dates: Start: 8 January 1991 End: 22 January 1991

Animal assignment and treatment: In an acute dermal toxicity study, a group of five male and five female (7-8 week old) Tif: RAI f (SPF) rats were given a single dermal dose of 4000 mg/kg of CGA163935 ME 250 (A8587B). Approximately 24 hours before treatment an area on the back of the rat of at least 10% of the body surface was shaved with an electric clipper. The required amount of the undiluted test substance was evenly dispersed on the skin at a rate of 10 ml/kg bodyweight. It was covered with a gauze-lined semi-occlusive dressing fastened around the trunk with an adhesive elastic bandage. After an exposure period of 24 hours the dressing was removed and the skin was cleaned with lukewarm water.

The animals were examined at least daily for mortality and clinical abnormalities during the study. Bodyweights were recorded immediately before application and on days 7 and 14. At the end of the scheduled observation period, all animals were necropsied and examined macroscopically.

Statistics: The dermal LD_{50} was estimated (limit dose, no mortalities).

RESULTS AND DISCUSSION

Mortality: There were no mortalities.

Clinical observations: Piloerection, abnormal body positions, and dyspnea were seen, being common symptoms in acute dermal tests. Additionally, reduced locomotor activity and trismus was observed during the application day. The animals recovered within 5 days.

Bodyweight: The bodyweight of the animals was within the range commonly recorded for this age and strain.

Necropsy: No macroscopic findings were observed at necropsy.

CONCLUSION: The acute dermal LD_{50} to males and females of CGA163935 ME 250 (A8587B) is in excess of 4000 mg/kg bw (limit dose, no mortalities), therefore no classification is required for acute dermal toxicity of A8587B according to Regulation (EC) No 1272/2008 as amended.

(Hartmann H, 1991a)

RMS comments:

The study follows the OECD TG 402 (1987) Limit Test conditions.

- Rat diet NAFAG 890 Tox and water were provided *ad libitum* according to the study report;
- the undiluted test substance was evenly dispersed on the skin at a rate of 4 ml/kg body weight according to the study report but not 10 ml/kg body weight;
- changes in body weight were not calculated and recorded in the study report. Should be noted that the body weight of males increased throughout the study period: body weight Day 0 - Day 7 increased 19.9% and Day 0 - Day 14 increased 38.9%, respectively. Whereas the body weight of females did not adequately increase during the first post exposure week (i.e. body weight Day 0 - Day 7 increased 2.2%; body weight of one female decreased) and slightly increased during the second observation week (i.e. body weight Day 0 - Day 14 increased 6.3%). The probable cause for the lack of increased body was not considered in the study report.
- The Certificate of Analysis corresponding of tested A8587B Bach No P.010001 was submitted on request.

The study is acceptable.

RMS conclusion:

The acute dermal LD_{50} of the test substance CGA163935 ME 250 (A8587B) in rats of both sexes was > 4000 mg/kg bw (limit dose). No classification is required for acute dermal toxicity of A8587B according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No.1272/2008 on the basis of this test result.

B.6.1.3. Inhalation toxicity

Previous evaluation	**A new study submitted for the purpose of renewal.**

Report:	Beebe D, 2016. Trinexapac-ethyl ME (250) (A8587F) - acute (four hour) inhalation study in rats. Envigo CRS Ltd, Huntingdon, Cambridgeshire, UK. Laboratory Report No. KH71 WS. Issue date 29 March 2016. Unpublished. (Syngenta File No. A8587F_10528)

GUIDELINES: Acute Inhalation Toxicity (rat) OECD 403 (2009)

GLP: Signed and dated GLP and Quality Assurance statements were provided.

There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

EXECUTIVE SUMMARY

The objective of this study was to investigate the acute inhalation toxicity of A8587F to male and female RccHan^{TM}: WIST rats in a single 4-hour exposure followed by a 14 day observation period.

The study design included a preliminary exposure of a single 4-hour exposure targeted at 5.0 mg/L to two male and two female animals and the main exposure of a single 4-hour exposure targeted at 5.0 mg/L to five male and five female animals followed by a 14 day observation period.

The achieved test atmosphere had the following characteristics:

Target concentration mg/l	**Achieved particulate concentration mg/L**	**MMAD* µm**	**GSD^{+}**
5	5.45	2.5	2.41

* Mass Median Aerodynamic Diameter (µm)
$^{+}$ Geometric Standard Deviation

The time weighted average mean aerosol concentration was close to target. The individual and mean calculated MMAD values were within the guideline expected range of 1 to 4 microns for the main study animals.

There were no unscheduled deaths in the preliminary or main exposures.

Clinical signs for the majority of animals immediately after exposure included wet rales with chin rubbing evident for one animal of each sex and irregular breathing apparent for one female. The signs observed at the end of exposure were generally present at the 1 hour and 2 hour post exposure and end of day checks and were accompanied by partially closed eyelids and irritable behaviour for a proportion of animals. Wet or dry rales were present for all animals on Day 2 and persisted up to Day 7 for some animals with males recovering slower when compared with females. Irregular breathing was observed for one animal of each sex at the initial check on Day 8; all animals were considered normal from the end of day check on Day 8 onwards.

Group mean weight loss was evident for both sexes on Day 2. A small increase in group mean body weight was apparent for females on Day 4 but further loss was observed for males. Increased group mean body weight was evident for both sexes from Day 8 of the observation period onwards.

Enlargement of the tracheobronchial lymph nodes was observed in one male and one female. The incidence and distribution of the other findings were consistent with the common background changes seen at these laboratories.

Under the conditions of this study the LC_{50} (4 hour) of A8587F is in excess of 5.45 mg/L for male and female rats.

MATERIALS AND METHODS

Materials:

Test Material:	A8587F (Trinexapac-ethyl ME (250)
Description:	Liquid
Lot/Batch number:	SMO4L0116
Purity:	25.3% w/w trinexapac ethyl
CAS#:	Not given
Stability of test compound:	Store at ambient temperature; expires 30th November 2018

Vehicle and/or positive control: The sample was tested as supplied.

Test Animals:

Species	Rat
Strain	RccHan™: WIST
Age/weight at dosing	Young adult; 9-10 weeks at start of treatment 257-296 g (males); 160-213 g (females) at the start of exposure
Source	Envigo RMS (UK) Ltd
Housing	Animals were housed 5 per cage according to sex in polycarbonate body cages with a stainless steel mesh lid.
Acclimatisation period	12 days
Diet	Teklad 2014C diet available *ad libitum* except during exposure.
Water	Mains water *ad libitum* except during exposure.
Environmental conditions	Temperature: 22 ± 3°C Humidity: 40-70% Air changes: Filtered fresh air was passed through atmosphere and not recirculated. Photoperiod: 12 hours light / 12 hours dark

Study Design and Methods:

In-life dates: Start: 16th February 2016 End: 1st March 2016

Exposure conditions: Animals were exposed for a period of 4 hours to the test item restrained in a polycarbonate snout-only restraint tube.

Animal assignment and treatment: In view of the limited data toxicity available, and as allowed for in the regulatory guidelines a preliminary exposure, using 2 male and 2 female rats, was conducted. A target exposure level of 5.0 mg/L for a period of 4-hours was administered in order to assess the likely response of rats to the test substance. As an exposure level of 5.1 mg/L was tolerated by the preliminary animals with no mortality, the main study test animals were also exposed to the target exposure level of 5.0 mg/L for a period of 4-hours. All animals were exposed to the test item via snout only exposure.

Table 6.1.3-1: Mortality / animals treated

Target exposure concentration mg/*l*	Mortality (Number dead / total)		
	Males	**Females**	**Combined**
5	0/5	0/5	0/10

Generation of the test atmosphere / chamber description: The test atmosphere was generated using a stainless steel concentric jet atomiser, designed to produce and maintain an atmosphere containing a high proportion of respirable droplets. The test item was supplied to the generator via a polyethylene feed line, driven

at a constant rate from an infusion pump. The exposure system was a flow through snout only chamber- an aluminium construction comprising a base unit, animal exposure section and a top section.

Test atmosphere concentration: A minimum of 6 samples of the test atmosphere were collected per exposure at irregular intervals. Aerosol samples were collected using a glass microfiber filter from the animal exposure port and analysed gravimetrically.

Particle size determination: The particle size distribution was determined with a Marple 298 cascade impactor using stainless steel substrates and a glass microfibre backup filter.

Two samples were collected per exposure. The MMAD and σg were derived.

Table 6.1.3-2: Summary of acute study test atmosphere characteristics

Parameter	Target concentration 5 mg/l
Measured particulate concentration	5.45 ± 0.382 mg/L
Nominal concentration	11 mg/L
Particle size MMAD; GSD (mean)	2.5 µm; 2.41
Size range (Effective cut-off diameter µm)	% by weight
Particles 21.3 µm (% w/w)	1.1
Particles 14.8 µm (% w/w)	0.5
Particles 9.80 µm (% w/w)	2.9
Particles 6.00 µm (% w/w)	13.0
Particles 3.50 µm (% w/w)	22.6
Particles 1.55 µm (% w/w)	21.3
Particles 0.93 µm (% w/w)	21.1
Particles 0.93µm (% w/w)	15.3
Filter - Particles <0.93µm (% w/w)	2.2
Flow rate (whole system)	20 L/min
Temperature	20.5-21.2°C
Humidity	50.4- 55.8%

Statistics: The acute inhalation LC_{50} was estimated (limit test, no mortalities).

RESULTS AND DISCUSSION

Mortality: There were no unscheduled deaths in the preliminary or main exposures.

Clinical observations: Clinical signs for the majority of animals immediately after exposure included wet rales with chin rubbing evident for one animal of each sex and irregular breathing apparent for one female. The signs observed at the end of exposure were generally present at the 1 hour and 2 hour post exposure and end of day checks and were accompanied by partially closed eyelids and irritable behaviour for a proportion of animals. Wet or dry rales were present for all animals on Day 2 and persisted up to Day 7 for some animals with males recovering slower when compared with females. Irregular breathing was observed for one animal of each sex at the initial check on Day 8; all animals were considered normal from the end of day check on Day 8 onwards.

Red staining to the head and/or muzzle observed for a proportion of animals and wet fur, observed for all animals, is considered to be a consequence of tube restraint during exposure and is not a direct effect related to A8587F exposure.

Bodyweight: Group mean weight loss was evident for both sexes on Day 2. A small increase in group mean body weight was apparent for females on Day 4 but further loss was observed for males. Increased group mean body weight was evident for both sexes from Day 8 of the observation period onwards.

Necropsy: Enlargement of the tracheobronchial lymph nodes was observed in one male and one female. The incidence and distribution of the other findings were consistent with the common background changes seen at these laboratories.

CONCLUSION: Under the conditions of this study the LC50 (4 hour) of A8587F is in excess of 5.45 mg/L for male and female rats.

(Beebe D, 2016)

RMS comments:

After the consultations with RMS the acute inhalation study was submitted whereas the notifier couldn't justify an alternative approach under Regulation (EC) No 1272/2008, i.e. acute inhalation toxicity of all components couldn't be provided or reliably predicted with validated methods.

The study follows the OECD TG 403 (2009) Limit Test conditions.

Should be noted that A8587B contains the co-formulant at sufficiently high concentration (>50 % w/w) which is self-classified as STOT SE 3 H335 "May cause respiratory irritation". Thought there aren't currently validated animal tests that deal specifically with respiratory tract irritation (RTI), this study provides some information in terms of clinical signs of RTI, i.e. wet and dry rales were present for all animals. All animals were only subject to a macroscopic examination which consisted of opening the cranial, thoracic and abdominal cavities. However, additional microscopic examination of the respiratory tract to provide evident of irritation (e.g. hyperaemia, oedema minimal inflammation, thickened mucous layer) was not performed. RTI is generally limited to local cytotoxic effects which induce tissue changes at the site of contact and these changes can be detected by pathological methods. On the other hand all these specific clinical signs observed were reversible from the end of Day 8.

The study is acceptable.

RMS conclusion:

Under the experimental conditions, the acute inhalation LC_{50} of formulation A8587B is greater than 5.45 mg/L air/4h (nose only) in rats of both sexes. Classification is not required according to Regulation (EC) No 1272/2008. Taking all considerations mentioned above the hazard statement **H335** "May cause respiratory irritation" is recommended for the representative formulation A8587B.

B.6.1.4. Skin irritation

Previous evaluation	**A new study submitted for the purpose of renewal.**

Report:	Hagemann C 1991. Acute Dermal Irritation/Corrosion Study in the Rabbit: CGA163935 ME 250 (A8587B). Experimental Toxicology, CIBA-GEIGY Limited, 4332 Stein, Switzerland. 901524. 21 February 1991 Unpublished. (Syngenta File No. CGA163935/0084)

GUIDELINES: Primary Dermal Irritation (rabbit) OECD 404 (2002): OPPTS 870.2500 (1998): 2004/73/EC B.4 (2004)

GLP: Signed and dated GLP and Quality Assurance statements were provided.

There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

EXECUTIVE SUMMARY

In a primary dermal irritation study, three young male New Zealand White rabbits were dermally exposed to 0.5 ml of CGA163935 ME 250 (A8587B) for 4 hours to a shaved area of the flank. Animals then were observed for 10 days. The irritant/corrosive potency of CGA163935 ME 250 (A8587B) was classified according to the Commission Directive83/467/EEC.

Under the experimental conditions employed CGA163935 ME 250 (A8587B) induced erythema and edema reactions when applied to the clipped albino rabbit skin.

Because the mean values of the recordings 24 to 72 hours after application are below the threshold of significance (2 score for erythema or oedema) CGA163935 ME 250 (A8587B) can be classified as non-irritant according to the Regulation (EC) No 1272/2008 as amended, therefore, no classification is required for skin irritating properties of A8587B.

MATERIALS AND METHODS

Materials:

Test Material:	CGA163935 ME 250 (A8587B)
Description:	Formulation, liquid.
Lot/Batch number:	P.010001
Purity:	Not reported
CAS#:	Not reported
Stability of test compound:	Not reported

Vehicle and/or positive control: Before application, the gauze patches (test and control) were moistened with distilled water.

Test Animals:

Species	Rabbit
Strain	New Zealand White (Chbb: NZW)
Age/weight at dosing	Approximately 9-13 weeks; 2430 – 2500 g
Source	Dr. K. Thomae GMBH, Chemisch-pharmazeutische Fabrik D-7950 Biberach/Riss
Housing	Individually in metal cages
Acclimatisation period	At least 5 days
Diet	Nafag No. 814 standard rabbit pellet diet *ad libitum*
Water	Mains water *ad libitum*
Environmental conditions	Temperature: 20±3°C Humidity: 30-70% Air changes: Not reported Photoperiod: 12 hours light; 12 hours darkness

Study Design and Methods:

In-life dates: Start: 15 January 1991 End: 25 January 1991

Animal assignment and treatment: In a primary dermal irritation study, three young male New Zealand White rabbits were dermally exposed to 0.5 ml of CGA163935 ME 250 (A8587B) for 4 hours to a shaved area of the flank.

An area of at least 36 cm^2 was shaved on both flanks of the animals approximately 24 hours before treatment. A gauze patch (approx.12-16 cm) bearing 0.5 ml of the test article was applied to the right flank of each animal. A control gauze patch was applied to the contralateral flank. Both patches were moistened before application with distilled water.

The patches were loosely covered with an aluminium foil (approx.36 cm^2) and held in place for 4 hours by an adhesive tape.

The animals were checked daily for systemic symptoms and mortality.

The skin reactions were evaluated 1, 24, 48, and 72 hours, 7 and 10 days after removing the gauze patches. The irritant/corrosive potency of CGA163935 ME 250 (A8587B) was classified according to the Commission Directive83/467/EEC.

RESULTS AND DISCUSSION

Because reactions were observed within 72 hours after removing the bandages, the observation period was extended to 10 days to determine the reversibility of the skin reactions.

Scaling was seen in all animals on day 3, and in two animals up to day 7.

A minimal loss of weight considered not to be an effect of the test article was observed on day 3 in two animals.

According to the EEC classification of the results obtained 24 to 72 hours after removing the bandages CGA163935 ME 250 (A8587B) can be classified as non-irritant in albino rabbits.

The skin reactions observed were reversible until the end of the observation period on day 10.

Table 6.1.4–1: Individual and mean skin irritation scores of CGA163935 ME 250 (A8587B)

Time	**Erythema**			**Oedema**		
Animal number	**597**	**547**	**573**	**597**	**547**	**573**
after 1 hour	1	2	1	1	1	1
after 24 hours	2	2	2	1	2	1
after 48 hours	1	2	1	1	1	0
after 72 hours	1s	1s	1s	1	0	0
mean score 24-72 h	1.33	1.67	1.33	1	1	0.33
after 7 days	0s	1s	0	0	0	0
after 10 days	0	0	0	0	0	0

S = scaling

CONCLUSION: Because the mean values of the recordings 24 to 72 hours after application are below the threshold of significance (2 score for erythema or oedema) CGA163935 ME 250 (A8587B) can be classified as non-irritant according to the Regulation (EC) No 1272/2008 as amended, therefore, no classification is required for skin irritating properties of A8587B.

(Hagemann C, 1991)

RMS comments:

The study follows the OECD TG 404 (adopted 12 May, 1981). After the study was performed, the OECD Test Guideline TG 404 has been revised in 1992, 2002 and 2015. Furthermore: *New Guidance document on Integrated Approached to Testing and Assessment (IATA) for Skin Irritation/Corrosion (OECD GD No 203; 2014)* and several Test Guidelines on *in vitro* methods for skin corrosion/irritation have been published. The study doesn't fulfil these current scientific knowledge/data requirements.

- There is significant departure from the OECD TG 404 (1981): a quite big shaved area 36 cm^2 and gauze patch 12-16 cm^2 is reported in the study report. Usually a shaved area 2.5 x 2.5 cm is used and approximately application area 6 cm^2 is required in all versions of the OECD TG 404. The application area was about 2-2.7 times larger than the area requested by the test guidelines, whereas the standard dose 0.5 ml was applied. Consequently, the sensitivity of the test might be reduced due to the thinner layer of substance on the skin.
- Though it is recommended to use a gauze patch and semi-occlusive dressing, the gauze patches were covered with an aluminium foil (36 cm^2) and held in place by an adhesive non-specified tape.
- While there is significant departure from an OECD TG 404 (1981), the study could be considered only as supplementary element of weight of evidence approach according to OECD Guidance document No 203 (2014).
- None local signs of skin irritation were reported at 4000 mg/kg bw (10% of the body surface) in *Hartmann H.* study (1991a; OECD GD 402). On the other hand negative results from other *in vivo* dermal toxicity data for substance (i.e. OECD TG 402, OECD TG 406, and OECD TG 410) cannot justify a non-classification according to OECD Guidance document No 203 (2014).
- Skin irritation potential findings were reported from the submitted skin sensitization study (*OECD TG 406; Buehler - 9 inductions, Simon C., 2009*). Epidermal application of the 25/50/75% test substance preparation (6 hours) produced necrosis, fissures and erythema grade 3 in the screening study for epidermal induction. Epidermal application of the 5/10/15% test substance preparation (6 hours) produced mild-to-moderate irritation in the screening study for epidermal challenge.
- The mean values of ≥2.0 and ≥2.3 for erythema or oedema in at least 2 of 3 tested animals from grading at 24,48 and 72 hours after application are the threshold of significance in accordance with Directive 67/548/EEC and Regulation (EC) No.1272/2008, respectively.
- On the basis of this study with the A8587B, mean erythema scores of the three animals were 1.33-1.67-1.33 and the mean oedema scores were 1.0-1.0-0.33, respectively. All signs of skin irritation had gone by the day 10 reading. The A8587B should not be warranted classification for skin irritation in accordance with Regulation (EC) No 1272/2008. In view of the fact that the sensitivity of the test might be reduced and the mean erythema scores were quite close the classification limits, no evident conclusion on the classification can be drawn and the skin irritation potential could not be excluded according this single study.
- Considering the detailed composition of the representative formulation and the classification of all ingredients the RMS finds it justified not to classify the formulation as skin irritant due to the non-presence of skin irritants in the composition of this PPP except one co-formulant. The existing amount of it (~1% w/w) doesn't fulfil the criteria for classification of PPP according to Regulation (EC) No 1272/2008. Should be noted that the co-formulants were determined to be non-irritants/irritants based only on

information provided by the suppliers Safety Data Sheets.

- On the other hand A8587B contains the co-formulant at sufficiently high concentration (>50 % w/w) for which supplemental hazard information EUH066 "Repeated exposure may cause skin dryness or cracking" is assigned in accordance with MSDS. The skin irritating or sensitization studies are not completely appropriate for identification of such property. However, observations of scaling in the skin irritation study and of fissures/scaling in the skin sensitization study justify the assigning of this supplemental hazard information EUH066.
- The Certificate of Analysis corresponding of tested A8587B Bach No P.010001 was submitted on request.

The study is limited but accepted as supporting information regarding the skin effect of the A8587B.

RMS conclusion:

While there is significant departure from an OECD TG 404 (1981) the study is considered to be of supporting information and as supplementary element of weight of evidence approach according to OECD Guidance document on Integrated Approached to Testing and Assessment (IATA) for Skin Irritation/Corrosion (No 203; 2014). CGA163935 ME 250 (A8587B) does not warrant classification for skin irritation in accordance with Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No.1272/2008 on the basis of weight of evidence analysis. The supplemental hazard information **EUH066** "Repeated exposure may cause skin dryness or cracking" is recommended for the representative formulation A8587B.

B.6.1.5. Eye irritation

Previous evaluation	**A new study submitted for the purpose of renewal.**

Report:	Hagemann C 1991a. Acute Eye Irritation/Corrosion Study in the Rabbit: CGA163935 ME 250 (A8587B). Experimental Toxicology, CIBA-GEIGY Limited, 4332 Stein, Switzerland. 901523. 15 March 1991 Unpublished. (Syngenta File No. CGA163935/0090)

GUIDELINES: Primary Eye Irritation (rabbit) OECD 405 (2002): OPPTS 870.2400 (1998): 2004/73/EC B.5 (2004)

GLP: Signed and dated GLP and Quality Assurance statements were provided.

There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

EXECUTIVE SUMMARY

In a primary eye irritation study, 0.1 ml of CGA163935 ME 250 (A8587B) was instilled into the conjunctival sac of the left eye of each of three female New Zealand White rabbits, after gently pulling away the lower lid from the eyeball. The lids were then held together for about one second in order to prevent loss of the test article. The right eye remained untreated and served as a control.

The animals were checked daily for systemic symptoms and mortality.

The ocular reactions were evaluated 1, 24, 48, and 72 hours after the instillation of CGA163935 ME 250 (A8587B) according to the OECD scoring system. A slit-lamp was used to facilitate the evaluation. The

irritant/corrosive potency of CGA163935 ME 250 (A8587B) was classified according to the Commission Directive 83/467/EEC.

Because the mean values of the readings 24 to 72 hours after instillation are above the threshold of significance, CGA163935 ME 250 (A8587B) can be classified as irritant to the rabbit eye (H319), according to the Regulation (EC) No 1272/2008 as amended.

MATERIALS AND METHODS

Materials:

Test Material:	CGA163935 ME 250 (A8587B)
Description:	Formulation, liquid.
Lot/Batch number:	P.010001
Purity:	Not reported
CAS#:	Not reported
Stability of test compound:	Not reported

Vehicle and/or positive control: None

Test Animals:	
Species	Rabbit
Strain	New Zealand White (Chbb: NZW)
Age/weight at dosing	Approximately 9-13 weeks; 2210 – 2440 g
Source	Dr. K. Thomae GMBH, Chemisch-pharmazeutische Fabrik D-7950 Biberach/Riss
Housing	Individually in metal cages
Acclimatisation period	At least 5 days
Diet	Nafag No. 814 standard rabbit pellet *ad libitum*
Water	Mains water *ad libitum*
Environmental conditions	Temperature: 20±3°C Humidity: 30-70% Air changes: Not reported Photoperiod: 12 hours light; 12 hours darkness

Study Design and Methods:

In-life dates: Start: 26 February 1991 End: 8 March 1991

Animal assignment and treatment: In a primary eye irritation study, 0.1 ml of CGA163935 ME 250 (A8587B) was instilled into the conjunctival sac of the left eye of each of three female New Zealand White rabbits, after gently pulling away the lower lid from the eyeball. The lids were then held together for about one second in order to prevent loss of the test article. The right eye remained untreated and served as a control.

The animals were checked daily for systemic symptoms and mortality.

The ocular reactions were evaluated 1, 24, 48, 72 hours and 7 and 10 days after the instillation of CGA163935 ME 250 (A8587B) according to the OECD scoring system. A slit-lamp was used to facilitate the evaluation. The irritant/corrosive potency of CGA163935 ME 250 (A8587B) was classified according to the Commission Directive 83/467/EEC.

RESULTS AND DISCUSSION

No deaths occurred. No systemic signs of toxicity were noted during the study. All animals gained body weight throughout the study.

Because reactions were observed within 7 days after instillation of the test article, the observation period was extended to 10 days to determine the reversibility of the eye reactions.

Table 6.1.5–1: Eye irritation scores of CGA163935 ME 250 (A8587B)

Time	Cornea			Iris			Conjunctiva					
							Redness			Chemosis		
Animal number	**84**	**138**	**104**	**84**	**138**	**104**	**84**	**138**	**104**	**84**	**138**	**104**
after 1 hour	1	1	1	1	1	1	2	2	2	2	3	2
after 24 hours	2	1	2	1	0	1	3	2	2	1	1	1
after 48 hours	1	1	1	1	0	1	2	2	2	1	1	1
after 72 hours	1	1	1	0	0	1	1	2	2	0	1	1
mean scores 24-72h	1.33	1	1.33	0.67	0	1	2	2	2	0.67	1	1
after 7 days	0	0	1	0	0	0	1	1	1	0	0	0
after 10 days	0	0	0	0	0	0	0	0	0	0	0	0

CONCLUSION: Because the mean values of the readings 24 to 72 hours after instillation are above the threshold of significance, CGA163935 ME 250 (A8587B) can be classified as irritant to the rabbit eye (H319), according to the Regulation (EC) No 1272/2008 as amended.

(Hagemann C, 1991a)

RMS comments:

The study follows the OECD TG 405 (adopted 12 May, 1981). After the study was performed, the OECD TG 405 was updated in 1987, 2002, and 2012.

- The last updated versions include some recommendations (e.g. a stepwise testing approach, the use of analgesics and anaesthetics). The study doesn't fulfil these current data requirements.
- The Certificate of Analysis corresponding of tested A8587B Bach No P.010001 was submitted on request.

The study is acceptable.

RMS conclusion:

CGA163935 ME 250 (A8587B) does not warrant classification for eye irritation in accordance with Directive 67/548/EEC and subsequent regulations.

The mean irritation scores 24 to 72 hours after application were above the threshold for conjunctival redness (≥2) and corneal effects (≥1) defined in Regulation (EC) No. 1272/2008. Therefore, CGA163935 ME 250 (A8587B) does warrant classification as an eye irritant Eye Irrit. 2, **H319** "Causes serious eye irritation".

B.6.1.6. Skin sensitization

Previous evaluation	**A new study submitted for the purpose of renewal.**

Report:	Simon C, 2009. Trinexapac-ethyl ME (A8587F) – Contact Hypersensitivity in Albino Guinea Pigs, Buehler Test (9-induction). Harlan Laboratories Ltd, Füllinsdorf, Switzerland. Laboratory Report No. C17543. 22 January 2009. Unpublished. (Syngenta File No. A8587F_10024)

GUIDELINES: Dermal Sensitisation (guinea pig) OECD 406 (1992): OPPTS 870.2600 (2003): Council Regulation (EC) No 440/2008: Japanese MAFF 12 NohSan No. 8147 (2000)

GLP: Signed and dated GLP and Quality Assurance statements were provided.

There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

EXECUTIVE SUMMARY

The "Buehler Test" modified by Ritz, H.L. and Buehler, E.V. (1980) was used. Twenty male animals of the test group were treated topically with Trinexapac-ethyl ME (A8587F) at 100 % (undiluted) three times a week for a 3-week induction phase. Ten days after the final induction application the animals were challenged with the test item concentrations of 1 % and 0.5 % in purified water.

The ten animals of the control group were treated in the same way as the test group but with purified water only during the induction.

There were no deaths and no signs of systemic toxicity were observed in the animals.

Two out of twenty test animals were observed with discrete/patchy erythema at the 24-hour reading after the challenge treatment with trinexapac-ethyl ME (A8587F) at a concentration of 1 % in purified water. No skin reactions were noted in all animals treated with 0.5 % in purified water.

Based on the results of this study, trinexapac-ethyl ME (A8587F) is considered not to be a skin sensitizer in the guinea pig.

MATERIALS AND METHODS

Materials:

Test Material:	Trinexapac-ethyl ME (A8587F)
Description:	Liquid; clear to slightly turbid, yellow to reddish brown
Lot/Batch number:	SMO8H147
Purity:	trinexapac-ethyl 26.8% w/w
CAS#:	Not available.
Stability of test compound:	Stable under storage conditions. Reanalysis date: End of September 2011

Vehicle and/or positive control: Purified water

Purified water was prepared at Harlan Laboratories Ltd (deionised water which was processed and treated by the PURELAB Option-R unit. This latter links four purification technologies: reverse osmosis, adsorption, ion-exchange and photo oxidation).

Test Animals:

Species	Guinea pig
Strain	Albino Dunkin Hartley Guinea Pig, CRL:(HA)BR, SPF
Age/weight at dosing	5-6 weeks / Test and control animals: 317 - 376 g, animals used for irritation screen: 298 - 363 g
Source	Charles River Deutschland GmbH, Stolzenseeweg 32-36, D-88353 Kisslegg / Germany
Housing	Individually in Makrolon type-4 cages with standard softwood bedding ("Lignocel", Schill AG, 4132 Muttenz/Switzerland).
Acclimatisation period	6 days (control and test group)
Diet	Pelleted standard Provimi Kliba 3418, batch no. 55/08 guinea pig breeding / maintenance diet, containing Vitamin C (Provimi Kliba AG, 4303 Kaiseraugst/Switzerland), *ad libitum.*
Water	Community tap water from Füllinsdorf, *ad libitum*.
Environmental conditions	Temperature: 22 ± 3 °C Humidity: 30-70 % (values above 70 % during cleaning process possible)

Test Animals:

Air changes: 10-15 / h
Photoperiod: 12 hours light and 12 hours dark

Study Design and Methods:

In-life dates: Start: 15 October 2008 End: 19 November 2008

Animal assignment and treatment: The "Buehler Test" modified by Ritz, H.L. and Buehler, E.V. (1980) was used. Twenty male animals (albino Dunkin Hartley guinea pigs) of the test group were treated topically with Trinexapac-ethyl ME (A8587F) three times a week for a 3-week induction phase. Ten days after the final induction application the animals were challenged. The concentrations for the induction and the challenge were selected based on the results of two irritation screens.

The control animals were treated in the same way with the vehicle (purified water) only and also covered occlusively.

After the last induction exposure the animals were left untreated for 9 days.

The skin responses were graded approximately 24 hours after the patches have been removed.

Challenge: The animals previously exposed during the induction period (i.e. test group) as well as the previously only with the vehicle treated control animals were challenged 10 days after the last induction exposure using the test item at 1 % and 0.5 % in purified water. The exposure period was 6 hours on a naive skin site.

The skin responses were graded approximately 24 and 48 hours after the patches had been removed.

RESULTS AND DISCUSSION

Mortality / Clinical observations: There were no deaths during the course of the study, hence no necropsies were performed. No signs of systemic toxicity were observed in the animals.

Induction reactions and duration: After three weeks of induction, discrete/patchy to intense erythema with swelling, crusts and scaling was observed in all test animals after treatment with the test item at 100 %. No skin effect was observed in the control animals treated with purified water only during the induction phase.

Challenge reactions and duration: Two out of twenty test animals were observed with discrete/patchy erythema at the 24-hour reading after the challenge treatment with trinexapac-ethyl ME (A8587F) at the concentration of 1 % in purified water. No skin reactions were noted in all animals treated with 0.5 % in purified water.

Bodyweights: There were no treatment-related effects on body weight during the study.

Table 6.1.6-1: Buehler test: Number of animals with positive signs of allergic skin reactions following challenge

	Test flank			
	Challenge at 1%		**Challenge at 0.5%**	
Scored after:	24 hours	48 hours	24 hours	48 hours
Main test – test group	2/20	0/20	0/20	0/20
Main test – negative vehicle control	0/10	0/10	0/10	0/10

Positive control: Seventy percent of the test animals were observed with discrete/patchy to moderate/confluent erythema after the challenge treatment performed with alpha-hexylcinnamaldehyde at a concentration of 3 % in PEG 300. Ten % of the test animals were observed with discrete/patchy erythema at the 24-hour reading after the challenge treatment performed with alpha-hexylcinnamaldehyde at a concentration of 1 % in PEG 300. All animals of the control group (representing 0% of the group) remained completely free of local signs following the challenge treatment. This demonstrates the sensitivity of the strain of animals used and the reliability of the experimental technique.

CONCLUSION: Based on the results of this study, trinexapac-ethyl ME (A8587F) is considered not to be a skin sensitizer in the guinea pig.

(Simon C, 2009)

RMS comments:

The study follows the OECD TG 406 (adopted 17 July, 1992) and Council Regulation (EC) No 440/2008 B.6. by using a Buehler assay with 9 induction applications. The positive response in the positive control study with alpha-hexylcinnamaldehyde Technical (HCA) validates the test system used in this study.

- The inadequate concentration of test substance for induction exposure was used. Epidermal application of the 25/50/75% test substance preparation (6 hours) produced necrosis, fissures and erythema grade 3 in the screening study for epidermal induction. However, the highest test item concentration of 100% was chosen for the induction phase. Consequently, intense erythema grade 3 with swelling, crusts and scaling was observed in most of test animals during induction.
- The use of the two concentrations1% & 0.5% of A8587F (instead of 1% alone) for challenge was not clarified.
- The allowable max temperature 23°C of the experimental animal room according to OECD TG was exceeded (22±3°C).
- According to Commission Regulation EU No 284/2013, the local lymph node assay (LLNA) is prescribed as the appropriate test to address skin sensitization. However it is specified that where a guinea pig assay (Maximisation or Buehler), meeting OECD guidelines and providing a clear result, is available, further testing shall not be carried out for animal welfare reasons.

The study is limited but accepted.

RMS conclusion:

Based on the sensitisation rate of 10% (below the threshold of significance 15%) following challenge with 1% test material, Trinexapac-ethyl 250 g/L ME (A8587F) does not warrant classification as a skin sensitiser in accordance with Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No.1272/2008.

B.6.1.7. Supplementary studies on the plant protection product

No studies submitted by the notifier.

B.6.1.8. Supplementary studies for combinations of plant protection products

Trinexapac-ethyl 250 g/L ME (A8587F) does not contain recommendations for combinations of this product with other plant protection products and/or with adjuvants as a tank mix. For this reason, supplementary studies are not required and not submitted by the notifier for Trinexapac-ethyl 250 g/L ME (A8587F).

B.6.2. DERMAL ABSORPTION

No experimental data on dermal absorption of trinexapac-ethyl in A8587F have been generated therefore worst case, default dermal absorption values have been assumed in accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2012; 10(4):2665). As stated in the Guidance (section 6): "a default dermal absorption value of 25% may be applied for products containing >5% (50 g/kg for solids or 50 g/L for liquids) active substance. A default dermal absorption value of 75% should be used for products or in use dilutions containing <5% active substance." Thus, using of the recommended default dermal absorption values of 25% for the concentrate and 75% for the in use dilution is considered appropriate in view of the concentrations of the active substance in the representative formulation (250 g/L trinexapac-ethyl corresponding to 27.5% w/w) and in the spray dilution (max. 2 g a.s/L corresponding to 0.2%) according to the critical GAP use of Trinexapac-ethyl 250 g/L ME (A8587F).

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

CONFIDENTIAL information – data provided in Volume 4.

Copies of the Safety Data Sheets for the other components of the formulation have been included in the dossier.

B.6.4. EXPOSURE DATA

Trinexapac-ethyl 250 g/L ME (A8587F) is a micro-emulsion formulation (ME) containing 250 g/L trinexapac-ethyl. A8587F is applied with a single foliar application between BBCH 25 and 49 in winter barley and winter wheat or between BBCH 25 and 37 in spring barley as a plant growth regulator to prevent lodging and brackling (crop leaning). The formulation will be applied on cereals (fields) by professional operators using vehicle mounted boom sprayers with hydraulic nozzles. The formulation is packaged in 1, 5 (cap closure 63 mm diameter) and 20 L containers.

Table 6.4-1: Summary of critical use patterns (i.e. worst case) for use of A8587F

Application equipment	Representative Crop (indoor / field)	Max Application rate		Spray dilution (L/ha)	Number applications	Application Interval (days)
		(L/ha product)	(g a.s./ha)			
Tractor-mounted boom sprayer	Cereals (winter barley)	0.8	200	100 - 400	1	-

A rate of 200 g a.s./ha diluted in 100 to 400 L/ha of water corresponds to a spray dilution of 2.0 - 0.5 g a.s./L.
The exposure estimations were compared to the Acceptable Operator Exposure Level of 0.34 mg/kg bw/day (see Volume 1, level 2, point 2.6.13). The systemic exposure was calculated based on default dermal penetration factors of 25 % for the concentrate and 75 % for the spray dilution (see point B.6.2).

It should be noted that the exposure of operators, workers, residents and bystanders was additionally estimated by RMS using *EFSA Guidance Exposure Calculator (version 30 Mar 2015)*:

- 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, doi: 10.2903/j.efsa.2014.3874. The implementation schedule and applicability of this Guidance follows SANTE-10832-2015 29 May 2015.

B.6.4.1. Operator exposure

Operator exposure was modelled using the *German BBA, UK POEM and a new Operator Outdoor Spray AOEM (EFSA Guidance Exposure Calculator; version 30 Mar 2015)* exposure models*:*

- Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protection), Mitteilungen aus der Biologischen Bundesanstalt für Land-und Forstwirtschaft, Berlin-Dahlem, Heft 277, 1992. ("German Model").
- Estimation of Exposure and Absorption of Pesticides by Spray Operators, Scientific subcommittee on Pesticides and British Agrochemical association Joint Medical Panel Report (UK MAFF), 1986 and the Predictive Operator Exposure Model (POEM) V 1.0, (UK MAFF), 1992, 2007 version. ("UK POEM").
- 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, doi: 10.2903/j.efsa.2014.3874. The implementation schedule and applicability of this Guidance follows SANTE-10832-2015 29 May 2015.

Estimations of operator exposure have been undertaken for A8587F using the critical uses (Table 6.4-1).
The following parameters were used in the operator exposure assessment:

UK POEM:

Application method:	Tractor-mounted boom sprayer
Treated area:	50 ha/day
Max. dose rate:	0.2 kg trinexapac-ethyl/ha (0.8 L product/ha)
Pack size:	10 L with 63 mm closure (worst case scenario)
Application volume:	100 L/ha
Operator body weight:	60 kg (UK POEM default body weight)
No PPE:	Operator wearing long-sleeved shirt, long trousers ("permeable") but no gloves
PPE:	Gloves during mixing/loading and application.

German Model (geometric mean):

Application method:	Tractor-mounted boom sprayer
Treated area:	20 ha/day
Max. dose rate:	0.2 kg trinexapac-ethyl/ha (0.8 L product/ha)
Operator body weight:	70 kg (German model default body weight)

No PPE: Operator wearing T-shirt and shorts.

Operator Outdoor Spray AOEM

Scenario: Application equipment, method and application: Vehicle-mounted, Downward spraying, Outdoor
Treated area: 50 ha/day
Max. dose rate: 0.2 kg trinexapac-ethyl/ha (0.8 L product/ha)
Operator body weight: 60 kg (Guidance default body weight)
No PPE (potential exposure): Operator in the absent of clothing.
No PPE (Workwear: consist of coveralls or long-sleeved jackets and trousers that were made of cotton (> 300 g/m^2) or cotton/polyester (> 200 g/m^2).

A summary of the estimated operator exposure to trinexapac-ethyl is presented in Table 6.4.1-1. The detailed estimations of exposure are provided in B.6.7 Annex I Tables [B.6.7-1] – [B.6.7-4].

Table 6.4.1-1: Summary of estimated operator exposure to trinexapac-ethyl

Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of AOEL (0.34 mg/kg bw/day)
Tractor-mounted boom sprayer application outdoors to low crops Application rate: 0.8 L A8587F/ha (200 g trinexapac-ethyl/ha)			
UK POEM 50 ha/day, 6 h/day 100 L/ha 60 kg operator	No PPE*	1.249	367.4
	Gloves during mixing/loading and application	0.184	54.1
German Model (geometric mean) 20 ha/day 70 kg operator	No PPE*	0.122	35.9
Operator Outdoor Spray AOEM 50 ha/day 60 kg operator	No PPE*	0.142	41.6

** - No PPE:*
German Model: Operator wearing T-shirt and shorts.
UK POEM: Operator wearing long-sleeved shirt, long trousers ("permeable") but no gloves.
Operator Outdoor Spray AOEM: Operator wearing workwear which consist of coveralls or long-sleeved jackets and trousers that were made of cotton (> 300 g/m^2) or cotton/polyester (> 200 g/m^2)

Conclusion

According to the UK POEM calculations, it can be concluded that the risk of exposure to trinexapac-ethyl for the operator using A8587F for the proposed uses is acceptable with the use of personal protective equipment: gloves during mixing/loading and application.

According to the German model calculations, it can be concluded that the risk of exposure to trinexapac-ethyl for the operator using A8587F for the proposed uses is acceptable without the use of personal protective equipment.

According to Operator Outdoor Spray AOEM calculations, it can be concluded that the risk of exposure to trinexapac-ethyl for the operator using A8587F for the proposed uses is acceptable without the use of personal protective equipment but with the use of workwear which consist of coveralls or long-sleeved jackets and trousers that were made of cotton or cotton/polyester.

Gloves should also be used for the maintenance of the sprayer during application.

Given the eye irritating potential of A8587F suitable eye/face protection should be worn when handling the concentrate.

B.6.4.2. Bystander and resident exposure

Bystanders and resident are not involved in application or handling plant protection products or the professional handling of treated crops.

Bystanders are persons who could be located directly adjacent to the area where PPP application or treatment is in process or has recently been completed; whose presence is quite incidental and unrelated to work involving PPPs, but whose position might lead them to be exposed; and who take no action to avoid or control exposure.

Residents are persons who live, work or attend school or any other institution adjacent to an area that is or has been treated with a plant protection product; persons whose presence is quite incidental and unrelated to work involving plant protection products but whose position might lead them to be exposed; persons who take no action to avoid or control exposure; or persons who might be in the location for 24 hours per day.

Estimations of bystander and residential exposure have been undertaken for A8587F using the critical uses (Table 6.4-1) and the *German guidance paper (Martin et al; 2008)* as well as *EFSA Guidance Exposure Calculator (version 30 Mar 2015):*

- Martin S, Westphal D, Erdtmann-Vourliotis M, Dechet F, Schulze-Rosario C, Stauber F, Wicke H and Chester G, 2008. Guidance for Exposure and Risk Evaluation for Bystanders and Residents exposed to Plant Protection Products during and after Application. J. Verbr. Lebensm. 3, 272-2811661-5751/08/030272-10 DOI 10.1007/s00003-008-0361-5, ©Birkhäuser Verlag, Basel, 2008.
- 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, doi: 10.2903/j.efsa.2014.3874. The implementation schedule and applicability of this Guidance follows SANTE-10832-2015 29 May 2015.

All assumptions made in the following are quoted in these guidance papers.

EFSA Guidance Exposure Calculator (version 30 Mar 2015) was used for long term risk assessment for resident. According to EFSA guidance (EFSA Journal 2014; 12(10):3874), for PPPs with no potential acute systemic toxicity longer term risk assessment for bystander is covered by the risk assessment for resident.

Resident exposure (both adult and child) to trinexapac-ethyl following application of Trinexapac-ethyl 250 g/L ME (A8587F) was estimated using the AOEL and assuming tractor mounted applications.

A summary of the estimated bystander/resident exposure to trinexapac-ethyl is presented in Table 6.4.2-1. The detailed estimations of exposure are provided in B.6.7 Annex I Tables [B.6.7-5] – [B.6.7-7].

Table 6.4.2-1: Estimated bystander/residential exposure to trinexapac-ethyl and % of the AOEL

	Trinexapac-ethyl (AOEL = 0.34 mg/kg bw/day)	
Bystander exposure		
German guidance paper		
	Adult	**Child**
Dermal exposure (mg/kg bw/day)	7.25×10^{-4}	5.66×10^{-4}
Inhalation exposure (mg/kg bw/day)	9.26×10^{-7}	1.98×10^{-6}
Total systemic exposure (mg/kg bw/day)	**7.26×10^{-4}**	**5.68×10^{-4}**
% of AOEL	**0.21**	**0.17**
*German guidance paper (additional option)**		
Dermal exposure (mg/kg bw/day)	69.25×10^{-4}	54.03×10^{-4}
Inhalation exposure (mg/kg bw/day)	9.26×10^{-7}	1.98×10^{-6}
Total systemic exposure (mg/kg bw/day)	**69.26×10^{-4}**	**54.05×10^{-4}**
% of AOEL	**2.04**	**1.59**
EFSA Guidance Exposure Calculator		
Residential exposure		
German guidance paper		
Dermal exposure (mg/kg bw/day)	5.29×10^{-5}	7.00×10^{-5}
Inhalation exposure (mg/kg bw/day)	2.76×10^{-4}	5.15×10^{-4}
Hand-to-mouth transfer (mg/kg bw/day)	-	7.18×10^{-6}
Object-to-mouth transfer (mg/kg bw/day)	-	1.80×10^{-6}
Total systemic exposure (mg/kg bw/day)	**3.29×10^{-4}**	**5.94×10^{-4}**
% of AOEL	**0.10**	**0.17**
*German guidance paper (additional option)**		
Dermal exposure (mg/kg bw/day)	50.55×10^{-5}	66.90×10^{-5}
Inhalation exposure (mg/kg bw/day)	2.76×10^{-4}	5.15×10^{-4}
Hand-to-mouth transfer (mg/kg bw/day)	-	68.61×10^{-6}
Object-to-mouth transfer (mg/kg bw/day)	-	17.2×10^{-6}
Total systemic exposure (mg/kg bw/day)	**7.82×10^{-4}**	**12.69×10^{-4}**
% of AOEL	**0.23**	**0.37**
EFSA Guidance Exposure Calculator		
Spray drift (75th percentile) mg/kg bw/day	0,0096383	0,0402650
Vapour (75th percentile) mg/kg bw/day	0,0002300	0,0010700
Surface deposits (75th percentile) mg/kg bw/day	0,0010220	0,0023464
Entry into treated crops (75th percentile) mg/kg bw/day	0,0140625	0,0253125
All pathways (mean) mg/kg bw/day	**0,0167689**	**0,0451444**
% of AOEL (mean)	**4,93%**	**13,28%**

** - additional option: the drift deposition 2.77% at 1 m (90th percentile; 1 application) parameter was used in the bystander and resident exposure assessment*

It is concluded that there is no undue risk to any bystander or resident from trinexapac-ethyl during and following local application of A8587F. This has no labelling implications.

B.6.4.2.1. Estimation of bystander exposure

The following parameters were used in the bystander assessment according to ***German guidance paper*** **(2008)**:

- Application method: Tractor-mounted boom sprayer
- Application rate: 200 g/ha for trinexapac-ethyl
- Area treated: 20 (ha/day)
- Drift deposition: 0.29% at 10 m (90th percentile; 1 application) and additional option : 2.77% at 1 m (90th percentile; 1 application)
- Exposure duration: 5 minutes
- Exposed body surface: 1 m² for an adult and 0.21 m² for a three to less than four-year old children
- Dermal absorption: 75%
- Body weights: 60 kg for adults and 16.15 kg for a two to less than five-year old child.

The detailed estimation of exposure is provided in B.6.7 Annex I Table B.6.7-5. A summary is provided in B.6.4.2.

During the commenting phase, an open point was identified by EFSA: it was requested the RMS to present both options (bystander exposure estimates for 1 m and 10 m distances) in a revised RAR.
In response to the Reporting table comment 2(65) at renewal, the RMS presents additional option (bystander exposure estimates for 1 m distances). The drift deposition 2.77% at 1 m (90th percentile; 1 application) parameter was used in the bystander exposure assessment according to ***German guidance paper*** **(2008).** The detailed estimation of exposure is provided in B.6.7 Annex I Table B.6.7-5a. A summary is provided in B.6.4.2.

The estimated bystander exposures are below the AOEL for trinexapac-ethyl. Therefore, it is concluded that according to German guidance paper (2008) there is no undue risk to any bystander during and following local application of A8587F.

B.6.4.2.2. Estimation of residential exposure

The following parameters were used in the resident assessment according to ***German guidance paper*** **(2008)**:

- Application rate: 200 g/ha for trinexapac-ethyl
- Drift deposition: 0.29% at 10 m (90th percentile; 1 application) and additional option : 2.77% at 1 m (90th percentile; 1 application)
- The vapour pressure: 2.16×10^{-3} Pa @ 25°C for trinexapac-ethyl, therefore, active substance is considered as semi-volatile
- Exposure duration: 2 hours for dermal exposure
- In the case of semi-volatile or volatile active substances, the inhalation exposure duration is 24 hours
- Dermal absorption: 75%
- Body weights: 60 kg for adults and 16.15 kg for children.

The following parameters were used in the resident assessment according to **EFSA Guidance Exposure Calculator (version 30 Mar 2015)**:

• Buffer strip	**2-3**	m
• Application rate of the product	**0,2**	kg a.s./ha
• Concentration of active substance (in-use dilution for liquid applications)	**2**	g a.s./l
• Dermal absorption of product	**25,00%**	
• Dermal absorption of in-use dilution	**75,00%**	
• Oral absorption	**100,00%**	

• Dislodgeable foliar residue (i_AppRate*i_DFR)	**0,6**	µg a.s./cm^2
• Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3 Pa	
• Concentration in air	**0,001**	mg/m^3
• 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
• Exposure duration inhalation	**24**	hours
• Exposure duration entry into treated crops	**0,25**	hours
• Light clothing adjustment factor	**18,0%**	
• Breathing rate adult	**0,23**	m^3/day/kg
• Breathing rate child (1-3 year old)	**1,07**	m^3/day/kg
• Drift percentage on surface (75th percentile)	**5,60%**	
• Drift percentage on surface (mean)	**4,10%**	
• Turf transferable residues percentage	**5,00%**	
• Transfer coeff. of surface deposits-adult	**7300**	cm^2/hour
• Transfer coeff. of surface deposits-child (1-3 year old)	**2600**	cm^2/hour
• Saliva extraction percentage	**50,00%**	
• Surface area of hands mouthed	**20**	cm^2
• Frequency of hand to mouth activity	**9,5**	events/hour
• Ingestion rate for mouthing of grass per day	**25**	cm^2
• Dislodgeable residues percentage transferability for object to mouth	**20,00%**	
• Transfer coefficient for entry into treated crops (75th percentile) - adult	**7500**	cm^2/h
• Transfer coefficient for entry into treated crops (75th percentile) - child	**2250**	cm^2/h
• Transfer coefficient for entry into treated crops (mean) - adult	**5980**	cm^2/h
• Transfer coefficient for entry into treated crops (mean) - child	**1794**	cm^2/h

The detailed estimation of exposure is provided in B.6.7 Annex I Tables [B.6.7-6] – [B.6.7-7]. A summary is provided in B.6.4.2.

During the commenting phase, an open point was identified by EFSA: it was requested the RMS to present both options (resident exposure estimates for 1 m and 10 m distances) in a revised RAR.

In response to the Reporting table comment 2(65) at renewal, the RMS presents additional option (resident exposure estimates for 1 m distances). The drift deposition 2.77% at 1 m (90th percentile; 1 application) parameter was used in the resident exposure assessment according to ***German guidance paper*** **(2008).** The detailed estimation of exposure is provided in B.6.7 Annex I Table B.6.7-6a. A summary is provided in B.6.4.2.

The estimated resident exposures are below the AOEL for trinexapac-ethyl according to both models.
Four pathways of exposure has been considered and has been summed (i.e. spray drift, vapour, surface deposits and entry into treated crops) in the calculation according to the EFSA Guidance. Thereby, exposure assessment calculation taken into account input data (above) recommended in 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) indicates acceptable levels of exposure for residents.
Therefore, it is concluded that there is no undue risk to any resident during and following local application of A8587F.

B.6.4.3. Worker exposure

Estimations of worker exposure have been undertaken for A8587F using the critical uses (Table 6.4-1) and the generic re-entry exposure approach approved for use in *Germany* and default parameters from the *EUROPOEM II re-entry model:*

- Krebs B. *et al* (1998) Uniform Principles for Safeguarding the Health of Worker Re-entering Crop Growing Areas after Application of Plant Protection Products. (Bulletin of the German Plant Protection Service) Nachrichtenblatt des Deutschen Pflanzenschutzdienstes.10/98; Vol 50, Verlag Eugen Ulmer , Stuttgart, Germany.
- Van Hemmen *et al* (2002). Post-application exposure of workers to pesticides in agriculture (Report of the re-entry working group). EUROPOEM II Project FAIR3-CT96-1406

Additionally, the exposure of worker was estimated by RMS using *EFSA Guidance Exposure Calculator (version 30 Mar 2015).*
Crop inspection in cereals has been presented as a worst case scenario.
The following parameters were used in the worker assessment according to *German* and the *EUROPOEM II re-entry model:*

Table 6.4.3-1: Parameters used for the worker risk assessment

	Parameter		**Units**
MR	Application rate considered for default worker exposure	0.2	kg a.i./ha
DF	Dermal absorption:	75%	
DFR	Default dislodgeable foliar residue:	3	µg/cm²/ kg a.i. applied/ha
BW	Re-entry worker body weight	60	kg
TC	Transfer coefficient:	2500	cm²/h x person
A	Working period:	2	h/day

Regarding the worker assessment according to *EFSA Guidance Exposure Calculator (version 30 Mar 2015)* different the TC value was used, i.e. 1400 cm²/h x person, assuming the worker wearing adequate work clothing (but no PPE) that covers the arms, body and legs, when re-entering crops treated with PPP. Additionally, the total potential exposure was calculated by using TC value of 12500 cm^2/h, assuming the worker without workwear.

The detailed estimations of exposure are provided in B.6.7 Annex I Tables [B.6.7-8] – [B.6.7-9]. A summary of the estimated worker exposure to trinexapac-ethyl is presented in Table 6.4.3-2.

Table 6.4.3-2: Estimated worker exposure to trinexapac-ethyl

	Exposure parameter		
Exposure scenario	**AOEL (mg/kg bw/day)**	**Unprotected worker**	
		Absorbed dose (mg/kg bw/day)	**% of AOEL**
German and EUROPOEM II re-entry model[1]			
Inspection	0.34	0.03750	11.0
EFSA Guidance Exposure Calculator			
Inspection[2]	0.34	0.18750	55.2
Inspection[3]		0.02100	6.2

1) Worker wearing shoes, socks, long-sleeved shirt, and long trousers;
2) Worker without workwear, total potential exposure
3) Worker wearing clothing/workwear that covers the arms, body and legs

It is concluded that there is no unacceptable risk anticipated from trinexapac-ethyl for the worker wearing adequate work clothing (but no PPE) that covers the arms, body and legs, when re-entering crops treated with A8587F. It should be noted, that worker exposure is acceptable even without workwear. 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.

B.6.5. EXPOSURE AND RISK ASSESSMENT

Estimates based on surrogate data contained in the German Model (geometric mean) predict that the proposed use of Trinexapac-ethyl 250 g/L ME (A8587F) through field crop sprayers will result in a level of systemic exposure to trinexapac-ethyl equivalent to 35.9% of the AOEL for an operator without the need for PPE.

According to UK POEM operator exposure to trinexapac-ethyl is predicted to be 54.1% of the AOEL for operators wearing gloves during all operations.

According to Operator Outdoor Spray AOEM calculations, it can be concluded that the risk of exposure to trinexapac-ethyl for the operator using A8587F for the proposed uses is acceptable without the use of personal protective equipment (i.e. 41.6% of the AOEL) but with the use of workwear which consist of coveralls or long-sleeved jackets and trousers that were made of cotton or cotton/polyester (section B.6.4.1.).

Additionally, on the basis of the classification of the product as an eye irritant (H319) and as EUH066 “Repeated exposure may cause skin dryness or cracking“ the use of a face shield and gloves for operator when handling the concentrate would be required.

The bystander and residential exposure estimations using the German guidance paper (2008) indicate that levels of exposure for bystander and resident will be within acceptable levels of the proposed systemic AOEL of trinexapac-ethyl. A first tier systemic exposure to bystanders results in 2.0% of the AOEL (adult) and 1.6% of the AOEL (child) applying the drift values for 1 m distance (2.77%). Systemic exposure to bystanders results in 0.21% of the AOEL (adult) and 0.17% of the AOEL (child) applying the drift values for 10 m distance (0.29%). A first tier systemic exposure to resident results in 0.23% of the AOEL (adult) and 0.37% of the AOEL (child) applying the drift values for 1 m distance (2.77%). Systemic exposure to resident results in 0.1% of the AOEL (adult) and 0.17% of the AOEL (child) applying the drift values for 10 m distance (0.29%) (section B.6.4.2.).
Regarding resident child and adult exposure levels of 13.3% of the AOEL for the child and 4.9% of AOEL for the adult are derived using EFSA Guidance Exposure Calculator (version 30 Mar 2015). According to EFSA guidance (EFSA Journal 2014; 12(10):3874) no bystander risk assessment is required for PPPs with no potential acute systemic toxicity. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure (section B.6.4.2.).

Estimates using German with the EUROPOEM II re-entry models and EFSA Guidance Exposure Calculator (version 30 Mar 2015) predict that the proposed use of Trinexapac-ethyl 250 g/L ME (A8587F) will result in a level of systemic exposure to trinexapac-ethyl equivalent to 11% and 6.2% of the AOEL, respectively, for the unprotected worker wearing adequate work clothing (but no PPE) when re-entering treated areas to carry out crop inspection (section B.6.4.3.). It should be noted, that worker exposure is acceptable even without workwear based on EFSA Guidance Exposure Calculator (version 30 Mar 2015).

Consequently, the risk to bystanders/residents and to workers undertaking crop inspection activities is considered acceptable.

B.6.6. REFERENCES RELIED ON

Search in the scientific peer reviewed open literature was conducted, covering a period from 2005 to 2015. The strategy for the review followed the EFSA Guidance "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009" (EFSA Journal 2011;9(2):2092. [49 pp.]).

The notifier included in the search the active substance trinexapac/trinexapac-ethyl, its four metabolites and three trade product names. After the rapid and the full-text assessment the notifier concluded that none of the articles retrieved was relevant regarding the properties of the formulations containing trinexapac/trinexapac-ethyl.

After assessment of the chosen approaches for the literature search, the RMS concluded that the notifier appropriately addressed the scientific peer reviewed open literature (for more information please refer to Volume 3 (AS), section B.6 point B.6.10.).

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCP 7.1.1 / 01	Hartmann H.R.	1991	CGA 163935 ME 250 (A-8587 B) - Acute oral toxicity in the rat. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Stein, Switzerland, 901522 GLP not published Syngenta File No CGA163935/0107	Y	Y	Eligible for data protection according to SANCO/12576/2012; dependent on national product registration status	SYN	Submitted for the purpose of renewal
KCP 7.1.2 / 01	Hartmann H.R.	1991a	CGA 163935 ME 250 (A-8587 B) - Acute dermal toxicity in the rat. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Stein, Switzerland, 901525 GLP not published Syngenta File No CGA163935/0106	Y	Y	Eligible for data protection according to SANCO/12576/2012; dependent on national product registration status	SYN	Submitted for the purpose of renewal
KCP 7.1.3 / 01	Beebe D.	2016	Trinexapac-ethyl ME (250) (A8587F) - Acute (Four-Hour) Inhalation Study in Rats Syngenta, KH71WS GLP not published Syngenta File No A8587F_10528	Y	Y	Eligible for data protection according to SANCO/12576/2012; dependent on national product registration status	SYN	Submitted for the purpose of renewal
KCP 7.1.4 / 01	Hagemann Ch.	1991	CGA 163935 ME 250 (A-8587 B) - Acute dermal irritation/corrosion study in the rabbit. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Stein, Switzerland, 901524 GLP not published Syngenta File No CGA163935/0084	Y	Y	Eligible for data protection according to SANCO/12576/2012; dependent on national product registration status	SYN	Submitted for the purpose of renewal
KCP 7.1.5 / 01	Hagemann Ch.	1991a	CGA 163935 ME 250 (A-8587 B) - Acute eye irritation/corrosion study in the rabbit. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Stein, Switzerland, 901523 GLP not published Syngenta File No CGA163935/0090	Y	Y	Eligible for data protection according to SANCO/12576/2012; dependent on national product registration status	SYN	Submitted for the purpose of renewal
KCP 7.1.6 / 01	Simon Christina	2009	A8587F - Trinexapac-ethyl ME (A8587F) - Contact Hypersensitivity in Albino Guinea Pigs, Buehler Test (9-Induction) Syngenta Harlan Laboratories Ltd., 4414 Fullinsdorf, Switzerland, C17543 GLP not published Syngenta File No A8587F_10024	Y	Y	Eligible for data protection according to SANCO/12576/2012; dependent on national product registration status	SYN	Submitted for the purpose of renewal

B.6.7. ANNEX I: DETAILED MODELLING

Table B.6.7-1: UK POEM – operator exposure to trinexapac-ethyl, no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles				
Product	**A8587F**		Active substance	**Trinexapac-ethyl**	
Formulation type	organic solvent-based		a.s. concentration	**250**	mg/ml
Dermal absorption from product	**25**	%	Dermal absorption from spray	**75**	%
Container	10 litres 63 mm closure				
PPE during mix/loading	None		PPE during application	None	
Dose	**0,8**	l/ha	Work rate/day	**50**	ha
Application volume	**100**	l/ha	Duration of spraying	**6**	h

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0,05	ml
Application dose	0,8	litres product/ha
Work rate	50	ha/day
Number of operations	4	/day
Hand contamination	0,2	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0,2	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	100	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	None	Permeable	Permeable	
Penetration	100%	5%	15%	
Dermal exposure	6,5	0,05	0,375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	41,55	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0,2	ml/day	41,55	ml/day
Concen. of a.s. product or spray	250	mg/ml	2	mg/ml
Dermal exposure to a.s.	50	mg/day	83,1	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	12,5	mg/day	62,325	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0,01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	2	mg/ml
Inhalation exposure to a.s.	0,12	mg/day
Percent absorbed	100	%
Absorbed dose	0,12	mg/day

PREDICTED EXPOSURE

Total absorbed dose	74,945	mg/day
Operator body weight	60	kg
Operator exposure	1,249083333	mg/kg bw/day

Table B.6.7-2: UK POEM – operator exposure to trinexapac-ethyl, with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles				
Product	**A8587F**		Active substance	**Trinexapac-ethyl**	
Formulation type	organic solvent-based		a.s. concentration	**250**	mg/ml
Dermal absorption from product	**25**	%	Dermal absorption from spray	**75**	%
Container	10 litres 63 mm closure				
PPE during mix/loading	Gloves		PPE during application	Gloves	
Dose	**0,8**	l/ha	Work rate/day	**50**	ha
Application volume	**100**	l/ha	Duration of spraying	**6**	h

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0,05	ml
Application dose	0,8	litres product/ha
Work rate	50	ha/day
Number of operations	4	/day
Hand contamination	0,2	ml/day
Protective clothing	Gloves	
Transmission to skin	10	%
Dermal exposure to formulation	0,02	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	100	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	Gloves	Permeable	Permeable	
Penetration	10%	5%	15%	
Dermal exposure	0,65	0,05	0,375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	6,45	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0,02	ml/day	6,45	ml/day
Concen. of a.s. product or spray	250	mg/ml	2	mg/ml
Dermal exposure to a.s.	5	mg/day	12,9	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	1,25	mg/day	9,675	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0,01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	2	mg/ml
Inhalation exposure to a.s.	0,12	mg/day
Percent absorbed	100	%
Absorbed dose	0,12	mg/day

PREDICTED EXPOSURE

Total absorbed dose	11,045	mg/day
Operator body weight	60	kg
Operator exposure	0,184083333	mg/kg bw/day

Table B.6.7-3: German model – operator exposure to trinexapac-ethyl, no PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles				
Product	**A8587F**		Active substance		**Trinexapac-ethyl**
Formulation type	Liquid		a.s. concentration		**250** g/l
Dermal absorption from product	**25** %		Dermal absorption from spray		**75** %
RPE during mix/loading	None		RPE during application		None
PPE during mix/loading	None				
PPE during application: Head	None	Hands	None	Body	None
Dose	**0,8** l product/ha		Work rate/day		**20** ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2,4	mg/kg a.s.
Hand contamination/day	9,6	mg/day
Protective clothing	none	
Transmission to skin	100	%
Dermal exposure to a.s.	9,6	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0,0006	mg/kg a.s.
Inhalation exposure/day	0,0024	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0,0024	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique: Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0,06	0,38	1,6	
Dermal contamination/day	0,24	1,52	6,4	
Protective clothing	none	none	none	
Transmission to skin	100	100	100	%
Total dermal exposure to a.s.	8,16	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0,001	mg/kg a.s.
Inhalation exposure/day	0,004	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0,004	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	9,6	mg/day	8,16	mg/day
Percent absorbed	25	%	75	%
Absorbed dose (dermal route)	2,4	mg/day	6,12	mg/day
Inhalation exposure to a.s.	0,0024	mg/day	0,004	mg/day
Total systemic exposure	2,4024	mg/day	6,124	mg/day

PREDICTED EXPOSURE

Total systemic exposure	8,5264	mg/day
Operator body weight	70	kg
Operator exposure	0,121805714	mg/kg bw/day

Table B.6.7-4: Operator Outdoor Spray AOEM - operator exposure to trinexapac-ethyl, no PPE

Operator exposure for A8587F outdoor spray applications

Application rate of active substance	0,2 kg a.s./ha	*i_AppRate*	
Assumed area treated	50 ha/day	*d_AreaTreated*	
Amount of active substance applied	10 kg a.s./day	*i_AmoutAS*	
Dermal absorption of the product	25,00%	*i_AbsorpProduct*	
Dermal absorption of in-use dilution	75,00%	*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		

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	28588	106902	AOEM	
	Body	17999	140606	AOEM	
	Head	519	2846	AOEM	
	Protected hands (gloves)	154	1981	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	183	1463	AOEM	
	Protected head (hood and face shield)	8	161	AOEM	
	Inhalation	7	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. 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	1483	12376	AOEM	
	Body	829	4275	AOEM	
	Head	39	118	AOEM	
	Protected hands (gloves)	148	4360	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	23	56	AOEM	
	Inhalation	3	11	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	13,5511274	8,4920647	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,2258521	0,1415344	
% of RVNAS	66,43%	41,63%	
Acute			

Table B.6.7-5: German guidance paper – bystander exposure to trinexapac-ethyl

Estimation of bystander exposure during/after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of bystander exposure:

Intended use(s):	Field crop		**Drift (D):**	0,29	% (FC, 10 m)
Application rate (AR):	0,2	kg a.s./ha	**Exposed body surface area (BSA):**	1	m² (adults)
	20	mg/m²		0,21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0,001	mg/kg a.s. (6 hours, adults)
	16,15	kg/person (children)		0,00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	75,00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on FCTM)
Inhalation absorption (IA):	100	%			
AOEL:	0,34	mg/kg bw/d	**Exposure duration (T):**	5	min

Bystander exposure towards Trinexapac-athyl					
Adults			**Children**		
Bystander: Systemic dermal exposure during/after application in Field crop (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(20 x 0,29% x 1 x 75%) / 60			(20 x 0,29% x 0,21 x 75%) / 16,15		
External dermal exposure	0,058	mg/person	External dermal exposure	0,01218	mg/person
External dermal exposure	0,0009667	mg/kg bw/d	External dermal exposure	0,0007542	mg/kg bw/d
Systemic dermal exposure	**0,000725**	**mg/kg bw/d**	**Systemic dermal exposure**	**0,000566**	**mg/kg bw/d**
Bystander: Systemic inhalation exposure during/after application in Field crop (via spray drift)					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,001 / 360 x 0,2 x 20 x 5 x 100%) / 60			(0,001 / 360 x 0,2 x 20 x 5 x 100%) / 16,15		
External inhalation exposure	5,556E-05	mg/person	External inhalation exposure	3,193E-05	mg/person
External inhalation exposure	9,259E-07	mg/kg bw/d	External inhalation exposure	1,977E-06	mg/kg bw/d
Systemic inhalation exposure	**0,000001**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0,000002**	**mg/kg bw/d**
Total systemic exposure: $SE_B = SDE_B + SIE_B$			Total systemic exposure: $SE_B = SDE_B + SIE_B$		
Total systemic exposure	0,0435556	mg/person	Total systemic exposure	0,0091669	mg/person
Total systemic exposure	**0,000726**	**mg/kg bw/d**	**Total systemic exposure**	**0,000568**	**mg/kg bw/d**
% of AOEL	**0,2135**	**%**	**% of AOEL**	**0,1669**	**%**

Table B.6.7-5a: German guidance paper – bystander exposure to trinexapac-ethyl*

Estimation of bystander exposure during/after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of bystander exposure:

Intended use(s):	Field crop		**Drift (D):**	2,77	% (FC, 10 m)
Application rate (AR):	0,2	kg a.s./ha	**Exposed body surface area (BSA):**	1	m² (adults)
	20	mg/m²		0,21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0,001	mg/kg a.s. (6 hours, adults)
	16,15	kg/person (children)		0,00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	75,00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on FCTM)
Inhalation absorption (IA):	100	%			
AOEL:	0,34	mg/kg bw/d	**Exposure duration (T):**	5	min

Bystander exposure towards Trinexapac-athyl					
Adults			**Children**		
Bystander: Systemic dermal exposure during/after application in Field crop (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(20 x 2,77% x 1 x 75%) / 60			(20 x 2,77% x 0,21 x 75%) / 16,15		
External dermal exposure	0,554	mg/person	External dermal exposure	0,11634	mg/person
External dermal exposure	0,00923333	mg/kg bw/d	External dermal exposure	0,007203715	mg/kg bw/d
Systemic dermal exposure	**0,006925**	**mg/kg bw/d**	**Systemic dermal exposure**	**0,005403**	**mg/kg bw/d**
Bystander: Systemic inhalation exposure during/after application in Field crop (via spray drift)					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,001 / 360 x 0,2 x 20 x 5 x 100%) / 60			(0,001 / 360 x 0,2 x 20 x 5 x 100%) / 16,15		
External inhalation exposure	5,5556E-05	mg/person	External inhalation exposure	3,19285E-05	mg/person
External inhalation exposure	9,2593E-07	mg/kg bw/d	External inhalation exposure	1,977E-06	mg/kg bw/d
Systemic inhalation exposure	**0,000001**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0,000002**	**mg/kg bw/d**
Total systemic exposure: SE_B = SDE_B + SIE_B			Total systemic exposure: SE_B = SDE_B + SIE_B		
Total systemic exposure	0,41555556	mg/person	Total systemic exposure	0,087286928	mg/person
Total systemic exposure	**0,006926**	**mg/kg bw/d**	**Total systemic exposure**	**0,005405**	**mg/kg bw/d**
% of AOEL	**2,0370**	**%**	**% of AOEL**	**1,5896**	**%**

***-** *In response to the Reporting table comment 2(65) at renewal, the RMS presents additional option (bystander exposure estimates for 1 m distances). The drift deposition 2.77% at 1 m (90th percentile; 1 application) parameter was used in this bystander exposure assessment.*

Table B.6.7.-6: German guidance paper –resident exposure to trinexapac-ethyl

Estimation of resident exposure after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of resident exposure:

Intended use(s):	Field crop		**Drift (D):**	**0,29**	% (FC, 10 m)
Application rate (AR):	**0,2**	kg a.s./ha	**Transfer coefficient (TC):**	**7300**	cm^2/hour (adults)
	0,002	mg/cm^2		**2600**	cm^2/hour (children)
Number of applications (NA):	**1**		**Turf Transferable Residues (TTR):**	**5**	%
Body weight (BW):	**60**	kg/person (adults)	**Exposure Duration (H):**	**2**	hours
	16,15	kg/person (children)	**Airborne Concentration of Vapour (AC_V):**	**0,001**	mg/m3
Dermal absorption (DA):	**75,0**	% ('worst case')	**Inhalation Rate (IR):**	**16,57**	m^3/day (adults)
Inhalation absorption (IA):	**100**	%		**8,31**	m^3/day (children)
Oral absorption (OA):	**100**	%	**Saliva Extraction Factor (SE):**	**50**	%
AOEL:	**0,3400**	mg/kg bw/d	**Surface Area of Hands (SA):**	**20**	cm^2
			Frequency of Hand to Mouth (Freq):	**20**	events/hour
			Dislodgeable foliar residues (DFR):	**20**	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	**25**	cm^2/day

Resident exposure towards Trinexapac-ethyl					
Adults			**Children**		
Residents: Systemic dermal exposure after application in Field crop (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0,002 x 1 x 0,29% x 5% x 7300 x 2 x 75%) / 60			(0,002 x 1 x 0,29% x 5% x 2600 x 2 x 75%) / 16,15		
External dermal exposure	0,004234	mg/person	External dermal exposure	0,001508	mg/person
External dermal exposure	7,0567E-05	mg/kg bw/d	External dermal exposure	9,33746E-05	mg/kg bw/d
Systemic dermal exposure	**0,0000529**	**mg/kg bw/d**	**Systemic dermal exposure**	**0,000070**	**mg/kg bw/d**
Residents: Systemic inhalation exposure after application in Field crop (via vapour)					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0,001 x 16,57 x 100%) / 60			(0,001 x 8,31 x 100%) / 16,15		
External inhalation exposure	0,01657	mg/person	External inhalation exposure	0,00831	mg/person
External inhalation exposure	0,00027617	mg/kg bw/d	External inhalation exposure	0,000514551	mg/kg bw/d
Systemic inhalation exposure	**0,000276**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0,000515**	**mg/kg bw/d**
			Residents: Systemic oral exposure (hand-to-mouth transfer)		
			$SOE_{R(H)}$ = (AR x NA x D x TTR x SE x SA x Freq x H x OA) / BW		
			(0,002 x 1 x 0,29% x 5% x 50% x 20 x 20 x 2 x 100%) / 16,15		
			External oral exposure	0,000116	mg/person
			External oral exposure	7,18266E-06	mg/kg bw/d
			Systemic oral exposure	**0,00000718**	**mg/kg bw/d**
			Residents: Systemic oral exposure (object-to-mouth transfer)		
			$SOE_{R(O)}$ = (AR x NA x D x DFR x IgR x OA) / BW		
			(0,002 x 1 x 0,29% x 20% x 25 x 100%) / 16,15		
			External oral exposure	0,000029	mg/person
			External oral exposure	1,79567E-06	mg/kg bw/d
			Systemic oral exposure	**0,0000018**	**mg/kg bw/d**
Total systemic exposure: SE_R = SDE_R + SIE_R			Total systemic exposure: SE_R = SDE_R + SIE_R + $SOE_{R(H)}$ + $SOE_{R(O)}$		
Total systemic exposure	0,0197455	mg/person	Total systemic exposure	0,009586	mg/person
Total systemic exposure	**0,000329**	**mg/kg bw/d**	**Total systemic exposure**	**0,000594**	**mg/kg bw/d**
% of AOEL	**0,097**	**%**	**% of AOEL**	**0,17**	**%**

Table B.6.7.-6a: German guidance paper –resident exposure to trinexapac-ethyl*

Estimation of resident exposure after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of resident exposure:

Intended use(s):	Field crop		**Drift (D):**	**2,77**	% (FC, 10 m)
Application rate (AR):	**0,2**	kg a.s./ha	**Transfer coefficient (TC):**	**7300**	cm^2/hour (adults)
	0,002	mg/cm^2		**2600**	cm^2/hour (children)
Number of applications (NA):	**1**		**Turf Transferable Residues (TTR):**	**5**	%
Body weight (BW):	**60**	kg/person (adults)	**Exposure Duration (H):**	**2**	hours
	16,15	kg/person (children)	**Airborne Concentration of Vapour (AC_V):**	**0,001**	mg/m3
Dermal absorption (DA):	**75,0**	% ('worst case')	**Inhalation Rate (IR):**	**16,57**	m^3/day (adults)
Inhalation absorption (IA):	**100**	%		**8,31**	m^3/day (children)
Oral absorption (OA):	**100**	%	**Saliva Extraction Factor (SE):**	**50**	%
AOEL:	**0,3400**	mg/kg bw/d	**Surface Area of Hands (SA):**	**20**	cm^2
			Frequency of Hand to Mouth (Freq):	**20**	events/hour
			Dislodgeable foliar residues (DFR):	**20**	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	**25**	cm^2/day

Resident exposure towards Trinexapac-ethyl					
Adults			**Children**		
Residents: Systemic dermal exposure after application in Field crop (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0,002 x 1 x 2,77% x 5% x 7300 x 2 x 75%) / 60			(0,002 x 1 x 2,77% x 5% x 2600 x 2 x 75%) / 16,15		
External dermal exposure	0,040442	mg/person	External dermal exposure	0,014404	mg/person
External dermal exposure	0,00067403	mg/kg bw/d	External dermal exposure	0,000891889	mg/kg bw/d
Systemic dermal exposure	**0,0005055**	**mg/kg bw/d**	**Systemic dermal exposure**	**0,000669**	**mg/kg bw/d**
Residents: Systemic inhalation exposure after application in Field crop (via vapour)					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0,001 x 16,57 x 100%) / 60			(0,001 x 8,31 x 100%) / 16,15		
External inhalation exposure	0,01657	mg/person	External inhalation exposure	0,00831	mg/person
External inhalation exposure	0,00027617	mg/kg bw/d	External inhalation exposure	0,000514551	mg/kg bw/d
Systemic inhalation exposure	**0,000276**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0,000515**	**mg/kg bw/d**
			Residents: Systemic oral exposure (hand-to-mouth transfer)		
			$SOE_{R(H)}$ = (AR x NA x D x TTR x SE x SA x Freq x H x OA) / BW		
			(0,002 x 1 x 2,77% x 5% x 50% x 20 x 20 x 2 x 100%) / 16,15		
			External oral exposure	0,001108	mg/person
			External oral exposure	6,86068E-05	mg/kg bw/d
			Systemic oral exposure	**0,00006861**	**mg/kg bw/d**
			Residents: Systemic oral exposure (object-to-mouth transfer)		
			$SOE_{R(O)}$ = (AR x NA x D x DFR x IgR x OA) / BW		
			(0,002 x 1 x 2,77% x 20% x 25 x 100%) / 16,15		
			External oral exposure	0,000277	mg/person
			External oral exposure	1,71517E-05	mg/kg bw/d
			Systemic oral exposure	**0,0000172**	**mg/kg bw/d**
Total systemic exposure: SE_R = SDE_R + SIE_R			Total systemic exposure: SE_R = SDE_R + SIE_R + $SOE_{R(H)}$ + $SOE_{R(O)}$		
Total systemic exposure	0,0469015	mg/person	Total systemic exposure	0,020498	mg/person
Total systemic exposure	**0,000782**	**mg/kg bw/d**	**Total systemic exposure**	**0,001269**	**mg/kg bw/d**
% of AOEL	**0,230**	**%**	**% of AOEL**	**0,37**	**%**

- *The drift deposition 2.77% at 1 m (90th percentile; 1 application) parameter was used in this bystander exposure

Table B.6.7.-7: EFSA Guidance Exposure Calculator (version 30 Mar 2015) – resident exposure to trinexapac-ethyl

Resident exposure for A8587F			
Croptype	Cereals		
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	0,2	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	2	g a.s./l	*d_ConcAS*
Dermal absorption of product	25,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	75,00%		*i_AbsorpInuse*
Oral absorption	100,00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,6	µg a.s./cm^2	*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/m^3	*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	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1,07	m^3/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	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50,00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9,5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20,00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - ad	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

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)	0,4026500	0,0107000	0,0234640	0,2531250	0,4514440
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0402650	0,0010700	0,0023464	0,0253125	0,0451444
% of RVNAS	11,84%	0,31%	0,69%	7,44%	13,28%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,5783000	0,0138000	0,0613200	0,8437500	1,0061364
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0096383	0,0002300	0,0010220	0,0140625	0,0167689
% of RVNAS	2,83%	0,07%	0,30%	4,14%	4,93%

Table B.6.7-8: *German* and the *EUROPOEM II re-entry model* - worker exposure to trinexapac-ethyl

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	3	µg/cm²/kg a.s.
Application rate (AR):	0.2	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	1		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	75	% ('worst case')			
			Work rate per day (WR):	2	h/d
AOEL	0.34	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in cereals					
Worker exposure towards trinexapac-ethyl					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 3600 x 2 x 0.2 x 1 x 75%) / 60			(3 x 300 x 2 x 0.2 x 1 x 75%) / 60		
External dermal exposure	4.32	mg/person	External dermal exposure	0.36	mg/person
External dermal exposure	0.07	mg/kg bw/d	External dermal exposure	0.01	mg/kg bw/d
Total systemic exposure	3.24	mg/person	Total systemic exposure	0.27	mg/person
Total systemic exposure	**0.054000**	**mg/kg bw/d**	**Total systemic exposure**	**0.004500**	**mg/kg bw/d**
% of AOEL	**15.9**	**%**	**% of AOEL**	**1.32**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 2200 x 2 x 0.2 x 1 x 75%) / 60			(3 x 2200 x 2 x 0.2 x 1 x 5% x 75%) / 60		
External dermal exposure	2.64	mg/person	External dermal exposure	0.13	mg/person
External dermal exposure	0.04	mg/kg bw/d	External dermal exposure	0.002	mg/kg bw/d
Total systemic exposure	3.30	mg/person	Total systemic exposure	0.01	mg/person
Total systemic exposure	**0.033000**	**mg/kg bw/d**	**Total systemic exposure**	**0.001650**	**mg/kg bw/d**
% of AOEL	**9.7**	**%**	**% of AOEL**	**0.49**	**%**

Total potential exposure	**0.087000**	**mg/kg bw/d**	**% of AOEL**	**25.6**	**%**
Total actual exposure	**0.037500**	**mg/kg bw/d**	**% of AOEL**	**11.0**	**%**
Total exposure with PPE	**0.006150**	**mg/kg bw/d**	**% of AOEL**	**1.8**	**%**

Table B.6.7-9: EFSA Guidance Exposure Calculator (version 30 Mar 2015) - worker exposure to trinexapac-ethyl

Worker exposure from residues on foliage for A8587F			
Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0,2	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	25,00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	75,00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,6	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*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	11,2500000	1,2600000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0,1875000	0,0210000		
% of RVNAS	55,15%	6,18%		