European Commission

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TRITICONAZOLE

Volume 3 – B.6 (PPP) – Premis 25 FS (BAS 595 01 F)

Rapporteur Member State: Austria
Co-Rapporteur Member State: United Kingdom

Version History

When	What
September/2003	Initial DAR
September/2004	Addendum 1
January/2005	Addendum 2
July/2018	DRAR

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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

Acute oral, dermal and inhalation study, as well as studies on skin and eye irritation and skin sensitisation (modified Buehler assay) have been submitted and evaluated already in the DAR (2003). An additional LLNA assay has been submitted for purpose of renewal since it was required by some authorities for product registration.

B.6.1.1. Oral

Previous evaluation:	DAR (2003)
DRAR (2016)	Additional information on material and methods added. No changes in the original conclusion

Reference:	EXP 80472: Acute oral toxicity in rats
Author(s), year:	[redacted] 1994
Report/Doc. number::	C016283 / -
Guideline(s):	OECD 401 (1987); US EPA Pesticide Assessment Guidelines, Subdivision F, No 81-1
GLP:	Yes
Deviations:	No
Acceptability:	Yes

Material and methods

Test Material:	BAS 595 01 F (identical to EXP 80472 B)
Description:	red liquid
Lot/Batch #:	OP930601
Purity/content:	Triticonazole: 24.3 g/L
Stability of test compound:	According to the CoA the formulation was stable until September 6, 1995 when stored at +2 to +30 °C in the dark.
Vehicle and/or positive control:	none
Test animals:	
Species:	Rat
Strain:	Sprague-Dawley, ICO: OFA-SD (IOPS Caw)
Sex:	5 males and 5 females
Age:	approx 6 weeks at the day of treatment
Weight at dosing (mean):	175 ± 11 g (males), 137 ± 7 g (females)
Source:	[redacted]
Acclimation period:	At least 5 days
Diet:	AO4 pelleted diet (U.A.R., 91360 Villemoisson-sur-Orge, France), ad libitum except prior to treatment.
Water:	Millipore membrane (0.22 µm) filtered water in bottles, ad libitum
Housing:	group housing in polycarbonate cages (48 x 27 20 cm) covered with a stainless steel lid. The cages contained graded, dust-free sawdust
Environmental conditions:	
Temperature:	21 ± 2 °C
Humidity:	30 - 70%
Air changes:	approx. 12 air changes per hour
Photo period:	12 h light / 12 h dark

Animal assignment and treatment:

Groups of five, 18 hour-fasted male and female rats received single doses of 2000 mg/kg bw of the undiluted formulation by oral gavage. The dosing volume was adjusted to the individual animal weight determined at the day of administration.

The animals were observed frequently during the hours following administration of the test substance for detection of possible treatment-related clinical signs. Observation of the animals was made at least once a day for a period of 14 days, to determine whether any of the clinical signs were reversible or not. Clinical signs were recorded for each animal individually.

The animals were checked frequently during the hours following administration of the test substance for mortality or signs of morbidity, then at least twice a day thereafter. The time of any deaths was recorded individually, in terms of the number of hours or days after dosing.

Body weights were recorded at day 0 (prior to dosing) and at days 8 and 15. The body weight gain of the treated animals was compared to a reference curve of control animals with the same initial weight.

Necropsy with gross-pathology examination was performed on the last day of the observation period after killing with CO_2. After opening the thoracic and abdominal cavities, a macroscopic examination of the main organs (digestive tract, heart, kidneys, liver, lungs, pancreas, spleen and any other organs with obvious abnormalities) was performed.

Results

No mortality and no clinical signs were observed in this study.

The mean body weight of all animals increased throughout the study period and was comparable to control.

Gross necropsy revealed no abnormal findings in any of the animals.

Conclusion

Under the conditions of this study the oral LD_{50} for BAS 595 01 F was determined to be greater than 2000 mg/kg body weight in rats.

Based on the study results no classification as to acute oral toxicity is required for the formulation BAS 595 01 F (Premis 25 FS) according to the criteria laid down in Regulation (EU) No. 1272/2008 (CLP).

B.6.1.2. Dermal

Previous evaluation:	DAR (2003)
DRAR (2016)	Additional information on material and methods added. No changes in the original conclusion

Reference:	Acute dermal toxicity in rats - EXP80472
Author(s), year:	[redacted], 1994
Report/Doc. number::	C016277 / -
Guideline(s):	OECD 402 (1987)
GLP:	Yes
Deviations:	No
Acceptability:	Yes

Material and methods

Test Material:	BAS 595 01 F (identical to EXP 80472 B)
Description:	red liquid
Lot/Batch #:	OP930601
Purity/content:	Triticonazole: 24.3 g/L
Stability of test compound:	According to the CoA the formulation was stable until September 6, 1995 when stored at +2 to +30 °C in the dark.
Vehicle and/or positive control:	none
Test animals:	
Species:	Rat
Strain:	Sprague-Dawley, ICO: OFA-SD (IOPS Caw)
Sex:	5 males and 5 females
Age:	approx. 8 weeks at the day of treatment
Weight at dosing (mean):	245 ± 1 g (males), 202 ± 3 g (females)
Source:	[redacted]
Acclimation period:	At least 5 days
Diet:	AO4 pelleted diet (U.A.R., 91360 Villemoisson-sur-Orge, France), ad libitum.
Water:	Millipore membrane (0.22 µm) filtered water in bottles, ad libitum
Housing:	group housing in polycarbonate cages (48 x 27 x 20 cm) covered with a stainless steel lid. The cages contained graded, dust-free sawdust. During treatment the rats were housed individually in cages of 35.5 x 23.5 x 19.3 cm
Environmental conditions:	
Temperature:	21 ± 2 °C
Humidity:	30 - 70%
Air changes:	approx. 12 air changes per hour
Photo period:	12 h light / 12 h dark

Animal assignment and treatment:

Groups of five male and female rats received single dermal doses of 2000 mg/kg bw of the undiluted formulation. The dosing volume was adjusted to the individual animal weight determined at the day of administration.

One day prior to treatment, the dorsal area (approx. 6 x 8 cm) of each animal was clipped free of hair using electric clippers. Only animals with intact skin were used in the study.

The undiluted formulation was applied directly to an area of the skin representing approximately 10% (5 x 6 cm for the females and 5 x 7 cm for the males) of the body surface of the animals. A hydrophilic gauze patch was then applied to the skin. The test substance and the patch were held in contact with the skin for 24 hours by means of an adhesive hypoallergenic aerated semi-occlusive dressing and a restraining bandage, thus preventing the ingestion of the test substance by the animals. At the end of the 24-hour application period the dressing was detached and any residual test substance was removed using a gauze patch moistened with paraffin oil.

The animals were observed frequently during the hours following administration of the test substance, for detection of possible treatment-related clinical signs. Observation of the animals was made at least once a day for a period of 14 days, to determine whether any of the clinical signs were reversible or not. Clinical signs were recorded for each animal individually.

The animals were checked frequently during the hours following administration of the test substance for mortality or signs of morbidity, then at least twice a day thereafter. The time of any deaths was recorded individually, in terms of the number of hours or days after dosing.

Body weights were recorded at day 0 (prior to dosing) and at days 8 and 15. The body weight gain of the treated animals was compared to a reference curve of control animals with the same initial weight.

Necropsy with gross-pathology examination was performed on the last day of the observation period after killing with CO_2. After opening the thoracic and abdominal cavities, a macroscopic examination of the main organs (digestive tract, heart, kidneys, liver, lungs, pancreas, spleen and any other organs with obvious abnormalities) was performed.

Results

No mortality and no clinical signs were observed in the study.

Due to the red coloration of the skin caused by residual test-substance, evaluation of Grade 1, 2, or 3 erythema was not possible on days 2 to 4. Thereafter, no cutaneous reactions were observed.

The mean body weight of all animals increased throughout the study period as and was comparable control.

Gross necropsy revealed no abnormal findings in any of the animals.

Conclusion

Under the conditions of this study the dermal LD_{50} for BAS 595 01 F was determined to be greater than 2000 mg/kg body weight in rats.

Based on the study results, no classification as to acute dermal toxicity is required for the formulation BAS 595 01 F (Premis 25 FS) according to the criteria laid down in Regulation (EU) No. 1272/2008 (CLP).

B.6.1.3. Inhalation

Previous evaluation:	DAR (2003)
DRAR (2016)	Additional information on material and methods added. No changes in the original conclusion

Reference:	EXP 80472: Acute inhalation toxicity study with four hour exposure (nose only) in the rat
Author(s), year:	[redacted] 1994
Report/Doc. number::	C016285 / -
Guideline(s):	OECD 403 (1981)
GLP:	Yes
Deviations from OECD 403 (2009):	No
Acceptability:	Yes

Material and methods

Test Material:	BAS 595 01 F (identical to EXP 80472)
Description:	red opaque liquid
Lot/Batch #:	OP930601
Purity/content:	Triticonazole: 24.3 g/L
Stability of test compound:	According to the CoA the formulation was stable until September 6, 1995 when stored at +2 to +30 °C in the dark.
Vehicle and/or positive control:	distilled water

Test animals:	
Species:	Rat
Strain:	Sprague-Dawley
Sex:	5 males and 5 females
Age:	8 to 10 weeks
Weight at dosing:	286.0 ± 12.6 g (males), 253.0 ± 3.4 g (females)
Source:	[redacted]
Acclimation period:	at least 5 days
Diet:	Rat and Mouse Expanded Diet No. 1, Special Diet Services Ltd., Witham, Essex, UK, ad libitum except during exposure
Water:	Tap water ad libitum, except during exposure
Housing:	group housing in solid floor, polypropylene cages with sawdust bedding.
Environmental conditions:	
Temperature:	20 - 23°C
Humidity:	59 - 78%
Air changes:	approx. 15/hour
Photo period:	12 h light / 12 h dark

Animal assignment and treatment:

For determination of the acute inhalation toxicity (single 4-hour-exposure) of BAS 595 01 F as a liquid aerosol groups of five male and 5 female rats were exposed to an aerosol at 3. 54 mg/L in a head-nose inhalation system. In order to facilitate the generation of an aerosol the formulation was diluted with distilled water (4 parts BAS 595 01 F + 1 part water).

Clinical examinations:

The body weight of the animals was determined just prior to exposure (day 0) and at days 7 and 14. All animals were observed for clinical signs at hourly intervals during the exposure, immediately on removal from the restraining tubes at the end of the exposure, one hour after termination of the exposure and subsequently once daily for 14 days.

Pathology:

At the end of the 14-day observation period the animals were sacrificed by an intravenous overdose of sodium pentobarbital. All animals were subjected to gross-pathological external and internal examination. The respiratory tract was subjected to a detailed macroscopic examination for signs of irritancy or local toxicity.

Statistics:

Not mentioned in the report

Generation of the test atmosphere / chamber description:

The diluted test material was aerosolized using a glass concentric jet nebuliser (Radleys, Saffron Walden, Essex) located at the top of the cylindrical exposure chamber of an approximate volume of 30 L. The nebuliser was connected to a glass syringe attached to a modified infusion pump, which provided a continuous supply of test material under pressure, and to a metered compressed air supply. The concentration within the exposure chamber was controlled by adjusting the rate of the infusion pump and the air flow rate through the chamber (16 L/min).

The extract from the exposure chamber passed through a 'scrubber' trap and was connected with a high efficiency filter to a metered exhaust system. The chamber was maintained under negative pressure.

Prior to the start of the study test material atmospheres were generated within the exposure chamber. The nature of the test material was such that it did not easily flow through the nebuliser resulting in frequent blockages. Several nebulisers with different orifice sizes were tried in combination with different test material dilution factors. Every effort was made to vary the combination of air flow settings with test material input rate to achieve maximum concentrations and optimum particle size distribution. A target concentration of 5 mg/L was used for the test exposure but due to the poor aerosolization properties of the test material this could not be achieved. The exposure was, therefore, performed at the maximum attainable concentration.

Each rat was individually held in a tapered, polycarbonate restraining tube fitted onto a single tier of the exposure chamber and sealed by means of a rubber '0' ring . Only the noses of the animals were exposed to the test atmosphere.

Analytical investigation:
The temperature, relative humidity inside the exposure chamber were measured by an electronic thermometer/humidity meter located in a vacant port in the animals' breathing zone of the chamber and recorded every thirty minutes throughout the four-hour exposure period. Oxygen levels within the exposure chamber were measured by an electronic oxygen meter located in a sampling port near the animals' breathing zone three times during the exposure period. The test atmosphere was generated to contain at least 19% oxygen.

Prior to the start of the study the moisture content of the test material was determined by adding a small amount of test material to glass fibre filters (Gelman, type A/E 25 mm) and recording their weights. The filters were then dried in a desiccators in an incubator at 37°C for approximately 24 hours and then weighed again. The difference in the two weights was taken as the moisture content of the test material and was calculated as a percentage. The mean moisture content was found to be 88.5% (n = 10).
Based on these results the study was performed using the dry weight of the test material to calculate the atmosphere concentration.
The chamber concentration was estimated at regular intervals (15 minutes) during the exposure period. A glass fibre filter was placed in a filter holder and temporarily sealed in a vacant port in the exposure chamber in the animals' breathing zone. Exposure chamber air was drawn through the filter at a measured rate using a vacuum pump for a suitable time period.
Each filter was weighed before sampling then dried in a desiccators, as previously described, and weighed again 24 hours later in order to calculate the weight of collected test material. The difference in the two weights divided by the volume of atmosphere sampled was representative of the chamber concentration.
Based on the results of the preliminary work these figures were adjusted for moisture content (88.5%) to obtain a true figure for the test material concentration in the chamber. The nominal chamber concentration was calculated by dividing the weight of the test material used by the total air flow through the chamber.

The particle size distribution of the aerosol was determined three times during the exposure period using a Cascade Impactor. This device consisted of six impactor stages with stainless steel collection substrates (10, 6, 3.5, 1.6, 0.9 and 0.5 µm cut-off points) and a back-up glass fibre filter housed in an aluminium sampler. The sampler was temporarily sealed in a sampling port in the animals' breathing zone. Exposure chamber air was drawn through the Cascade Impactor using a vacuum pump for a suitable time period.
The collection substrates were weighed before and after sampling and the weight of test material, collected at each stage, calculated by difference. From the results obtained the weight distribution of particles in the respective size ranges was calculated.

Results
No mortality was observed in this study.
Specific signs of systemic toxicity consisted of hunched posture and piloerection. These clinical signs were observed in all animals immediately after removal of the animals from the restraining tubes and one hour after the exposure. None of these signs were noted the day after exposure or later during the observation period.
Unspecific observations due to the red color of the test article consisted of red staining on head and forelimbs or over whole body as well as wet fur. Red staining was observed with decreasing incidence and severity up to day 10. Wet fur was observed during the 4 hour exposure period only.
Overall mean body weights of the animals increased throughout the study period and appeared normal for rats of this age.
Gross necropsy revealed no abnormal findings in any of the animals.

The concentration analysis revealed mean actual aerosol concentrations of 3.54 ± 1.47 mg/L and represents the maximum attainable concentration for this formulation. The calculated nominal concentration was 167.4 mg/L.

The mass mean aerodynamic diameter (MMAD) was 4.5 µm with a geometric standard deviation (GSD) of 0.46 µm. Forty-four percent of the aerosol particles had a diameter less or equal than 4 µm and thus might have reached the alveolar region of the lung.

Conclusion
Under the conditions of this study the 4 hour inhalation LC_{50} for BAS 595 01 F was determined to be greater than 3.45 mg/L (maximum attainable concentration) in male and female rats.
Based on the study results, no classification for acute inhalation toxicity is required for the formulation BAS 595 01 F (Premis 25 FS) according to the criteria laid down in Regulation (EU) No. 1272/2008 (CLP).

B.6.1.4. Skin irritation

Previous evaluation: DRAR (2016)	DAR (2003) Additional information on material and methods added. No changes in the original conclusion

Reference:	EXP 80472: Acute dermal irritation in rabbits
Author(s), year:	[redacted] 1994
Report/Doc. number::	C016281 / -
Guideline(s):	OECD 404 (1981)
GLP:	Yes
Deviations from OECD (2015):	No deviations in study design: OECD 404 (2015) describes how to integrate and use existing testing and non-testing data for the assessment of the skin irritation and skin corrosion potentials of chemicals and proposes an approach when further testing is needed
Acceptability:	Yes

Material and methods

Test Material:	BAS 595 01 F (identical to EXP 80472 B)
Description:	red liquid
Lot/Batch #:	OP930601
Purity/content:	Triticonazole: 24.3 g/L
Stability of test compound:	According to the CoA the formulation was stable until September 6, 1995 when stored at +2 to +30 °C in the dark.
Vehicle and/or positive control:	none
Test animals:	
Species:	Rabbit
Strain:	New Zealand White
Sex:	3 males
Age:	not indicated in the report
Weight at dosing:	2.5 ± 0.1 kg
Source:	[redacted]
Acclimation period:	at least 5 days
Diet:	112 C pelleted diet, U.A.R., 91360 Villemoisson-sur-Orge, France, ad libitum
Water:	F.G. Millipore membrane (0.22 µm) filtered drinking water in bottles, ad libitum
Housing:	individual housing in polystyrene cages (35 x 55 x 32 cm or 48.2 x 58 x 36.5 cm)
Environmental conditions:	
Temperature:	18 ± 3°C
Humidity:	30 - 70%
Air changes:	not indicated in the report
Photo period:	12 h light / 12 h dark

In-vitro pre-test:
No *in vitro* pre-test was performed.

Animal assignment and treatment:

The potential of BAS 595 01 F to cause acute dermal irritation or corrosion was assessed by a single topical application of 0.5 mL of the test substance for 4 hours to the intact skin of three male New Zealand White rabbits.

The day before treatment, the flanks of the animals were clipped. Only animals without obvious signs of skin irritation were used in the study. A dose of 0.5 mL of the undiluted formulation was applied to a 6 cm² hydrophilic gauze patch which was then applied to the right flank of the animals for 4 hours. The gauze patch

was held in place by means of an adhesive hypo-allergenic aerated semi-occlusive dressing and a restraining bandage.

After 4 hours the dressings were removed and any residual test substance removed by means of a gauze patch moistened with paraffin oil.

The cutaneous reactions were assessed approximately 1, 24, 48 and 72 hours after removal of the patch.

Results

No edema was observed throughout the 72 hour post application observation period. After removal of the dressing, a red colouration of the treatment site by residual substance in all 3 animals prevented the evaluation of skin erythema. However, this colouration which could cover an eventual erythema was equivalent to a well-defined erythema (score of 2) during 24 hours and then of a very slight erythema (score of 1) after 48 and 72 hours in all three rabbits. No higher graded erythema was observed in the skin at any time point. Based on the individual scores the mean score would be at most 1.3 for "erythema".

Conclusion

Under the experimental conditions, the formulation BAS 595 01 F could possibly provoke slight to moderate irritant effects, when administered by cutaneous route in rabbits. However, considering the mean irritation score of 1.3 for "erythema", classification would not be justified according to Regulation (EU) No. 1272/2008 (CLP).

Only one co-formulant in BAS 595 01 F is classified for skin effects (H314) but it is present at very low amount (< 1%); by applying calculation method for BAS 595 01 F also no classification for skin irritation would result.

B.6.1.5. Eye irritation

Previous evaluation:	DAR (2003)
DRAR (2016)	Additional information on material and methods added. No changes in the original conclusion

Reference:	EXP 80472: Acute eye irritation in rabbits
Author(s), year:	[redacted] 1994
Report/Doc. number::	C016279 / -
Guideline(s):	OECD 405 (1987)
GLP:	Yes
Deviations from OECD (2012):	No deviations in study design: OECD 405 (2012). A preferred sequential testing strategy, which includes the performance of validated in vitro or ex vivo eye corrosion/irritation tests, is included as a Supplement to this Guideline (2012). It is recommended that this testing strategy be followed prior to undertaking in vivo testing.
Acceptability:	Yes

Material and methods

Test Material:	BAS 595 01 F (identical to EXP 80472 B)
Description:	red liquid
Lot/Batch #:	OP930601
Purity/content:	Triticonazole: 24.3 g/L
Stability of test compound:	According to the CoA the formulation was stable until September 6, 1995 when stored at +2 to +30 °C in the dark.

Vehicle and/or positive control:	none
Test animals:	
Species:	Rabbit
Strain:	New Zealand White
Sex:	3 males
Age:	not indicated in the report
Weight at dosing:	2.6 ± 0.1 kg
Source:	[redacted]
Acclimation period:	at least 5 days
Diet:	112 C pelleted diet, U.A.R., 91360 Villemoisson-sur-Orge, France, ad libitum
Water:	F.G. Millipore membrane (0.22 µm) filtered drinking water in bottles, ad libitum
Housing:	individual housing in polystyrene cages (35 x 55 x 32 cm or 48.2 x 58 x 36.5 cm)
Environmental conditions:	
Temperature:	18 ± 3°C
Humidity:	30 - 70%
Air changes:	not indicated in the report
Photo period:	12 h light / 12 h dark

In-vitro pre-test:

No *in vitro* pre-test was performed.

Animal assignment and treatment:

The potential of BAS 595 01 F to cause acute eye irritation was assessed by instillation of 0.1 mL of the test substance into the conjunctival sac of the left eye. The lower and upper eyelids were held together for about one second to avoid any loss of test substance. The right eye, which remained untreated, served as a control. The eyes were not rinsed after administration of the test substance.

The ocular reactions were assessed approximately 1, 24, 48 and 72 hours after the administration of the test substance.

Results

No effects on the cornea, iris or the conjunctiva were observed throughout the 72 hour post administration observation period. Thus the study was terminated after 72 hours.

Conclusion

Based on the study results, no classification as to eye irritant is required for the formulation BAS 595 01 F (Premis 25 FS) according to the criteria laid down in Regulation (EU) No. 1272/2008 (CLP).

B.6.1.6. Skin sensitization

B.6.1.6.1. Modified Buehler assay

Previous evaluation:	DAR (2003)
DRAR (2016)	Additional information on material and methods and results added. No changes in the original conclusion

Reference:	Skin sensitization test in Guinea-pigs (Modified Buehler test: 9 applications)
Author(s), year:	[redacted] 1995
Report/Doc. number::	C016286 / -
Guideline(s):	OECD 406 (1992)
GLP:	Yes
Deviations from OECD (1992):	
Acceptability:	Yes

Material and methods

Test Material:	BAS 595 01 F (identical to EXP 80472 B)
Description:	red liquid
Lot/Batch #:	OP930601
Purity/content:	Triticonazole: 24.3 g/L
Stability of test compound:	According to the CoA the formulation was stable until September 6, 1995 when stored at +2 to +30 °C in the dark.
Vehicle and/or positive control:	distilled water, dinitro-2,4-chlorobenzene
Test animals:	
Species:	Guinea pig
Strain:	Dunkin-Hartley
Sex:	15 males and 15 females
Age:	1 to 3 months
Weight at dosing:	males: 321 ± 28 g; females: 311 ± 15 g
Source:	[redacted]
Acclimation period:	at least 5 days
Diet:	Guinea-pigs sustenance reference 106 diet, U.A.R., 91360 Villemoisson-sur-Orge, France
Water:	F.G. Millipore membrane (0.22 µm) filtered drinking water in bottles, ad libitum
Housing:	individual housing in polycarbonate cages (48 x 27 x 20) with sawdust
Environmental conditions:	
Temperature:	21 ± 2°C
Humidity:	30 - 70%
Air changes:	approximately 12/hour
Photo period:	12 h light / 12 h dark

Animal assignment and treatment:

The treatment regime followed the Modified Buehler test procedure involving 9 topical induction treatments of 10 male and 10 female guinea pigs during a three-week period using the undiluted formulation. The control group (5 males and 5 females) was treated with distilled water.

After a 10-day recovery period control and treated animals were topically challenged with a 10% (w/w) aqueous dilution of BAS 595 01 F.

The skin at the application site was clipped and/or shaved free of hair 24 hours before each application. For induction the anterior left flank and for challenge the posterior right and left flanks (each 4 x 4 cm) were clipped free of hair.
The test substance concentrations used for induction and challenge applications were selected based on the results of a pre-test. In this preliminary test the undiluted and 50%, 25% and 10% (w/w) aqueous dilutions of the formulation were administered once for six hours under occlusive conditions to the shaved skin of groups of 2 (mainly) female Guinea pigs as described below. Skin reactions were assessed 24 and 48 hours after application.

Induction:
The inductions were performed on study days 1, 3, 5, 8, 10, 12, 15, 17 and 19. For this 4 cm² gauze patches containing 0.5 ml of the undiluted test substance were applied to the skin of the left anterior flank under an occlusive dressing. The gauze patch was held in place using an adhesive anallergic waterproof plaster placed around the trunk of the animals. After removal of the dressings, any residual test substance was removed by means of a gauze pad moistened with paraffin oil.
The test group animals were exposed to the undiluted test substance whereas control animals were exposed to the vehicle (bi-distilled water) for six hours. Skin reactions were assessed 24 hours after removal of the dressings.

Challenge:
A challenge was performed after 10 treatment-free days at study day 29. A volume of 0.5 mL of the 10% aqueous dilution (w/w) of the test substance was applied to each animal as described above. Both, the test group and control group were treated with the test substance. The duration of exposure was 6 hours; the test substance was applied on the posterior right flank. Readings were performed at 24 and 48 h after the removal of the dressings.

Positive control:
A positive control (reliability check) with a known sensitizer was performed in April 1994. The positive control with 2,4-dinitro chlorobenzene showed that the test system was able to detect sensitizing compounds under the laboratory conditions chosen (see results).

Evaluation
Only animals of the treated group showing well-defined macroscopic cutaneous reactions (erythema and/or edema, score ≥ 2) or "doubtful" (erythema and/or edema, score of 1) macroscopic reactions observed after 24 and 48 hours, confirmed by microscopic exanimation as being due to a sensitization process, were retained for the determination of the allergic potential level of the test substance.
The evaluation "sensitizing" results if at least 15% of the test animals exhibit skin reactions in accordance to the criteria of Annex VI of the Commission Directive 67/548/EEC (as adapted to the technical process for the 18th time by Commission Directive 93/21/EC) that were in place at the time the study was conducted.

The animals were observed for clinical signs and mortality twice a day throughout the study.

The animals were weighted on the day of allocation into the groups, on the first day of the study (day 1) and each week until the end of the study.

A macroscopic examination of the main organs of the animal found dead during the study was performed. On day 31, after the 48-hour observation period, the surviving animals were killed by CO_2 inhalation. No skin samples were taken.

Results

Pre-test:

No edema was observed in any of the animals 24 and 48 hours after removal of the dressings. The determination of erythema was obscured by the red coloration of the skin due to the red dye in the formulation (Table 6.1.6.1-1)

Table 6.1.6.1-1: Results of the pre-test for determination of skin reactions after administration of BAS 595 01 F

Animal number	Concentration of the test substance [%]	Flank	Scoring after removal of the dressings 24 hours		48 hours	
			E	O	E	O
First assay						
male 01	100%	RF	C2	0	C2	0
		LF	C2	0	C2	0
female 01	100%	RF	C2	0	C2	0
		LF	C2	0	C2	0
Second assay						
female 01	50%	RF	C2	0	C1	0
		LF	C2	0	C1	0
female 02	50%	RF	C2	0	C1	0
		LF	C2	0	C1	0
Third assay						
female 03	25%	RF	C1	0	0	0
		LF	C1	0	0	0
female 04	25%	RF	C1	0	0/C	0
		LF	C1	0	0/C	0
Forth assay						
female 05	10%	RF	0	0	0	0
		LF	0	0	0	0
female 06	10%	RF	0	0	0	0
		LF	0	0	0	0

RF: right flank; LF: Left Flank; E: erythema; O: edema
C : red coloration of the skin
C1 : red coloration of the skin which could obscure an eventual erythema at grade 1
C2 : red coloration of the skin which could obscure an eventual erythema at grades 1 or 2

Based on the results of this pre-test concentrations of 100% and 10% were chosen for induction and challenge, respectively.

Main test:

A very slight to slight red coloration of the skin was observed throughout the induction period.

No skin reactions indicating an allergic response were observed in any of the treated animals after challenge.

Twenty-four hours after removal of the dressings a very slight red coloration of the application site was observed in 9/10 control and 17/19 treated animals. This was no longer seen after 48 hours.
The positive control study was performed using female animals. Induction was performed with a 0.05% (probably aqueous) dilution of 2,4-dinitro chlorobenzene with 9 inductions according to the method described above. The challenge was performed with a 0.1% dilution at the right flank and a 0.5% dilution at the left flank.
No signs of allergic skin reactions were observed with the 0.1% dilution after 24 or 48 hours. The challenge with the 0.5% dilution resulted in allergic skin reactions in 5/5 females after 24 hours and 4/5 females after 48 hours.

Two animals of the treated group showed clinical signs during the induction period consisting of piloerection and/or hypo-activity (animal #6: days 3 to 15) and sedation, lateral decubitus and dyspnea were noted a few hours prior to death in animal #7. Such spontaneous clinical signs and mortality are commonly observed in guinea-pigs and they were not attributed to treatment
There were no effects on body weight development
Macroscopic evaluation of the main organs of the animal found dead did not reveal any abnormalities.

Conclusion
Based on the results of this study it is concluded that BAS 595 01 F has no sensitizing properties under the test conditions chosen. No classification as to skin sensitizing is warranted according to the criteria laid down in Regulation (EU) No. 1272/2008 (CLP).

B.6.1.6.2. Local lymph node assay (LLNA)

Previous evaluation:	No
DRAR (2016)	New study

Reference:	BAS 595 01 F - Murine local lymph node assay (LLNA)
Author(s), year:	[redacted] 2008
Report/Doc. number::	2007/1053388 / -
Guideline(s):	OECD 429 (2002)
GLP:	Yes
Deviations from OECD (2010):	-Last periodic positive control test (June 2007) has been conducted with acetone and not with Pleuronic. However, it is clear from the periodic positive control tests that once a year acetone and once Pleuronic has been tested and that the sensibility of the system has been proven
Acceptability:	Yes

Materials and methods

Test Material:	BAS 595 01 F
Description:	not provided in the report
Lot/Batch #:	84108
Purity/content:	Triticonazole: 25.2 g/L
Stability of test compound:	According to the CoA the formulation was stable until May 29, 2008 when stored at +5 to +30 °C.
Vehicle and/or positive control:	1% Pluronic® L92 in bi-distilled water, Alpha-Hexylcinnamaldehyde
Test animals:	
Species:	Mouse

Strain:	CBA/J
Sex:	20 females
Age:	6 to 12 weeks
Weight at dosing:	20.5 ± 1.1 g
Source:	[redacted]
Acclimation period:	at least 14 days
Diet:	Kliba-Labordiät (Maus / Ratte Haltung "GLP"), Provimi Kliba SA, Kaiseraugst, Basel, Switzerland, ad libitum
Water:	tap water ad libitum
Housing:	individual housing in Makrolon Type II cages with Lignocel FS 14 (SSNIFF) bedding and environmental enrichment: Nest-building material (wood wool) (Type NBF E-011); Abedd® Lab. and Vet. Service GmbH Vienna, Austria
Environmental conditions:	
Temperature:	20 - 24°C
Humidity:	30 - 70%
Air changes:	not indicated in the report
Photo period:	12 h light / 12 h dark (06:00 - 18:00/18:00 – 06:00)

Animal assignment and treatment:

The skin sensitizing potential of BAS 595 01 F was assessed using the radioactive Murine Local Lymph Node Assay. For this, female mice were allocated to groups of 5 animals according to the randomization instructions of „Nijenhuis, A. and Wilf, H.S.: Combinatorial Algorithms, Academic Press, New York, San Francisco, London, 1978, pp. 62 – 64".

The groups were treated either with

- the vehicle (1% aqueous Pluronic®),
- a 30% (w/w) dilution of the test article in 1% aqueous Pluronic®,
- a 50% w/w) dilution of the test article in 1% aqueous Pluronic®, or
- the undiluted test article containing 1% Pluronic®.

Analysis of treatment solutions:

The stability of the test substance in the vehicle was determined indirectly by the concentration control or homogeneity analysis. For this purpose, the samples taken were stored at room temperature over the maximum duration of the application period and were subsequently deep-frozen. Afterwards, these samples were analyzed. The homogeneity of the 30% dilution of BAS 595 01 F was determined. The actual test substance concentration was determined once for the 30% and 50% dilution.

The 30% dilution of test article was homogenous and the concentration control analyses revealed the correct preparation of the dilutions. As the concentration of the solutions were analyzed after 5 days of storage at room temperature, the test article is considered to be stable for this period of time. For details see raw data.

Statistics:

Not performed in this study

Clinical observation:
Mortality was checked twice daily on working days and one on weekends and public holidays. No detailed clinical examination of the individual animals was performed but any obvious signs of systemic toxicity and/or local inflammation at the application sites were recorded.

Body weights:
Individual body weights were determined on day 0 prior to the first application and on day 5 prior to the sacrifice of the animals.

Treatment of animals:
The dosing solutions were applied daily to the dorsal part of the ears at a volume of 25 µL per ear for 3 consecutive days. On study day five, i.e. 66 to 72 hours after the last application, 20 µCi of ^{3}H-thymidine in 250 µL sterile saline was injected into the tail vein of each mouse.

Terminal procedures:
Approximately 5 hours after ^{3}H-thymidine injection the animals were killed by cervical dislocation.
Immediately after the death of each animal a circular piece of tissue (diameter 0.8 cm) was punched out of the apical part of each ear of all animals. The weight of the pooled punches was determined for each test group. These measurements served for the detection of a potential inflammatory ear swelling.
Immediately after removal of the ear punches the left and right auricular lymph nodes were dissected. The weight of the pooled lymph nodes from both sides was determined for each animal.
After weight determination, a single cell suspension was prepared per test group from the pooled lymph nodes by carefully passing all lymph nodes through an iron mesh (mesh size 200 µm) into 40 mL of phosphate-buffered physiological saline. Subsequently the cell counts were determined with an aliquot of each suspension using a Casy®- Counter.
The remaining cell suspensions were washed twice with phosphate buffered saline (PBS) and precipitated with 5% trichloroacetic acid. Each precipitate was transferred to scintillation fluid and incorporation of ^{3}H-thymidine into the cells was measured in a β-scintillation counter.

Data evaluation and interpretation
The stimulation indices (SI) of cell count, 3H-thymidine incorporation, lymph node weight and ear weight were calculated as the ratio of the test group values for these parameters divided by those of the vehicle control group.

The lymph node cell count and the ^{3}H-thymidine incorporation into the lymph node cells as well as to a certain extent lymph node weight are used to determine the potential sensitizing properties of a test article. Because not only sensitization induction but also irritation of the ear skin by the test substance may induce lymph node responses, the weight of ear punches taken from the area of test-substance application is determined as a parameter for inflammatory ear swelling as an indicator for the irritant action of the test substance.

Stimulation indices of >1.5 for cell count and/or of ≥ 3 for ^{3}H-thymidine incorporation are generally considered as indicative for a sensitizing potential of a test substance. If applicable, the EC (estimated concentration) leading to the respective SI values were calculated by linear or semi-logarithmical regression.

If the increase in cell count, ^{3}H-thymidine incorporation and/or lymph node weight is accompanied by a biologically relevant increases in ear weights it cannot be ruled out that the lymph node response was caused by irritation and not by skin sensitization. Depending on the magnitude of lymph node response, based on expert judgment, the evaluation of the sensitizing potential may be modified or additional studies might be necessary.

If a test article – despite of concentration related increase - does not elicit a biological relevant increase in cell count and/or ^{3}H-thymidine incorporation, further investigation of the sensitization potential at higher concentrations may be considered.

Positive controls

A concurrent positive control (reliability check) with a known sensitizer was not included into this study. Studies using the positive control substance Alpha-Hexylcinnamaldehyde are performed twice a year in the laboratory in order to show that the test system is able to detect sensitizing compounds under the test conditions chosen.

Results

No clinical observations or mortality were observed.

There were no effects on body weight development. The increase of body weights during the study was within the expected range.

The stimulation indices (SI) for lymph node cell counts, ^{3}H-thymidine incorporation and lymph node and ear weights are given in Table 6.1.6.2-1.

Table 6.1.6.2-1: Stimulation indices for cell counts, ^{3}H-thymidine incorporation, lymph node and ear weight in mice after treatment with BAS 595 01 F

Test Group	Treatment	Parameter evaluated	Stimulation index[1]
		Cell count [counts/lymph node pair]	
1	vehicle 1% aqueous Pluronic®	6182667	1.0
2	30% in 1% aqueous Pluronic®	5536000	0.9
3	50% in 1% aqueous Pluronic®	4680000	0.8
4	test substance + Pluronic® (99+1)	7181333	1.2
		^{3}H-Thymidine incorporation [DPM/lymph node pair]	
1	vehicle 1% aqueous Pluronic®	352.5	1.0
2	30% in 1% aqueous Pluronic®	349.1	1.0
3	50% in 1% aqueous Pluronic®	459.1	1.3
4	test substance + Pluronic® (99+1)	738.8	2.1
		Lymph node weight [mg/lymph node pair]	
1	vehicle 1% aqueous Pluronic®	4.4	1.0
2	30% in 1% aqueous Pluronic®	4.2	1.0
3	50% in 1% aqueous Pluronic®	4.4	1.0
4	test substance + Pluronic® (99+1)	4.8	1.1
		Ear weight [mg/animal]	
1	vehicle 1% aqueous Pluronic®	30.4	1.0

2	30% in 1% aqueous Pluronic®	31.4	1.0
3	50% in 1% aqueous Pluronic®	34.7	1.1
4	test substance + Pluronic® (99+1)	36.3	1.2

[1] test group x / test group 1 (vehicle control)

At any concentration tested, topical treatment of mouse ears with BAS 595 01 F did not result in a biologically significant increase of the stimulation index for auricular lymph node cell counts, ^{3}H-thymidine incorporation and lymph node weight.

The undiluted test article and the 50% dilution caused a slight increase in ear weights. Due to the red coloration of the test article a red discoloration of the ears was observed on the 2nd and 3rd day of application and on the day of lymph node removal. Additionally, residues of the test substance were observed on the ears of the mice treated with the undiluted test article. Due to these observations the increase in ear weights cannot unequivocally attributed to ear skin irritation.

The sensitivity of mice (CBA/CaOlaHsd, Harlan Winkelmann GmbH, Borchen, Germany or CBA/J, Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, 97633 Sulzfeld) and the reliability of experimental techniques is assessed regularly using a known sensitiser. Positive results were consistently obtained over the years using several variations of the methods and different vehicles. The results of 6 control studies are presented in Table 6.1.6.2-2.

Table 6.1.6.2-2: Positive control LLNA studies performed

Project No.	45H0288/ 982036[#]	45H0288/ 982059[#]	58H0288/ 982068[#]	58H0288/ 982075[#]	58H0508/ 062114[#]	58H0288/ 982082[6]
Strain used	CBA/CaOla Hsd	CBA/CaOla Hsd	CBA/CaOla Hsd	CBA/CaOla Hsd	CBA/CaOla Hsd	CBA/J
Date of performance	Apr 04	Apr / May 2005	Aug 05	Feb 06	Aug 06	Jun 07
Name of test substance	Alpha-Hexylcinnamaldehyde, techn. 85%	Alpha-Hexylcinnamaldehyde, techn. 85%	Alpha-Hexylcinnamaldehyde, techn. 85%	Alpha-Hexylcinnamaldehyde, techn. 85%	Alpha-hexylcinnamaldehyde, 95+%	Alpha-Hexylcinnam-aldehyde, techn. 85%
Concentrations tested	3%, 10%, 30%	1%, 3%, 10%	2.5%, 5%, 10%	3%, 10%, 30%	3%, 10%, 30%	1%, 3%, 10%
Vehicle	1% Pluronic® L92 Surfactant in bi-distilled water	acetone	AOO 4:1 (acetone : olive oil 4:1 v/v)	acetone	1% Pluronic® L92 Surfactant in bi-distilled water	acetone
Stimulation index Cell counts[a]	1.43, 2.28, 2.92	1.28, 1.63, 2.94	1.13, 1.30, 1.83	1.75, 2.36, 2.98	1.13, 2.20, 3.38	1.42, 1.97, 2.75
Stimulation index 3H-thymidine incorporation[b]	-	-	1.12, 1.19, 2.84[1]	4.56, 6.63, 9.86	1.16, 4.64, 17.98	1.81, 3.24, 3.74
Evaluation of study results	Positive	Positive	Positive	Positive	Positive	Positive

[a] = Ratio of test group values to control group values (Stimulation index) greater than 1.5 indicates a positive result
[b] = Ratio of test group values to control group values (Stimulation index) greater than 3.0 indicates a positive result
[#] = Individual lymph nodes
[6] = Pooled lymph nodes
[1] = Borderline SI at 10% in accordance with published results using AOO as the vehicle

Conclusion

Based on the results of this study it is concluded that BAS 595 01 F has no sensitizing properties under the test conditions chosen. No classification as to skin sensitization is warranted according to the criteria laid down in Regulation (EU) No. 1272/2008 (CLP).

B.6.1.7. Supplementary studies on the plant protection product

No further studies were either required or conducted for the product.

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

Not required, not needed.

B.6.2. DERMAL ABSORPTION

Previous evaluation:	No
DRAR (2016)	New study

Reference:	Triticonazole - Radiolabelled Triticonazole in BAS 595 01 F - In vitro study to investigate the dermal penetration through human skin
Author(s), year:	Bernard F., 2013
Report/Doc. number::	2013/1323932 / -
Guideline(s):	OECD Guideline for testing of chemicals No. 428 (Skin absorption: In vitro method (2004)), (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to (EC) No 1907/2006 of European Parliament and of Council on the REACH - Part B No. B.45
GLP:	Yes
Deviations from OECD:	No
Acceptability:	Yes

Materials and methods

Test Material**:**	a) ^{14}C-BAS 595 F (Triticonazole-C14) b) Unlabeled BAS 595 F c) BAS 595 X0 F B (blank formulation) d) BAS 595 01 F (Premis 25 FS)
Lot/Batch #:	a) 866-1401 b) COD-001440 c) FD-130827-0005 d) 0008117231
Purity:	a) radiochemical purity: 99.5%; specific activity: 5.95 MBq/mg b) 91.3% c) no triticonazole content d) 25 g active ingredient per 1 kg formulation
Stability of test compound:	a) The radiochemical purity was checked at the time point of administration. Therefore no expiration date is needed. b) The test substance is stable in the formulation; the expiry date of the formulation: 11-Feb-2014. c) The test substance is stable in the formulation; the expiry date of the formulation: 27-Aug-2015. d) The test substance is stable in the formulation; the expiry date of the formulation: 27-May-2015.
Vehicle:	tap water

Human skin preparations:
Human cadaver skin (upper leg dorsal or abdominal) from Caucasian donors was obtained from the "Institut für Pathologie, Kantonsspital Basel", Basel, Switzerland. Upon receipt the skin was wrapped in aluminium foil and stored at about -20°C until preparation of the skin membranes.

Preparation of formulations:
Stock Solution
[^{14}C]Triticonazole was provided as a solution in toluene. This solution was used as stock solution. The actual stock solution concentration was 1.90 mg/mL.

Dose Formulation A1 (low dose level)
1 mL of dose formulation A2 was diluted with 5 mL of deionised water. The formulation was sonicated for a few minutes and kept agitated by magnetic stirring until the end of application.
The final formulation was measured by LSC and had a concentration of radioactivity of 1719 kBq/mL corresponding to 4.04 mg [^{14}C]Triticonazole/mL (425.4 kBq/mg).

Dose Formulation A2 (high dose level)
47.0 mg (51.5 mg, 91.3 %) unlabeled Triticonazole was placed in a flask and a volume of the stock solution containing about 3.5 mg [^{14}C]Triticonazole (3.6 mg, 97.97% purity) was added. The solvent of the stock solution was removed by a gentle stream of N_2. The test item was re-dissolved in 2 mL of ethyl acetate. This procedure led to a new specific radioactivity of 425.4 kBq/mg, which was determined by LSC. The solvent was removed under a gentle stream of nitrogen. Once dried, 2091.5 mg of blank formulation BAS 595 X0 F was added to give 2142 mg BAS 595 01 F formulation with a density of 1.07 g/mL. The formulation was sonicated for a few minutes and kept on magnetic stirring until the end of application.
The final formulation was measured by LSC and had a concentration of radioactivity of 10950 kBq/mL corresponding to 25.7 mg [^{14}C]Triticonazole/mL.

Determination of applied dose
The exact radioactivity administered was determined by 3 control doses for each dose group.

Dose Formulation Stability:
The stability of the test item in the formulation at the time of the application was checked by HPLC.

The study was designed to examine the *in vitro* dermal absorption of [^{14}C]Triticonazole, batch no.: 866-1401 (5.95 MBq/mg) formulated as BAS 595 01 F (test preparation), a Flowable Slurry (FS) formulation, and one dilution, through human split-thickness skin using flow-through diffusion cells. The test preparation was tested at two target concentrations: 25 g a.i./L (concentrate), and 4 g a.i./L (1:5).

The study was performed using flow through diffusion cells with human skin samples (upper leg dorsal, or abdomen) and an suitable receptor fluid (Ethanol/tap water, 1:9 v:v) as a test system. Human skin membranes

were prepared from three separate donors (n=7) per test concentration tested. After thawing the frozen skin samples, the skin was dermatomed to a thickness of ca. 400 µm. The integrity of the skin membranes was assessed using tritiated water. Five cells were excluded from testing as they failed the integrity testing, leaving n= 5 for the concentrate and n=4 for the in-use dilution. The receptor fluid was Ethanol/tap water (1:9; v:v). The solubility of Triticonazole in the receptor fluid (estimated at 20 µg/mL) was considered to meet the requirements of the OECD guideline. The exposed area of each skin membrane (0.64 cm^2) remained in contact with the test material formulation for a contact period of 8 h (normal working hours/day) with a post-exposure time of 16 h (i.e. the study duration was 24 h). Washing was performed both at the end of the contact exposure and post-exposure period. The donor chamber was covered with permeable tape (FLAWA).

In order to determine dermal absorption, the amount of [^{14}C]Triticonazole was determined in:

- treatment formulation
- receptor fluid samples collected at 1 hour intervals until 8 h after application, then 2 hour intervals until study termination at 24 h.
- residues remaining in/on the skin membranes
- residues remaining in the stratum corneum (the first five stripping tapes were analysed individually (Tape Strips 1-5) and the stripping tape 6 to 10 and 11 to 15 were pooled).
- residues remaining into receptor and donor compartment
- washes

Results

The stability, homogeneity and content of the test item in the application medium were confirmed by analysis. Details are available in the raw-data.

The applied doses are given in Table 6.2-1.

Table 6.2-1: Target dose for the concentrate and in-use dilution

Dose group	Target dose [µg/cm²]
1 (concentrate)	241.3
2 (in-use dilution)	37.0

The mean values of the kinetic parameters determined from the linear region of the cumulative absorbed dose curve are presented in Table 6.2-2. An absorption rate of 0.15 and 0.04 µg/cm²·h was obtained for the formulation concentrate and in-use dilution. After 12 hours, the absorption of neither the formulation concentrate nor the in-use dilution was essentially complete as less than 75% of the total accumulated dose was found in the receptor medium after half of the study period. Within 12 hours 57.9% and 71.0% of the total dose were absorbed after application of the formulation concentrate and the in-use dilution, respectively

Table 6.2-2: *In-vitro* dermal penetration of Triticonazole formulated as BAS 595 01 F through human skin – Penetration kinetics

Dose group	High dose (formulation concentrate)	Low dose (1:5 dilution)

Target concentration [mg/mL]	25		4.0	
Target dose [µg/cm²]	234.4		37.5	
Mean actual applied dose [µg/cm²]	241.0		37.0	
Number of cells used/Valid cells	5/7		4/7	
	Mean cumulative absorption		Mean cumulative absorption	
	[µg/cm^2]	[%]	[µg/cm^2]	[%]
Sample time [h]				
8	0.28	0.12	0.19	0.50
12	0.89	0.38	0.33	0.90
24	1.54	0.64	0.46	1.25
Kp [*10^{-5} cm/h]	1.50		1.57	
Absorption rate [µg/cm^2·h]	0.15		0.04	
Lag time [h]	n.c.		n.c.	
% absorbed within 12 hours	57.90%		71.00%	

n.c. = not calculated, but steady state is achieved between 8 and 12 hours

The mean total recovery of Triticonazole in human skin was 97.8 ± 0.86% for the concentrate and 101.0 ± 2.33% for the dilution. 0.44% (concentrate) and 2.24% (dilution) radioactivity was associated with the stratum corneum (tape strips). For the concentrate, the mean cumulative absorption of Triticonazole into the receptor fluid after 24 h was 1.54 µg/cm^2, i.e. 0.64% of the dose applied and the mean maximal flux was 0.153 µg/cm^2/h. For the dilution, the mean cumulative absorption of Triticonazole into the receptor fluid after 24 h was 0.462 µg.cm^{-2}, i.e. 1.25% of the dose applied and the mean maximal flux was 0.040 µg/cm^2/h. In accordance with EFSA 2012, where less than 75% of the absorption occurs within half the duration of the study, the absorbed dose is defined as receptor fluid + receptor chamber washes + skin sample (including all tape strips except the first 2). For this study, at both concentrations the mean absorption was less than 75%, therefore tape strip samples 2 (strips 3 -15) have been included. As this was a flow-through chamber study, chamber washes were not performed.

The mean absorbed dose, defined as receptor fluid + skin sample (including all but the first two tape strips, in accordance with EFSA 2012, where less than 75% of the absorption occurs within half the duration of the study – see Table 6.2-3) was 0.85 ± 0.11% of the dose applied from concentrate and 1.87 ± 0.21% from the in-use dilution. Furthermore, as the standard deviation was >25% for the absorbed dose for the concentrate and in-use dilution, one standard deviation was added to the mean value for calculation of the absorption estimate used for risk assessment.

Table 6.2-3: *In-vitro* dermal penetration of BAS 595 F formulated as BAS 595 01 F through human skin - Recovery data

Dose group		**High dose (formulation concentrate)**	**Low dose (1:5 dilution)**
Target concentration	25	4.0	0.065
Target dose	234.4	37.5	0.65
Mean actual applied dose	241.0	37.0	0.68

Number of cells used/Valid cells	5/7		4/7	
	Recovery [%]		Recovery [%]	
	Mean	S.D.	Mean	S.D.
Unabsorbed dose				
Skin washing after 8 hours	94.30	3.49	92.63	3.50
Skin washing after 24 hours	1.14	0.71	3.64	1.88
Donor chamber	1.20	1.56	1.20	1.19
Dose associated to skin				
Tape strips: 1st sample, strips 1 + 2	0.28	0.17	1.69	1.20
Tape strips: 2nd sample; strips 3 - 15	0.16	0.07	0.55	0.49
Skin preparation	0.05	0.05	0.07	0.09
Absorbed dose				
Receptor fluid	0.64	0.49	1.25	0.80
Receptor chamber wash	-	-	-	-
Total recovery[#]	97.77	0.86	101.01	2.33
Absorption essentially complete at end of study (>75% absorption within half the study duration)	**No**		**No**	
Absorption estimates when absorption not essentially completed (= absorbed dose + dose associated to skin + tape strips sample 2)[a]	0.85.	0.61.	1.87	1.38
Absorption estimates when absorption essentially completed (= absorbed dose + dose associated to skin)	n.a.	n.a.	n.a.	n.a.
Absorption estimate normalized[b]	n.a.	n.a.	n.a.	n.a.
Relevant absorption estimate[c]	1.46		3.25	
Absorption estimates used for risk assessment[c]	**1**		**3**	

[#] values may not be calculated exactly due to rounding of figures

[a] In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665) the radioactivity in the second tape-strip pool (3rd to 15th tape strip) is considered potentially absorbable if less than 75% of the absorption occurred in the first half of the study. Finally, the skin preparation is also considered potentially absorbable.

[b] Cells with insufficient recovery (<95%) were corrected by normalization of absorption estimate to 100% recovery

[c] In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665) one standard deviation was added to the mean % dermal penetration in cases where the standard deviation was ≥ 25% of the mean value. This value was then rounded to the required number of significant figures.

n.a.: not applicable

Conclusion

On the basis of an *in vitro* dermal absorption study in human skin with BAS 595 01 F, dermal absorption values for Triticonazole to be used in the risk assessment are 1% and 3% for the concentrate and the in-use dilution, respectively.

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

Information on co-formulants is considered to be confidential and therefore included in Volume 4.

B.6.4. EXPOSURE DATA

B.6.4.1. Operator exposure

Estimations of potential operator exposure have been undertaken using the following exposure models:

SeedTropex UK Version (geometric mean values)

SeedTropex-worker-version 19(190506)FR (75th percentile values)

An exposure assessment for BAS 595 01 F used in static and mobile seed treatment stations has also been performed using surrogate data, originating from studies performed on behalf of the SeedTropex industry task force, to provide a higher tier exposure assessment.

The EFSA (2014) guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products having assessed the SeedTropex model 1996 states a data gap for seed treatment exposure scenarios as well as seed sowing. MS UK and France have conducted individual reviews of the initial model data in 2006 and accepted adopted versions of this model on national level. The notifier stated that however this initial model does not cover relevant exposure scenarios for BAS 595 01 F and does not represent the technical state of the art range of product and use scenarios. For example, data on mobile seed-treatment units are missing and low concentration application rates as relevant for BAS 595 01 F are not covered. The notifier further stated that these data gaps forced the further development of the SeedTropex model as provided in the 2014 version and are therefore considered the relevant database to be used for seed-treatment assessment of BAS 595 01 F in the absence on an EU agreed model. It should be noted that the exposure studies provided are included into this updated study database.

As a worst case the 20 L container size has been assumed as this gives the highest number of separate mixing/loading operations, i.e. a total of 8. In practice it is expected that the larger container sizes will be used when higher volumes of seed are to be treated. Based on an assumed throughput of 75 or 100 tons seed/day and an application rate of 2 L product per ton seeds, 150 to .200 L product are required per day. Therefore a 20 L container = use of 8 to 10 containers per day is considered a reasonable worst case. The available smaller container size of 5 L would require loading of 30 to 40 containers which is not considered reasonable. Regarding the assumed throughput it should be noted that the old model versions assumed a treatment rate of 75 tons per day while the updated risk assessments based on the recent SeedTropex model assumes a throughput of 100 tons per day. The UK and France model version consider individual container filling as single operations, whereas the recent SeedTropex model considers the total daily amount of active ingredient used for mixing/loading as basis for the assessment being the same approach as in the EFSA guidance operator model.

The updated SeedTropex database and model development includes a set of further studies extending the different exposure scenarios for cereal uses already included into the initial model version of 1996 with scenarios for mobile treatment units and extends the application rate range to low concentration products like BAS 595 01

F. Furthermore, other crop groups were included. The model version V15 of 2014 used in this risk assessment covers in comparison to the UK and France review versions of the model the following additional exposure studies:

1. Exposure study in cereals in static seed-treatment units in UK (2005)
2. Exposure study in cereals in static seed-treatment units in France (2005)
3. Exposure study in cereals in mobile seed-treatment units in France (2008)
4. Exposure study in sugar-beet in static seed treatment units in France (2006)
5. Study on seed sowing of treated corn in Germany and Italy (2007)
6. Exposure study in cereals in static seed treatment units in France (2008)
7. Exposure study in cereals in static seed treatment units in Germany, UK and France (2009).

Furthermore, the 2014 model version is more flexible in selection of evaluation parameters e.g. selection of breathing rate, percentile values, and PPE level.

Consequently estimates on this new extended model are presented as well.
The SeedTropex model version V15 of 2014 allows the assessment on different percentile data including 95th percentile. Therefore, an additional acute assessment based on 95th percentile exposure data and the proposed AAOEL is provided as well.

Estimations of exposure were compared to the AOEL agreed for the Annex I inclusion for triticonazole and the AAOEL proposed in this renewal assessment report. Dermal absorption data for BAS 595 01 F are now available.

End-Point	**Active Substance**
Dermal penetration	Concentrate: 1% Dilution: 3%
AOEL	0.025 mg/kg bw per day
AAOEL	0.05 mg/kg bw per day

Risk assessment for operator

Estimations of potential operator exposure using the UK and French versions of the SeedTropex model are summarised below.

Table 6.4.1-1:Estimated operator exposure to triticonazole from use of BAS 595 01 F during seed treatment

Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of AOEL**
Product used undiluted. Application rate = 5 g a.s./100 kg seed.			
UK SeedTropex Model 60 kg operator	Gloves and coveralls worn during mixing/loading, calibration and cleaning. Coveralls worn during bagging.	0.0097	39
Product diluted 1:5 Product:Water. Application rate = 5 g a.s./100 kg seed.			

UK SeedTropex Model 60 kg operator	Gloves and coveralls worn during mixing/loading, calibration and cleaning. Coveralls worn during bagging.	0.0061	24
Product used undiluted. Application rate = 5 g a.s./100 kg seed.			
France SeedTropex Model 70 kg operator	Gloves and coveralls worn during mixing/loading, calibration and cleaning. Coveralls worn during bagging. RPE worn during cleaning.	0.0137	55
Product diluted 1:5 Product:Water. Application rate = 5 g a.s./100 kg seed.			
France SeedTropex Model 70 kg operator	Gloves and coveralls worn during mixing/loading, calibration and cleaning. Coveralls worn during bagging. RPE worn during cleaning.	0.0172	69

In the SeedTropex studies included in the model workers wore a two part coverall and protective gloves for all tasks except bagging, where the task was performed with bare hands.

A higher tier assessment is also presented which addresses both static seed treatment plants and on-farm treatments carried out using mobile seed treatment equipment. As the SeedTropex model (static plants) is based on exposure data for products applied at higher application rates (g a.s./ton seed) than those recommended for triticonazole in BAS 595 01 F, it is expected that the predicted exposures using this exposure model will overestimate actual levels of exposure for seed treatment workers and the assessment based on a representative exposure study provides a more realistic estimate of their exposures.

Table 6.4.1-2: Estimated operator exposure to triticonazole from use of BAS 595 01 F during seed treatment using higher tier data

Scenario	Level of PPE	Total absorbed dose* (mg/kg/day)	% of AOEL
Static seed treatment	Cotton/polyester work clothing for mixing/loading, calibration and bagging. An impermeable coverall is worn over work clothing with suitable protective gloves during cleaning operations	6.3×10^{-5}	0.25
Mobile seed treatment	Cotton/polyester work clothing and suitable protective gloves for mixing/loading, calibration and bagging.	7.9×10^{-5}	0.32

*Assumes 3% dermal absorption

Table 6.4.1-3: Estimated operator exposure to triticonazole from use of BAS 595 01 F during seed treatment using updated SeedTropex model approach

Long-term exposure assessment			
Scenario	**Level of PPE**	**Total absorbed dose* (mg/kg/day)**	**% of AOEL**
Static seed treatment (75th percentile)	Cotton/polyester work clothing for mixing/loading, calibration and bagging. An impermeable coverall is worn over work clothing with suitable protective gloves during cleaning operations	0.00116	4.7
Mobile seed treatment (75th percentile)	Cotton/polyester work clothing for mixing/loading, calibration and bagging.	0.00078[5]	3.1
Acute exposure assessment			
Scenario	**Level of PPE**	**Total absorbed dose* (mg/kg/day)**	**% of AAOEL**
Static seed treatment (95th percentile)	Cotton/polyester work clothing for mixing/loading, calibration and bagging. An impermeable coverall is worn over work clothing with suitable protective gloves during cleaning operations	0.00394	7.9
Mobile seed treatment (95th percentile)	Cotton/polyester work clothing for mixing/loading, calibration and bagging.	0.00775	15.5

*Assumes 1% dermal absorption mixing/loading and 3% dermal absorption for all other operations

Table 6.4.1-4: Estimated operator exposure to triticonazole from sowing seed treated with BAS 595 01 F

Dermal exposure (mg/day)	**Inhalation exposure (mg/day)**	**Total systemic exposure* (mg/kg bw per dayay)**	**AOEL (mg/kg bw per dayay)**	**% AOEL**
Triticonazole				
7.33	0.2	0.007	0.025	28

*Assumes 3% dermal absorption

Table 6.4.1-5: Estimated operator exposure to triticonazole from sowing seed treated with BAS 595 01 F using updated SeedTropex model approach

Long-term exposure assessment				
Dermal exposure (mg/kg bw per dayay)	**Inhalation exposure (mg/kg bw per dayay)**	**Total systemic exposure* (mg/kg bw per dayay)**	**AOEL (mg/kg bw per dayay)**	**% AOEL**
0.124	0.0014	0.0037	0.025	15
Acute exposure assessment				
Dermal exposure (mg/kg bw per dayay)	**Inhalation exposure (mg/kg bw per dayay)**	**Total systemic exposure* (mg/kg bw per dayay)**	**AAOEL (mg/kg bw per dayay)**	**% AAOEL**
0.256	0.0031	0.0076	0.05	15

*Assumes 3% dermal absorption

Conclusion

According to the UK and French SeedTropex model calculations, it can be concluded that the risk for the operator using BAS 595 01 F to treat cereal seeds is acceptable with the use of personal protective equipment. A higher tier exposure assessment which addresses both static seed treatment plants and on-farm treatments carried out using mobile seed treatment equipment confirms levels of exposure for seed treatment operators are within the AOEL. This higher tier assessment is based on exposure studies which are more representative in terms of application rate to BAS 595 01 F than the initial SeedTropex studies and is therefore expected to give more realistic estimates of exposure for seed treatment operators using BAS 595 01 F. Protective gloves and coveralls should be worn during mixing/loading, calibration and cleaning operations. Suitable protective clothing (coveralls) should be worn during bagging operations. An impermeable coverall, in addition to work clothing, should be worn during cleaning operations.

The estimates based on the revised SeedTropex model (Version 15 of 2014) further substantiate the safe use for seed treatment of cereals with triticonazole when applied in BAS 595 01 F. The estimates considered coveralls worn during mixing/loading, calibration and bagging operations. An impermeable coverall, in addition to work clothing and protective gloves were considered during cleaning operations.

Estimates of exposure for triticonazole for operators sowing BAS 595 01 F treated seed are within the AOEL where protective clothing (coveralls) are worn during the seed sowing operation. This conclusion was confirmed by the estimates based on the revised SeedTropex sowing model. Furthermore, the acute assessment considering the proposed AAOEL and 95th percentile of the SeedTropex sowing model data demonstrates a safe use as well.

B.6.4.1.1. Estimation of operator exposure

The UK assessment using the SeedTropex model (geometric mean values) assumes the use of a static plant with a low level of automation, which achieves a throughput of 75 tons treated seed/day. Although more highly automated plants would normally achieve higher work rates and involve the handling of greater amounts of product, levels of exposure during the bagging task (which contributes most to overall exposure) would be lower for these plants. It is assumed that a single 60 kg operator performs 1 calibration and cleaning operation per day and 8 hours bagging. The assessment also assumes this worker performs 8 separate mixing/loading operations per day.

The French version of SeedTropex uses the same underlying database of studies but the indicative exposure values are based on 75th percentile values. This model also assumes a single worker performs all four tasks, but the bagging task is 7 hours and the worker body weight is 70 kg.

In the SeedTropex studies workers wore coveralls and gloves for all tasks except bagging where only coveralls were worn. The estimated actual dermal exposure values therefore reflect this level of PPE.

Table 6.4.1.1-1: UK SeedTropex estimate of operator exposure to triticonazole from use of BAS 595 01 F applied undiluted during seed treatment

TASK	Total Potential Dermal Exposure (mg/op)*	Estimated Actual Dermal Exposure (mg/op)*	Inhalation Exposure (mg/op)*	***Frequency of operation ** / day***	Total Potential Dermal Exposure (mg/day)	Estimated Actual Dermal Exposure (mg/day)	Inhalation Exposure (mg/day)
Calibration	0.81	0.36	0.025	***1***	0.81	0.3557	0.025
Mixing / Loading	0.1298	0.130	0.003	***8***	1.04	1.0384	0.026
Bagging (mg/hr) worst case scenario	1.84	0.698	0.0054	***8***	14.7	5.58	0.0432
Cleaning	22	2.08	0.4	***1***	22	2.0841	0.4
Total route specific exposure (mg/person/day)					**38**	**9.1**	**0.49**
Dermal absorption/Inhaltion absorption (incl RPE reduction)					n/a	1.0%	100%
Route specific absorbed dose (mg/kg bw/day)						**0.0015**	**0.008**
Total absorbed dose (mg/kg bw/day)						**0.0097**	

* exposure during bagging mg/hour

** frequency during bagging in hours/day

Table 6.4.1.1-2: UK SeedTropex estimate of operator exposure to triticonazole from use of BAS 595 01 F when diluted during seed treatment

TASK	Total Potential Dermal Exposure (mg/op)*	Estimated Actual Dermal Exposure (mg/op)*	Inhalation Exposure (mg/op)*	***Frequency of operation ** / day***	Total Potential Dermal Exposure (mg/day)	Estimated Actual Dermal Exposure (mg/day)	Inhalation Exposure (mg/day)
Calibration	0.16	0.07	0.005	***1***	0.16	0.0711	0.005
Mixing / Loading	0.1298	0.130	0.003	***8***	1.04	1.0384	0.026
Bagging (mg/hr) worst case scenario	1.84	0.698	0.0054	***8***	14.7	5.58	0.0432
Cleaning	4	0.42	0.08	***1***	4	0.4168	0.08
Total route specific exposure (mg/person/day)					**20**	**7.1**	**0.15**
Dermal absorption/Inhaltion absorption (incl RPE reduction)					n/a	3%	100%
Route specific absorbed dose (mg/kg bw/day)						**0.0036**	**0.003**
Total absorbed dose (mg/kg bw/day)						**0.0061**	

* exposure during bagging mg/hour

** frequency during bagging in hours/day

Table 6.4.1.1-3: French SeedTropex estimate of operator exposure to triticonazole from use of BAS 595 01 F applied undiluted during seed treatment

Task	Actual dermal exposure (mg/day)	Inhalation exposure (mg/day)
Calibration	0.362	0.062
Mixing/Loading	0.227	0.4
Bagging	7.945	0.214
Cleaning	4.527	1.515
Total	**13.06**	**2.191**
Total systemic dose (mg/day)	2.322	
% AOEL	**133**	

Table 6.4.1.1-4: French SeedTropex estimate of operator exposure to triticonazole from use of BAS 595 01 F when diluted during seed treatment

Task	Actual dermal exposure (mg/day)	Inhalation exposure (mg/day)
Calibration	0.07	0.062
Mixing/Loading	0.23	0.4
Bagging	7.95	0.214
Cleaning	4.53	1.515
Total	**12.77**	**2.191**
Total systemic dose (mg/day)	2.57	
% AOEL	**147**	

The revised SeedTropex model (Version 15, 2014) includes more studies meanwhile available and allows more flexible state of the art data evaluation. The revised model also covers the studies presented below. For the estimates the following parameters were taken into account:

The following parameters have been used:		
AOEL Value	0.025	mg/kg bw per dayay
Body weight	60	kg
Inhalation ventilation rate	21	L/min.
Dermal penetration M/L/loading	1.00	%
Dermal Penetration Calibration	3.00	%
Dermal penetration Bagging / Sowing	3.00	%
Dermal penetration Cleaning	3.00	%

PPE			
Task	**Gloves**	**Body**	**Respiration**
Mixing/Loading	No	Coverall	No
Calibration	No	Coverall	No
Bagging	No	Coverall	No
Cleaning	Yes	Coverall and Tyvek	No

Miscellaneous statistical parameters	
Selection of statistical endpoint	75th percentile
Protections: actual or actual+calculated	Actual + calculated

Table 6.4.1.1-5: Revised SeedTropex model: estimate of operator exposure to triticonazole from use of BAS 595 01 F in seed treatment plants

Cereal Seed in plant	Mixing/Loading	Calibration	Bagging	Cleaning	Total	
Total actual dermal exposure	7.021	0.766	3.216	0.306	11.308	µg/kg bw/day
Total inhalation exposure	0.258	0.007	0.251	0.026	0.541	µg/kg bw/day
Total dose absorbed	0.598	0.028	0.500	0.039	1.164	µg/kg bw/day
% AOEL	**2.393**	**0.110**	**1.998**	**0.156**	**4.657**	**%**

Table 6.4.1.1-6: Revised SeedTropex model: estimate of operator exposure to triticonazole from use of BAS 595 01 F in mobile seed treatment units

Cereal Seed Mobile	Combined	
Total actual dermal exposure	18.40	µg/kg bw/day
Total inhalation exposure	0.00	µg/kg bw/day
Total dose absorbed	0.78	µg/kg bw/day
% AOEL	**3.13**	**%**

An acute exposure assessment based on the revised SeedTropex model (Version 15, 2014) and the proposed AAOEL is presented below. For the estimates the following parameters were taken into account:

The following parameters have been used:		
AAOEL Value	0.05	mg/kg bw per dayay
Body weight	60	kg
Inhalation ventilation rate	21	L/min.
Dermal penetration M/L/loading	1.00	%
Dermal Penetration Calibration	3.00	%
Dermal penetration Bagging / Sowing	3.00	%
Dermal penetration Cleaning	3.00	%

PPE			
Task	**Gloves**	**Body**	**Respiration**
Mixing/Loading	No	Coverall	No
Calibration	No	Coverall	No
Bagging	No	Coverall	No
Cleaning	Yes	Coverall and Tyvek	No

Miscellaneous statistical parameters	
Selection of statistical endpoint	95th percentile
Protections: actual or actual+calculated	Actual + calculated

Table 6.4.1.1-7: Revised SeedTropex model: estimate of acute operator exposure to triticonazole from use of BAS 595 01 F in seed treatment plants

Cereal Seed in plant	Mixing/Loading	Calibration	Bagging	Cleaning	Total	
Total actual dermal exposure	229.689	0.766	18.572	1.812	250.839	µg/kg bw/day
Total inhalation exposure	0.571	0.007	1.066	0.102	1.746	µg/kg bw/day
Total dose absorbed	2.581	0.028	1.152	0.183	3.944	µg/kg bw/day
% AAOEL	**5.163**	**0.055**	**2.303**	**0.366**	**7.887**	**%**

Table 6.4.1.1-8: Revised SeedTropex model: estimate of acute operator exposure to triticonazole from use of BAS 595 01 F in mobile seed treatment units

Cereal Seed Mobile	Combined	
Total actual dermal exposure	468.31	µg/kg bw/day
Total inhalation exposure	0.71	µg/kg bw/day
Total dose absorbed	7.75	µg/kg bw/day
% AAOEL	**15.5**	**%**

For operators sowing treated seed the exposure assessment has been performed in accordance with the UK approach. This assumes a 60 kg worker sowing treated seed for 10 hours. The indicative dermal and inhalation exposures are 0.733 mg/hour and 0.02 mg/day respectively. The dermal exposure value assumes a protective coverall is worn but loading and sowing operations are performed with bare hands.

Table 6.4.1.1-9: Estimated operator exposure to triticonazole from sowing seed treated with BAS 595 01 F

Dermal exposure (mg/day)	Inhalation exposure (mg/day)	*Total systemic exposure (mg/kg bw per dayay)	AOEL (mg/kg bw per dayay)	% AOEL
7.33	0.2	0.007	0.025	28

Estimates based on the revised SeedTropex seed sowing model (SeedTropex Model Version 15, 2014) are presented as well.

Table 6.4.1.1-10: Estimated operator exposure to triticonazole from sowing seed treated with BAS 595 01 F (revised SeedTropex model V15)

Cereal Seed Sowing	Loading	Sowing	Total	
Total actual dermal exposure	86.17	38.1472	124.32	µg/kg bw/day
Total inhalation exposure	0.686	0.7517	1.44	µg/kg bw/day
Total dose absorbed	1.2	2.5552	3.71	µg/kg bw/day
% AOEL	**4.6**	**10.2**	**14.9**	**%**

Acute estimates based on the revised SeedTropex seed sowing model (SeedTropex Model Version 15, 2014, 95th percentile) and the proposed AAOEL are presented below.

Table 6.4.1.1-11: Estimated acute operator exposure to triticonazole from sowing seed treated with BAS 595 01 F (revised SeedTropex model V15, 95th percentile)

Cereal Seed Sowing	Loading	Sowing	Total	
Total actual dermal exposure	126.39	129.4911	255.88	µg/kg bw/day
Total inhalation exposure	1.506	1.6095	3.12	µg/kg bw/day
Total dose absorbed	2.3	5.2623	7.58	µg/kg bw/day
% AOEL	**4.6**	**10.5**	**15.2**	**%**

As estimates of exposure for triticonazole using the French version of SeedTropex are above the AOEL further estimates of exposure are given, which consider the use of additional PPE to those routinely worn by seed treatment workers. The cleaning task, whilst being of short duration, contributes significantly to the workers' total exposure from the four seed treatment tasks. The use of respiratory protective equipment (RPE) with a protection factor of 90% (i.e. APF of 10) is therefore considered for this task. This task is typically of short duration but offers the potential for significant inhalation exposure. The use of RPE is therefore a realistic refinement for reducing levels of exposure from this task.

Table 6.4.1.1-12: French SeedTropex estimate of operator exposure to triticonazole from use of BAS 595 01 F applied undiluted during seed treatment with RPE for cleaning task

Task	Actual dermal exposure (mg/day)	Inhalation exposure (mg/day)
Calibration	0.362	0.062
Mixing/Loading	0.227	0.4
Bagging	7.945	0.214
Cleaning	4.527	0.151
Total	**13.06**	**0.828**
Total systemic dose (mg/day)	0.958	
% AOEL	**55**	

Table 7.2.1.1-13: French SeedTropex estimate of operator exposure to triticonazole from use of BAS 595 01 F when diluted during seed treatment with RPE for cleaning task

Task	Actual dermal exposure (mg/day)	Inhalation exposure (mg/day)
Calibration	0.072	0.062
Mixing/Loading	0.227	0.4
Bagging	7.945	0.214
Cleaning	4.527	0.152
Total	**12.77**	**0.83**
Total systemic dose (mg/day)	1.21	
% AOEL	**69**	

B.6.4.1.2. Measurement of operator exposure

a) Static Seed Treatment

Since the risk assessment carried out using the SeedTropex model is based on exposure data for products applied at significantly higher application rates (g a.s./ton seed) than those recommended for triticonazole in BAS 595 01

F, it is expected that the predicted exposures using this exposure model will overestimate actual levels of exposure for seed treatment workers using BAS 595 01 F. A higher tier assessment for BAS 595 01 F is therefore presented below, based on an exposure study which more closely reflects the use conditions recommended for triticonazole in BAS 595 01 F.

Previous evaluation:	No
DRAR (2016)	New study

Reference:	Fluquinconazole and Prochloraz: Determination of operator exposure during cereal seed treatment with Jockey fungicide in Germany, United Kingdom and France
Author(s), year:	Wilson A.J., 2009
Report/Doc. number::	2009/1049020 / -
Guideline(s):	OECD/GD(97)148 No. 9
GLP:	Yes
Deviations from OECD (1997):	No
Acceptability:	Yes

Material and methods

Test Material:	Prochloraz copper chloride complex, Fluquinconazole, Anthrachinon BAS 61700F
Batch/purity #:	1159541 (UK), 1556013 (FR), 1239029 (UK), 1970163 (UK), 1816396 (DE), 1460359 (DE), 1859936 (UK), 1387219 (DE), 1816396 (DE), 1443159 (DE), 1816393 (DE), Fluquinconazole: 167 g/L nominal; Prochloraz: 31.2 g/L nominal; Prochloraz copper chloride complex: 34 g/L nominal
Dates of work:	08/23/2007 00:00:00 - 12/19/2007 00:00:00

Levels of exposure were determined by passive dosimetry on volunteer operators during seed treatment operations (mixing/loading/calibration), bagging of treated small grain cereal seed and cleaning the seed treatment equipment. The treatment was conducted with the fungicide BAS 617 00 F (Jockey Plus AB) containing nominally 167 g/L fluquinconazole, 31.2 g/L prochloraz (34 g/L as prochloraz copper chloride complex) and 111 g/L anthraquinone. The product was applied at the recommended use rate of 4.5 L product per ton of seed equivalent to 751.5 g fluquinconazole, 140.4 g prochloraz and 499.5 g anthraquinone. The active ingredients monitored were fluquinconazole and prochloraz. Anthraquinone was not monitored in this study.

The study was performed to determine the dermal and inhalation exposure of workers during typical seed treatment activities, i.e. mixing/loading, bagging of treated seed and cleaning of seed treatment equipment. Nine operators were monitored during mixing/loading, twenty two operators were monitored during bagging activities and eight were monitored when cleaning the treatment chamber. The dosimeters used for the specific tasks are summarized below.

Table 6.4.1.2-1: Dosimeters used in seed treatment tasks

Task	Outer dosimeter	Inner dosimeter	Hands Outer dosimeter	Actual exposure hands	Actual exposure face/neck	Inhalative exposure
Mixing/Loading Calibration	Long sleeved jacket and long trousers (cotton)	Longs sleeved vest and long-johns (cotton)	Glove wash, nitrile gloves when touching contaminated surfaces	Hand wash	Face/neck wipes	Personal air sampler, glass fibre filter
Bagging	Long sleeved jacket and long trousers (cotton)	Longs sleeved vest and long-johns (cotton)	Glove wash, optional on decision of operator nitrile gloves when touching contaminated surfaces	Hand wash	Face/neck wipes	Personal air sampler, glass fibre filter
Cleaning	Long sleeved jacket and long trousers (cotton) = outer dosimeter 1 additional impermeable coverall including hood (Tyvek®) = outer dosimeter 2	Longs sleeved vest and long-johns (cotton)	Glove wash, nitrile gloves	Hand wash	Face/neck wipes	Personal air sampler, glass fibre filter

The Tyvek® dosimeters and inner and outer cotton dosimeters were cut into four sections.

The test locations were situated at various sites across Germany (6 sites), the United Kingdom (4 sites) and France (1 site). The test sites comprised of commercial stationary seed treatment facilities. Continuous flow seed treatment equipment was used at five of the test sites and batch treatment equipment was used at six sites. The continuous flow equipment is typically used to treat larger quantities of seed per day. Selection of these different types of equipment addresses the potential variability in this aspect of the seed treatment operation at static treatment sites.

For mixing/loading/calibration activities, operators generally worked only in the vicinity of the chemical mixing area, except for operator 36 who also assisted in some bagging activities. For this reason this operator is not included in the mixing/loading/calibration dataset. For the bagging activities, operators generally worked in the vicinity of the bagging area only.

a) Mixing/Loading/Calibration

This task involved the transfer of the product from its original 200 litre container into a slurry tank prior to being connected to the treatment equipment. This procedure was done manually at one site. At other sites the treatment equipment (suction hose) was either placed directly into the original product container, where the product was manually transferred to the mixing chamber or, connected directly to the container using a dry break coupling system (where the suction hose is connected to a spigot on the outside of the container). In some cases the product was diluted with water prior to treatment, either in the slurry tank or directly at the treatment chamber. In

most cases calibration was automated and therefore not monitored. All operators involved in this task worked individually.

b) Bagging

The tasks involved filling either small bags (25 or 50 kg) or large bags (250, 500, 1000 kg). In addition, open metal containers (1875 kg) were also filled. One to three operators worked on each bagging line.

c) Cleaning

Cleaning involved cleaning the treatment chamber using one or more of the following tools: spatula, brushes (wet and dry), water hose (tap and high pressure) or compressed air. The duration of each activity was between 0.12 to 0.55 hours. In France the cleaning task also included cleaning the filter at the slurry tank, and this activity was also monitored.

A summary of the operator activities is given in Appendix 3-5 and information for the individual operators is given in Appendix 3-6.

Field fortification samples were prepared on three days of monitoring, to assess the stability of the test item under field, storage and transit conditions. Three specimens of each dosimeter type were fortified at two rates. Blank specimens were also prepared.

Glove wash samples and hand wash samples were diluted and directly injected into the LC chromatograph. Garment parts (Tyvek® or cotton) and face/neck wipe specimens were extracted with methanol and extracts were diluted prior to injection. The glass fibre filters were extracted with acetone and extracts were diluted prior to injection. All samples were analysed for prochloraz and fluquinconazole by LC/MS/MS.

Results

The results from the field fortification samples showed that mean recoveries were in the range of 92% to 110% for all matrixes, therefore the results for the operators' dosimeters did not require correction for field recovery.

The exposure levels determined during mixing/loading, bagging and cleaning normalized to µg/kg operator body weight based on the individual operator weights (see Appendix 3-6) and based on 75th percentile data are summarized in the following table. Further details of these calculations are provided in the Appendices 3-7, 3-8 and 3-9.

The values determined for bagging are furthermore normalised to an 8 h work rate based on the actual bagging durations provided in Appendix 3-8.

Table 6.4.1.2-2: Exposure to fluquinconazole and prochloraz normalized to 8 h work rate and mg/kg operator body weight based on 75th percentile data of the operator exposure study

	Fluquinconazole		Prochloraz	
	Dermal	**Inhalation**	**Dermal**	**Inhalation**
	(mg/kg bw per dayay)		(mg/kg bw per dayay)	
Mixing	0.01463	0.0000003	0.00511	0.00000005
Bagging	0.00773	0.0000158	0.00303	0.00000356
Cleaning	0.29484	0.0000062	0.06071	0.00000430
Sum	**0.31720**	**0.0000224**	**0.06884**	**0.00000791**
Mixing	0.00014	0.0000003	0.00006	0.00000005
Bagging	0.00476	0.0000158	0.00151	0.00000356
Cleaning	0.00070	0.0000062	0.00028	0.00000430
Sum	**0.00559**	**0.0000224**	**0.00185**	**0.00000791**

The sum of the total outer dosimeter values and total inner dosimeter values represent potential dermal exposure, while the sum of total inner dosimeters is actual dermal exposure.

The study results for fluquinconazole and prochloraz for actual and potential exposure based on the 75th percentile values are summarized in the following table. It should be noted that potential exposure assumes exposure without any type of clothing.

Table 6.4.1.2-3: Potential and actual exposure to fluquinconazole and prochloraz determined in a seed treatment operator exposure study conducted with BAS 617 00 F

Scenario	**PPE level**	**Fluquinconazole**		**Prochloraz**	
		Dermal	**Inhalation**	**Dermal**	**Inhalation**
		(mg/kg bw per dayay)		(mg/kg bw per dayay)	
		Potential exposure			
Mixing/loading	None	0.01477	0.0000003	0.00517	0.00000005
Bagging	None	0.01249	0.0000158	0.00454	0.00000356
Cleaning	None	0.29553	0.0000062	0.06099	0.00000430
Sum		**0.32279**	**0.0000224**	**0.07070**	**0.00000791**
		Actual exposure			
Mixing/loading	Gloves and work clothing	0.00014	0.0000003	0.00006	0.00000005
Bagging	Work clothing	0.00476	0.0000158	0.00151	0.00000356
Cleaning	Gloves and protective clothing (Tyvek)	0.00070	0.0000062	0.00028	0.00000430
Sum		**0.00559**	**0.0000224**	**0.00185**	**0.00000791**

Conclusion

Based on these study data the principal exposure of an unprotected operator occurs when cleaning the seed treatment equipment, where the operator may have direct contact with the undiluted product. Levels of inhalation exposure are not significant when compared to dermal exposure, being a factor of 1000 or more lower than (potential) dermal exposure. Work clothing typically worn by workers in combination with personal protective equipment significantly reduces dermal exposure levels during the mixing/loading and cleaning operations.

During these activities the main source of exposure is expected to result from selective local exposure to the undiluted/partially diluted product. The reduction in dermal exposure from clothing and PPE is less pronounced during the bagging task, as exposure is expected to occur more typically from airborne dust and where movement of the worker during various activities allows penetration through their clothing, e.g. around openings via the bellows effect.

Extrapolation of the results to triticonazole

The data given above are obtained from an operator exposure study, conducted with a product (BAS 617 00 F) containing 30 g/L prochloraz and applied at 140.4 g a.s./ton seed). This GLP study was performed to modern standards, and included a range of treatment equipment, covering both large scale and smaller scale use. A number of different activities were performed within the monitored tasks, which involved various procedures for adding the product to the seed treater, different levels of automation at the bagging station and different tasks and equipment used for cleaning operations. These data therefore capture the variability between static seed treatment plants, and provide a realistic and reliable basis with which to evaluate operator exposure to BAS 595 01 F during seed treatment operations. Further, the study will provide a precautionary estimate of exposure for triticonazole, as the amount of active substance in BAS 595 01 F (25 g/L) and the seed loading (50g a.s./ton seed) are lower than those of prochloraz used in the exposure study.

In the exposure study operators wore typical (cotton) working clothing except for cleaning operations. During this task an impermeable coverall (i.e. a Tyvek® suit) and nitrile gloves were worn in addition to the workers normal work clothing. Thus, actual dermal exposure estimates for the cleaning scenario represent workers wearing two layers of outer clothing and protective gloves.

Table 6.4.1.2-4: BAS 595 01 F: Summary of predicted exposures and risk assessment for triticonazole when using PPE during cleaning operations based on higher tier data

Scenario	Dermal exposure		Inhalation exposure	Combined systemic exposure	% of AOEL
	Actual dermal (mg/kg bw per dayay)	Systemic dermal exposure* (mg/kg bw per dayay)	(mg/kg bw per dayay)	Dermal (mg/kg bw per dayay)***	
Mixing/calibration	6×10^{-5}	4.8×10^{-6}	1.8×10^{-6}	1.9×10^{-6}	0.007
Bagging	0.0015	1.2×10^{-4}	4.5×10^{-5}	4.9×10^{-5}	0.20
Cleaning	2.8×10^{-4}	2.2×10^{-5}	8.4×10^{-6}	1.3×10^{-5}	0.05
Sum of all operations	1.9×10^{-3}	1.5×10^{-4}	5.6×10^{-5}	6.3×10^{-5}	**0.25**

*based on a dermal absorption rate of 3%
** based on a dermal absorption rate of 3% and 100% for absorption by inhalation
***based on actual worker body weight

b) Mobile Seed Treatment

Previous evaluation:	No
DRAR (2016)	New study

Reference:	Determination of worker exposure during treatment of cereal seeds by mobile treaters in

	France
Author(s), year:	Pontal P-G.,Thouvenin I., 2008
Report/Doc. number::	2008/1056997 / -
Guideline(s):	OECD/GD(97)148 No. 9
GLP:	Yes
Deviations from OECD Guideline (1997)	No
Acceptability:	Yes

For the use of BAS 595 01 F in mobile seed treatment stations a higher tier exposure assessment, based on data originating from a study performed on behalf of the SeedTropex industry task force, were used to estimate levels of exposure for workers.

Material and methods

Test Material: Anthrachinon, Fludioxonil, Imidacloprid

Batch/purity #: Austral Plus, Anthraquinone: 100 g/L; Fludioxonil: 10 g/L; Celest Rev, Anthraquinone: 250 g/L; Fludioxonil: 25 g/L; Ferial Ble, Anthraquinone: 125 g/L; Imidacloprid: 175 g/L; Ferial Orge, Imidacloprid: 350 g/L; Jockey Plus AB, Anthraquinone: 111 g/L; Seman TS, Anthraquinone: 333 g/L

Stability of test compound: Stable over duration of study

Dates of work: 08/25/2004 00:00:00 - 09/03/2007 00:00:00

Twelve operators from four different seed treatment companies (2 to 4 subjects per company) in four different regions of the Northern part of France (departments of Moselle, Pas-de Calais, Côtes d'Armor, Finistère and Calvados) participated in the study. Two different mobile treaters were used by each company. The treatments were performed on a total of 17 farms. The seed treatment equipment used covered the major types of mobile seed treatment equipment presently used in France. All seed treaters were equipped with a seed cleaning and a seed treatment unit. The bagging units were positioned either on a truck or on a trailer adjacent to the seed treatment unit.

The seed treatment products used contained the active substances anthraquinone, imidacloprid and fludioxonil in various compositions. A summary on the preparations used is presented below:

Table 6.4.1.2-5: Summary of seed treatment formulations used in mobile seed treatment exposure study

Product name	**Active substance and concentration (g/l)**			
	Anthraquinone	**Fludioxonil**	**Imidacloprid**	**Other**
Austral Plus	100	10	-	40 (Tefluthrin)
Celest Rev	250	25	-	-
Ferial Ble	125	-	175	37.5 (Bitertanol)
Ferial Orge	-	-	350	15 (Tebuconazoele) 10 (Triazoxide)
Jockey Plus AB	111	-	-	167 (Fluquinconazole) 34 (Prochloraz)
Seman TS	333	-	-	100 (Prochloraz)

For all formulations used, the target application rates were 500 g anthraquinone, 700 g imidacloprid and 50 g fludioxonil per ton of seeds.

Operators performed one or several of the following tasks: mixing/loading, bagging and cleaning according to their individual working habits. The study was designed to measure the exposure from each task, occurring during a single day. Therefore, the dermal and inhalation exposure for subjects performing various activities were combined for exposure evaluations, as the variability in daily tasks is considered to be representative of the specific conditions of mobile seed treatment operations. Since the nature of this type of seed treatment operation requires travelling from one farm to another, actual seed treatment times over a typical working day are less then would be expected for static treatment units, and this is reflected in the periods monitored for the individual workers. For the same reason, the actual quantities of active substance used per day are less than the typical requirements of static seed treatment facilities. In a number of cases operators began their seed treatment operations with ready to use product still remaining in the container of the treatment unit from the preceding treatment day. Consequently, when mixing and loading a formulation on the day of monitoring, they often did so using partially filled product containers of the treatment unit. In addition, for operations requiring only a small quantity of seed treatment product, no mixing/loading was performed as a sufficient amount of ready to use formulation was already present in the product tank. This explains why the amount of active substance handled during the mixing/loading operations does not correspond exactly to the amount handled during 'application' (i.e. treatment and bagging). Mixing/loading was performed manually on all treaters with the exception of operators 1 and 2, who had an automatic loading system on their treatment unit.

An overview on the daily working time and amounts of active substance handled in the study is presented in Appendix 3-10.

Air temperature and relative humidity were monitored, when possible, at approximately two to four hour intervals at each site. On two of the test sites the treatment operations were performed indoors in big barns with at least one door widely opened (operators 5 and 7). All other operations were performed outdoors. The air temperature ranged from 11°C to 23°C and the relative humidity ranged from 55% to 92% over all sites. The wind speed ranged from 0.2 to 6 m/second.

Dermal exposure to the body was measured using the whole body dosimetry method. The clothing adopted for the study was considered to represent what operators would typically wear under the prevailing conditions. The following dosimeters were evaluated: cotton long underwear (inner dosimeter: long-sleeved cotton shirt and long cotton johns) under a cotton shirt or a cotton/polyester jacket and cotton/polyester trousers (outer dosimeter). At the end of the exposure period the inner dosimeters were sectioned into three parts: arms, legs and torso. Outer dosimeters were sectioned similarly into torso including the upper parts of the arms and of the thighs, lower limbs and higher limbs (lower arms and lower parts of upper arms). Exposure to the hands and face/neck was measured using hand wash and face/neck wiping procedures. Some operators wore protective gloves which were not analyzed. The use of protective gloves was up to the discretion of each operator and followed their personal working habits (Appendix 3-10).

Inhalation exposure was measured using a Millipore air sampling cassette fitted with glass fibre filters, connected to personal air sampling pumps. The sampling device was located in the breathing zone of the operators.

Anthraquinone residues were determined by HPLC-UV while fludioxonil and imidacloprid residues were determined by LC-MS/MS. Limits of quantification were as shown below:

Table 6.4.1.2-6: Limits of quantification for dosimeter matrix

	Limit of quantification in µg/specimen		
	Anthraquinone	**Imidacloprid**	**Fludioxonil**
Cotton shirt	5	5	1
Cotton/polyester jacket or trouser	5	5	1
Cotton inner dosimeter	2.5	0.5	0.5
Air filter	0.05	0.02	0.01
Hand wash	0.5	0.5	0.05
Face/neck wipe	0.5	0.1	0.05

The field recoveries obtained were within acceptable limits (i.e. 70 – 110%), with the exception of the inner dosimeters and filters, which were on some occasions lower than 70% for anthraquinone and fludioxonil. Appropriate recovery corrections were made for these media.

Results

Due to the design of the study, which monitored the actual practices of the mobile seed treatment operatives, the duration of the seed treatment operations varied considerably, ranging from 46 to 415 minutes. For imidacloprid treatment two operators (Nos. 7 and 8) had a working time of just 9 minutes each. Whilst this may reflect the specific needs for mobile seed treatment operations, the data for these two operators are not considered representative of exposure during a typical work day for mobile seed treatment operations. Consequently, data for these workers has not been considered for this specific evaluation.

In general, the amount of active substance used in the seed treatment operations was about 5.5 to 19 kg for anthraquinone (500 g a.s. per ton of seeds), 0.1 to 1.6 kg for fludioxonil (50 g a.s. per ton of seeds) and 0.3 to 7.4 kg for imidacloprid (700 g a.s. per ton of seeds). Full details are presented in Appendix 3-10.

Results of actual dermal and inhalation exposure for the individual operators are presented in Appendices 3-11 to 3-13. Twelve operators handled anthraquinone (Appendix 3-11). Total actual dermal exposure for this active substance was in the range of 44 to 2108 µg/operator. Maximum dermal exposure values of 1408 (operator No. 11) and 2108 µg/operator (operator No. 3) were mainly due to high body exposure rather than hand exposure. Inhalation exposure was in the range 1.3 to 191 µg/operator. Eight of the study subjects handled fludioxonil (Appendix 8). Total actual dermal exposure was in the range of 1.09 to 2105.1 µg/operator. The maximum dermal exposure value of 2105.1 µg/operator for these operators was principally (operator No. 3 who did not use protective gloves) due to high hand exposure (1985 µg or 94% of total dermal exposure). Inhalation exposure was in the range of 0.07 to 4.04 µg/operator. For imidacloprid a restricted set of four operators was monitored, two of which handled only a small amount of active substance each (about 0.3 kg Imidacloprid) during a period of about 9 minutes. The other two subjects handled about 10 and 16 kg active substance (Appendix 9). The total

actual dermal exposure for these workers was in the range of 20 to 537 µg/operator. Inhalation exposure was in the range of 0.14 to 71.2 µg/operator. Operator No. 11 was observed to be working in a dusty environment, as indicated by the maximum values found for dermal (536.6 µg/operator) and inhalation exposure (71.2 µg/operator). These results are consistent with the inhalation exposure level of the same subject relative to anthraquinone. Similarly, his dermal exposure was notably high despite handling fairly small quantities of this active substance (1.5 kg for mixing/loading and 4.02 kg for application, Appendix 11).

Conclusion

The exposure data from this study includes findings for high application rates (anthraquinone, 500 g a.s. per ton of seeds and imidacloprid, 700 g a.s. per ton of seeds), as well as for a low application rate: fludioxonil (50 g a.s. per ton of seeds). Evaluation of these data was performed by keeping the two data sets for high and low application rates discrete, as the amount of test substances used over the whole working day is considered too different for the data to be combined. The evaluation of exposure data for the high application rate scenario is presented in Appendix 3-14 (anthraquinone and imidacloprid combined). This dataset includes all operators except the imidacloprid data of operators No. 7 & 8. The data for these study subjects has not been included as their working time (i.e. 9 min each) and amount of active substance handled (i.e. about 0.3 kg each) are too low to be compatible with the other operator exposure situations which were monitored.

Geometric mean values and 75th percentile values were calculated for both sets and are summarized in the table below.

Table 6.4.1.2-7: Geometric means and 75th percentiles for dermal and inhalation exposure when handling anthraquinone, imidacloprid and fludioxonil in mobile seed treatment stations (µg/operator/day)

	Dermal exposure		**Inhalation exposure**	
	Geometric mean	75th percentile	Geometric mean	75th percentile
High application rate* (Anthraquinone & Imidacloprid) n = 14	296.14	978.10	14.56	50.13
Low application rate ** (Fludioxonil) n = 8	14.01	91.26	0.60	2.00

*Appendix 14
**Appendix 12

For both dermal and inhalation exposure, the high application rate dataset resulted in about a 10-25 fold higher exposure when compared to the low application rate data. The amount of anthraquinone and imidacloprid from those operators used is about 10 times higher than the amount of fludioxonil handled (Appendix 3-10). This finding supports the conclusion that, for this study, the amount of active substance handled per day has a significant influence on levels of exposure. For exposure assessment purposes, the application rate of the active substance under consideration therefore needs to be taken into account when choosing which of the two datasets should be applied.

Extrapolation of the results to triticonazole

BAS 595 01 F is applied to cereal crop seeds at a recommended application rate of 50 g triticonazole per ton of seeds. This application rate is the same as that used for fludioxonil in the exposure study, i.e. the low application rate dataset. In the exposure study the amount of active substance used ranged from 0.187 to 1.085 kg per day. This amount of triticonazole would treat 3.7 to 22 tons of seed. Seed treatment workers were monitored over periods of 46 minutes to 249 minutes. As a conservative approach, the indicative 75th percentile values have been assumed for the exposure assessment for BAS 595 01F. These indicative exposure values are 91.26 µg/operator/day for actual dermal exposure and 2.0 µg/operator/day for inhalation exposure (Appendix 3-12). A dermal absorption value of 3% (worst case) and a worker body weight of 60 kg are assumed to estimate levels of systemic exposure on a mg/kg bw per dayay basis.

Table 6.4.1.2-8: Predicted exposures and % of the AOEL for triticonazole for workers treating cereal seed with mobile seed treatment equipment

Scenario	Dermal exposure		Inhalation exposure	Combined systemic exposure		% of AOEL
	Actual dermal (mg/day)	Systemic dermal exposure* (mg/day)	(mg/day)	Dermal (mg/day)	Dermal (mg/kg bw per dayay)***	
Cereals – mobile seed treatment unit	0.091	0.003	0.002	0.005	0.0001	0.3

* based on a dermal absorption rate of 3%
** based on a dermal absorption rate of 3% and 100% for absorption by inhalation
*** based on a 60 kg body weight

In summary, the predicted total systemic exposure for triticonazole is significantly below the AOEL value, i.e. less than 1%. The exposure study monitored actual mobile seed treatment operations, which showed that typically, these operations are of shorter duration than those conducted in static plants. When the time to travel between farms is also factored in, this shows that workers involved in this type of treatment operation are often treating seed for significantly less than the 8 hours routinely assumed for regulatory risk assessments.

The exposure study performed in France is a modern study conducted to modern standards. Where field recoveries for some dosimeters were found to be low, appropriate adjustments to the respective exposure samples were made. The equipment used in the study shows that variability does exist within mobile seed treatment equipment, in terms of the mixing/loading procedure and when bagging the treated seed. These variables have been captured in the study design. Similarly, whilst the study subjects were expected to use the recommended personal protective equipment for the products they were using, the dataset includes data for operators who consistently chose to use their bare hands rather than put on protective gloves. This study may therefore be considered to be a realistic and representative study upon which to base an exposure assessment for workers using mobile seed treatment equipment to treat cereal seeds with BAS 595 01 F.

B.6.4.2. Bystander and resident exposure

Dressing of seeds with BAS 595 01 F is typically performed in professional plants, where persons whose presence is quite incidental and unrelated to the work (i.e. bystanders) will not be present. However, workers who are not directly involved in the seed treatment process, such as forklift operators, may be present. An assessment is given which considers this scenario.

During loading/sowing of the seed treated with BAS 595 01 F it is highly unlikely that bystander exposure will occur. However, even in the theoretical case that exposure to dust from the treated seed could occur, e.g. as treated seed is loaded into the seed drill hopper, levels of exposure for bystanders would not be expected to exceed those of operators involved in bagging treated seed, where exposure is predominately from airborne dust. For operators wearing a single layer of clothing and no gloves the predicted exposures for this task (5.58 mg/person dermal exposure and 0.043 mg/person inhalation exposure) were within acceptable levels for triticonazole (14% of the AOEL), using the UK SeedTropex model.

Risk assessment for bystander and resident

In the SeedTropex model, forklift operators were monitored at three static plants in the UK to assess background exposure levels. Three measurements of potential exposure were obtained.

Table 6.4.2-1: Potential exposure of forklift operators at three UK Seed treatment plants.

	Potential dermal exposure (mg/hour)	Potential inhalation exposure (µg/hour)
Arithmetic mean	0.15	2.15
Geometric mean	0.14	1.62

The indicative geometric mean values are used to provide an exposure assessment for fork lift operators.

B.6.4.2.1. Estimation of bystander and resident exposure

Levels of exposure for forklift operators are predicted assuming a 10 hour working day and a 60 kg body weight.

Table 6.4.2.1-1: Estimated exposure to triticonazole for forklift operators working in seed treatment plants

Dermal exposure (mg/day)	Inhalation exposure (mg/day)	Total systemic exposure* (mg/kg bw per dayay)	AOEL (mg/kg bw per dayay)	% AOEL
1.4	0.016	0.001	0.025	4

*Assumes 3% dermal absorption for triticonazole

B.6.4.2.2. Measurement of bystander and resident exposure

Not required as estimated levels of exposure using data taken from SeedTropex confirm levels of exposure for bystanders (fork-lift operators) will be within the AOEL.

B.6.4.3. Worker exposure

The only intended use of BAS 595 01 F is treating seeds prior to sowing. There is no worker re-entry scenario for this product.

B.6.4.3.1. Estimation of worker exposure

The only intended use of BAS 595 01 F is treating seeds prior to sowing. There is no worker re-entry scenario for this product.

B.6.4.3.2. Measurement of worker exposure

The only intended use of BAS 595 01 F is treating seeds prior to sowing. There is no worker re-entry scenario for this product.

B.6.5. EXPOSURE AND RISK ASSESSMENT (TRITICONAZOLE)

Appendix 3-1: French SeedTropex model: Triticonazole used undiluted. Gloves and coverall worn during calibration, mixing and loading and cleaning. Coverall worn during bagging.

Formulation concentration	25	mg/ml
Dilution factor	1	
Dermal penetration	1.00%	
Application dose	50	g a.s./ton
Systemic AOEL	0.025	mg/kg/day
Body weight	70	kg

Actual dermal	13.06	mg/day
Inhalation	2.191	mg/day
Internal dose	2.32161	mg/day
% AOEL	133%	

CALIBRATION

Number of operations	1
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.209 ml/ope	0.014 ml/ope	0.062 mg/ope
5.22 mg/ope	0.362 mg/ope	0.062 mg/ope
0.00 mg/day	0.36 mg/day	0.062 mg/day

Mixing/Loading

Number of operations	8
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.0113 ml/ope	0.0011 ml/ope	0.050 mg/ope
0.28 mg/ope	0.028 mg/ope	0.050 mg/ope
0.000 mg/day	0.23 mg/day	0.400 mg/day

BAGGING (normal)

Number of hours	7
Protective gloves	no
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.00 mg/hr	1.14 mg/hr	0.031 mg/hr
0.00 mg/day	7.95 mg/day	0.214 mg/day

CLEANING

Number of operations	1
Protective gloves	yes
Mask	no
Ventilated helmet	no
Protective overall	no

Gloves	Actual dermal	Inhalation
18.50 mg/ope	4.53 mg/ope	1.515 mg/ope
0.00 mg/day	4.53 mg/day	1.515 mg/day

Appendix 3-2: French SeedTropex model estimates of exposure : Triticonazole used undiluted. Gloves and coverall worn during calibration, mixing and loading and cleaning. Coverall worn during bagging.

Formulation concentration	25	mg/ml
Dilution factor	5	
Dermal penetration	3.00%	
Application dose	50	g a.s./ton
Systemic AOEL	0.025	mg/kg/day
Body weight	70	kg

Actual dermal	12.77	mg/day
Inhalation	2.191	mg/day
Internal dose	2.574149	mg/day
% AOEL	147%	

CALIBRATION

Number of operations	1
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.209 ml/ope	0.014 ml/ope	0.062 mg/ope
1.04 mg/ope	0.072 mg/ope	0.062 mg/ope
0.00 mg/day	0.07 mg/day	0.062 mg/day

Mixing/Loading

Number of operations	8
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.0113 ml/ope	0.0011 ml/ope	0.050 mg/ope
0.28 mg/ope	0.028 mg/ope	0.050 mg/ope
0.000 mg/day	0.23 mg/day	0.400 mg/day

BAGGING (normal)

Number of hours	7
Protective gloves	no
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.00 mg/hr	1.14 mg/hr	0.031 mg/hr
0.00 mg/day	7.95 mg/day	0.214 mg/day

CLEANING

Number of operations	1
Protective gloves	yes
Mask	no
Ventilated helmet	no
Protective overall	no

Gloves	Actual dermal	Inhalation
18.50 mg/ope	4.53 mg/ope	1.515 mg/ope
0.00 mg/day	4.53 mg/day	1.515 mg/day

Appendix 3-3: French SeedTropex model: Triticonazole used undiluted. Gloves and coverall worn during calibration, mixing and loading and cleaning. Coverall worn during bagging. RPE worn for cleaning task only.

Formulation concentration	25	mg/ml
Dilution factor	1	
Dermal penetration	1.00%	
Application dose	50	g a.s./ton
Systemic AOEL	0.025	mg/kg/day
Body weight	70	kg

Actual dermal	13.06	mg/day
Inhalation	0.828	mg/day
Internal dose	0.958284	mg/day
% AOEL	55%	

CALIBRATION

Number of operations	1
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.209 ml/ope	0.014 ml/ope	0.062 mg/ope
5.22 mg/ope	0.362 mg/ope	0.062 mg/ope
0.00 mg/day	0.36 mg/day	0.062 mg/day

Mixing/Loading

Number of operations	8
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.0113 ml/ope	0.0011 ml/ope	0.050 mg/ope
0.28 mg/ope	0.028 mg/ope	0.050 mg/ope
0.000 mg/day	0.23 mg/day	0.400 mg/day

BAGGING (normal)

Number of hours	7
Protective gloves	no
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.00 mg/hr	1.14 mg/hr	0.031 mg/hr
0.00 mg/day	7.95 mg/day	0.214 mg/day

CLEANING

Number of operations	1
Protective gloves	yes
Mask	yes
Ventilated helmet	no
Protective overall	no

Gloves	Actual dermal	Inhalation
18.50 mg/ope	4.53 mg/ope	1.515 mg/ope
0.00 mg/day	4.53 mg/day	0.151 mg/day

RPE assumed for the cleaning task are assumed to reduce inhalation exposure by 90% (APF 10). These will be a minimum of a filtering half-mask (FFP2).

Appendix 3-4: French SeedTropex model : Triticonazole used diluted. Gloves and coverall worn during calibration, mixing and loading and cleaning. Coverall worn during bagging. RPE worn for cleaning task only.

Formulation concentration	25	mg/ml
Dilution factor	5	
Dermal penetration	3.00%	
Application dose	50	g a.s./ton
Systemic AOEL	0.025	mg/kg/day
Body weight	70	kg

Actual dermal	12.77	mg/day
Inhalation	0.828	mg/day
Internal dose	1.210822	mg/day
% AOEL	69%	

CALIBRATION

Number of operations	1
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.209 ml/ope	0.014 ml/ope	0.062 mg/ope
1.04 mg/ope	0.072 mg/ope	0.062 mg/ope
0.00 mg/day	0.07 mg/day	0.062 mg/day

Mixing/Loading

Number of operations	8
Protective gloves	yes
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.0113 ml/ope	0.0011 ml/ope	0.050 mg/ope
0.28 mg/ope	0.028 mg/ope	0.050 mg/ope
0.000 mg/day	0.23 mg/day	0.400 mg/day

BAGGING (normal)

Number of hours	7
Protective gloves	no
Mask	no
Protective overall	no

Gloves	Actual dermal	Inhalation
0.00 mg/hr	1.14 mg/hr	0.031 mg/hr
0.00 mg/day	7.95 mg/day	0.214 mg/day

CLEANING

Number of operations	1
Protective gloves	yes
Mask	yes
Ventilated helmet	no
Protective overall	no

Gloves	Actual dermal	Inhalation
18.50 mg/ope	4.53 mg/ope	1.515 mg/ope
0.00 mg/day	4.53 mg/day	0.151 mg/day

RPE assumed for the cleaning task are assumed to reduce inhalation exposure by 90% (APF 10). These will be a minimum of a filtering half-mask (FFP2).

Appendix 3-5: Summary of test sites and operator activities

Location	Equipment	Amount of active substance handled	Number of bags and size	Activity	Operator
Site 1	Batch	35.58 kg (F)	100 x 500 kg	Bagging	8
Bracebridge Heath		7.020 kg (P)		Cleaning	43
(UK)			Total = 50,000 kg	Mixing/Loading/Calibration	32
Site 2	Continuous flow	17.07 kg (F)	1002 x 25 kg	Bagging	10
La Bâtie Rolland		3.189 kg (P)		Cleaning	40
(France)			Total = 25,050 kg	Mixing/Loading/Calibration	33
Site 3	Batch	36.82 kg (F)	97 x 500 kg	Bagging	1 + 3
Little Airmyn		6.880 kg (P)	2 x 250 kg	Cleaning	-
(UK)			Total = 49,000 kg	Mixing/Loading/Calibration	35
Site 4	Continuous flow	49.86 kg (F)	127 x 500 kg 11 x 250 kg	Bagging	11 + 13
Holton-le-Clay		9.316 kg (P)	2 x 50 kg	Cleaning	47
(UK)			Total = 66,350 kg	Mixing/Loading/Calibration	31
Site 5	Batch	48.85 kg (F)	62 x 1000 kg	Bagging	16
Neubrandenburg		9.126 kg (P)	6 x 500 kg	Cleaning	-
(Germany)			Total = 65,000 kg	Mixing/Loading/Calibration	36
Site 6	Continuous flow	21.11 kg (F)	18 x 1000 kg	Bagging	7 + 14 + 20
Bisdorf		3.941 kg (P)	201.5 x 50 kg	Cleaning	48
(Germany)			Total = 28,075 kg	Mixing/Loading/Calibration	34
Site 7	Batch	23.67 kg (F)	63 x 500 kg	Bagging	5 + 18
Colsterworth		4.423 kg (P)		Cleaning	44
(UK)			Total = 31,500 kg	Mixing/Loading/Calibration	26
Site 8	Batch	26.30 kg (F)	8 x 1875 kg	Bagging	6 + 17
Altenweddingen		4.914 kg (P)	20 x 1000 kg	Cleaning	38
(Germany)			Total = 35,000 kg	Mixing/Loading/Calibration	28
Site 9	Continuous flow	64.63 kg (F)	86 x 1000 kg	Bagging	21 + 22 + 23
Lensahn		12.08 kg (P)		Cleaning	39
(Germany)			Total = 86,000 kg	Mixing/Loading/Calibration	-
Site 10	Batch	57.41 kg (F)	67 x 1000 kg	Bagging	4 + 19 + 24
Martensrade		10.73 kg (P)	188 x 50 kg	Cleaning	-
(Germany)			Total = 76,400 kg	Mixing/Loading/Calibration	27
Site 11	Continuous flow	62.37 kg (F)	83 x 1000 kg	Bagging	15 + 25
Demmin		11.65 kg (P)		Cleaning	45
(Germany)			Total = 83,000 kg	Mixing/Loading/Calibration	-

(F) = Fluquinconazole
(P) = Prochloraz

Appendix 3-6

Operator information

Operator identification	Activity	Height (cm)	Weight (kg)	Equipment type	Location
8	Bagging	178	81	batch	Bracebridge heath, UK
10	Bagging	170	65.6	continuous flow	La Bâtie-Rolland, France
1	Bagging	175	63.2	batch	Little Airmyn, UK
3	Bagging	174	80.5	batch	Little Airmyn, UK
11	Bagging	181	90.1	continuous flow	Holton-le-Clay, UK
13	Bagging	179	81.3	continuous flow	Holton-le-Clay, UK
16	Bagging	170	97.3	batch	Neubrandenburg, Germany
7	Bagging	165	83.7	continuous flow	Bisdorf, Germany
14	Bagging	163	88.7	continuous flow	Bisdorf, Germany
20	Bagging	187	105.2	continuous flow	Bisdorf, Germany
5	Bagging	188	63	batch	Colsterworth, UK
18	Bagging	178	71	batch	Colsterworth, UK
6	Bagging	165	75	batch	Altenweddingen, Germany
17	Bagging	174	76.2	batch	Altenweddingen, Germany
21	Bagging	186	105.1	continuous flow	Lensahn, Germany
22	Bagging	178	100.7	continuous flow	Lensahn, Germany
23	Bagging	180	90	continuous flow	Lensahn, Germany
4	Bagging	179	84	batch	Martensrade, Germany
19	Bagging	180	100	batch	Martensrade, Germany
24	Bagging	185	118	batch	Martensrade, Germany
15	Bagging	178	109	continuous flow	Demmin, Germany
25	Bagging	178	97.7	continuous flow	Demmin, Germany
Arithmetic mean	**Bagging**	**177**	**87.6**		
43	Cleaning	178	81	batch	Bracebridge heath, UK
40	Cleaning	170	65.6	continuous flow	La Bâtie-Rolland, France
47	Cleaning	179	100.1	continuous flow	Holton-le-Clay, UK
48	Cleaning	187	105.2	continuous flow	Bisdorf, Germany
44	Cleaning	186	96.8	batch	Colsterworth, UK
38	Cleaning	174	76.2	batch	Altenweddingen, Germany
39	Cleaning	180	90	continuous flow	Lensahn, Germany
45	Cleaning	178	109	continuous flow	Demmin, Germany
Arithmetic mean	**Cleaning**	**179**	**90.5**		
32	Mixing/loading	178	81	batch	Bracebridge heath, UK
33	Mixing/loading	170	65.6	continuous flow	La Bâtie-Rolland, France
35	Mixing/loading	186	70.1	batch	Little Airmyn, UK
31	Mixing/loading	179	100.1	continuous flow	Holton-le-Clay, UK
36	Mixing/loading	180	89.1	batch	Neubrandenburg, Germany
34	Mixing/loading	187	105.2	continuous flow	Bisdorf, Germany
26	Mixing/loading	186	96.8	batch	Colsterworth, UK
28	Mixing/loading	174	76.2	batch	Altenweddingen, Germany
27	Mixing/loading	179	84	batch	Martensrade, Germany
Arithmetic mean	**Mixing/loading**	**180**	**85.3**		

Appendix 3-7

Exposure of operators during mixing/loading normalized to µg/kg operator bodyweight

Site	Operator	Dermal Exposure [µg/kg bw]				Air filter [µg/kg bw]	
		"Total Inner Dosimeter"		"Total Outer Dosimeter"			
		Pz	Fq	Pz	Fq	Pz	Fq
Neubrandenburg	36	1.185	0.810	12.341	4.806	0.002247	0.000827
Bisdorf	34	0.017	0.137	4.618	23.760	0.000066	0.000425
Altenweddingen	28	0.077	0.011	5.107	14.630	0.000046	0.000028
Martensrade	27	0.040	0.174	62.563	335.286	0.000012	0.000028
Bracebridge Heath	32	0.010	0.026	0.019	0.148	0.000000	0.000000
Colsterworth	26	0.006	0.004	0.005	0.015	0.000000	0.000000
Little Airmyn	35	0.004	0.003	0.011	0.061	0.000000	0.000000
Holton Le Clay	31	0.060	0.034	0.014	0.026	0.000006	0.000000
La Batie-Rolland	33	0.001	0.027	0.572	6.075	0.000026	0.000348
	Geometric mean	0.021	0.033	0.382	1.315	0.00005	0.00016
	Arithmetic mean	0.156	0.136	9.472	42.756	0.00027	0.00018
	Min	0.001	0.003	0.005	0.015	0.00000	0.00000
	Max	1.185	0.810	62.563	335.286	0.00225	0.00083
	75^{th} percentile	0.060	0.137	5.107	14.630	0.00005	0.00035
	90^{th} percentile	0.299	0.301	22.385	86.065	0.00050	0.00051

Appendix 3-8

Exposure of operators during bagging normalized to µg/kg operator bodyweight and 8 hour work rate

Site	Operator	Work duration [min]	Dermal Exposure [µg/kg bw]				Air filter [µg/kg bw]	
			"Total Inner Dosimeter"		"Total Outer Dosimeter"			
			Pz	Fq	Pz	Fq	Pz	Fq
Neubrandenburg	16	458	2.1534	2.2560	7.4089	17.2206	0.0035	0.0026
Demmin	25	394	0.2983	0.5042	0.4014	1.1033	0.00062	0.0025
Demmin	15	267	1.5725	7.5624	38.2220	197.4727	0.0032	0.014
Bisdorf	14	267	0.1436	1.1235	0.6722	3.7813	0.0017	0.0095
Bisdorf	7	177	0.1437	1.3852	0.4800	3.4025	0.0046	0.019
Bisdorf	20	402	0.1678	1.4581	0.4254	2.6696	0.0018	0.010
Altenweddingen	6	177	1.1997	1.0041	3.5831	3.7594	0.0087	0.028
Altenweddingen	17	408	1.2728	2.0048	5.1534	7.9235	0.013	0.047
Lensahn	21	286	2.1243	9.0155	5.0416	13.4558	0.0036	0.016
Lensahn	22	285	0.2437	0.6192	0.2856	0.9791	0.00023	0.00072
Lensahn	23	460	2.5755	11.5760	1.2455	5.0386	0.0019	0.008
Martensrade	4	177	1.3086	5.5933	3.3680	15.7054	0.0061	0.031
Martensrade	19	408	0.2028	1.0765	0.6096	2.9822	0.0022	0.012
Martensrade	24	463	1.9944	12.1243	1.5235	8.3281	0.031	0.16
Bracebridge Heath	8	177	0.1650	1.1634	0.4444	2.3359	0.00091	0.0051
Colsterworth	18	408	0.0659	0.3153	0.2397	1.2688	0.0023	0.013
Colsterworth	5	177	0.0847	0.4157	0.3805	1.9846	0.0017	0.0091
Little Airmyn	1	177	0.0916	0.3313	0.0831	0.1568	0.00022	0.00087
Little Airmyn	3	177	0.0469	0.0918	0.2044	0.4686	0.000149	0.00060
Holton Le Clay	11	265	2.8208	13.2435	2.0182	7.1587	0.00033	0.0013
Holton Le Clay	13	267	0.8455	1.1590	1.6153	1.9883	0.00050	0.0015
La Batie-Rolland	10	177	0.0035	0.0910	0.0048	0.1046	0.000098	0.00055
Geometric mean		273.7	0.3547	1.3804	0.8316	3.0987	0.00154	0.00630
Arithmetic mean		293.4	0.8875	3.3688	3.3368	13.6040	0.00400	0.01784
Min		177.0	0.0035	0.0910	0.0048	0.1046	0.00010	0.00055
Max		463.0	2.8208	13.2435	38.2220	197.4727	0.03075	0.16028
75th percentile		406.5	1.5065	4.7590	3.0306	7.7323	0.00356	0.01580
90th percentile		453.0	2.1505	11.3200	5.1422	15.4805	0.00841	0.03086

Pz = Prochloraz
Fq = Fluquinconazole

Appendix 3-9

Exposure of operators during cleaning normalized to µg/kg operator bodyweight

Site	Operator	Dermal Exposure [µg/kg bw]				Air filter [µg/kg bw]	
		"Total Inner Dosimeter"		"Total Outer Dosimeter"			
		Pz	Fq	Pz	Fq	Pz	Fq
Demmin	45	1.050	4.994	232.561	1094.862	0.00547	0.02682
Bisdorf	48	0.080	0.635	14.046	80.218	0.01600	0.00023
Altenweddingen	38	0.326	0.400	9.092	13.639	0.00391	0.00512
Lensahn	39	0.268	0.885	42.316	199.489	0.00176	0.00703
Bracebridge Heath	43	0.010	0.045	10.845	38.574	0.00145	0.00596
Colsterworth	44	0.023	0.057	3.707	19.527	0.00047	0.00241
Holton Le Clay	47	0.270	0.532	115.882	580.880	0.00030	0.00044
La Batie-Rolland	40	0.006	0.048	9.413	44.332	0.00058	0.00452
	Geometric mean	0.085	0.304	22.011	90.836	0.00171	0.00299
	Arithmetic mean	0.254	0.950	54.733	258.940	0.00374	0.00657
	Min	0.006	0.045	3.707	13.639	0.00030	0.00023
	Max	1.050	4.994	232.561	1094.862	0.01600	0.02682
	75^{th} percentile	0.284	0.698	60.708	294.836	0.00430	0.00622
	90^{th} percentile	0.543	2.118	150.886	735.075	0.00863	0.01297

Pz = Prochloraz
Fq = Fluquinconazole

Appendix 3-10

Overview on activities of individual operators												
Operator No.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Active substance	**Anthraquinone**											
Activity performed	Application *	Application *	Application	All operations	All operations	Application	Application	All operations	Application	All operations	All operations	All operations
Hand protection**	PP	P	U	PP	PP	U	P	P	P	P	PP	P
Kg of active substance handled [mixing / loading & bagging]	11,57	10,27	7,22	8,00 & 7,22	8,00 & 8,09	8,09	10,48	8,99 & 10,48	10,83	5,995 & 10,83	1,5 & 4,022	5,748 & 5,123
Working time [min]	186	219	230	249	273	237	378	415	270	300	153	305
Active substance	**Fludioxonil**											
Kg of active substance handled [mixing / loading & bagging]	1,085	0,705	0,722	0.800 & 0,722	0.800 & 0,809	0.809			0,187	0,100 & 0,187		
Working time [min]	171	147	230	249	273	237			46	51		
Active substance	**Imidacloprid**											
Kg of active substance handled [mixing / loading & bagging]							0.315	0.315			2.800 & 7.366	7.00 & 6.139
Working time [min]							9	9			197	287
* Mixing/loading was substantially done automatically, thus no amount of active substance measured for this operation												
** U: unprotected hands P: protected hands PP: partially protected hands (gloves worn mainly or only during the mixing/loading phase)												

Appendix 3-11

Anthraquinone actual dermal and inhalation exposure [µg/day] including correction for field recoveries when required

Operator No	1	2	3	4	5	6	7	8	9	10	11	12
Task	All operations**	All operations**	Bagging	All operations	All operations	Bagging	Bagging	All operations	Bagging	All operations	All operations	Al operat
Mixing/loading & bagging [kg a.s. handled per day]	11.57	10.27	7.22	8,00 & 7,22	8,00 & 8,09	8.09	10.48	8,99 & 10,48	10.83	5,995 & 10,83	1,5 & 4,022	5,748 &
Duration [min]	186	219	230	249	273	237	378	415	270	300	133	305
Hand Protection	PP	P	U	PP	PP	U	P	P	P	P	PP	P
Inner dosimeter total	22.7	39.7	797	53.8	36.3	132	525	255	368	359	681	71.
Face/neck wipes	7.17	5.45	37.9	10.7	96.9	10.5	4.65	4.48	10.3	3.39	23	6.5
Hand washes	14.5	44.1	1273	357.1	900	686	43.7	151	339	141	704	9.7
Total dermal exposure	44.37	89.25	2107.9	421.6	1033.2	828.5	573.35	410.48	717.3	503.39	1408	87.9
Calculated inhalation exposure*	1.3	2.76	48.4	11.1	5.71	27.4	50.7	41.3	62.7	15.4	191	3.5

* Calculated inhalation exposure using a standard respiration rate of 14 L/min

** Mixing/loading was performed using a fast coupling system

Hand protection: U: unprotected hands P: protected hands PP: partially protected hands (gloves worn mainly or only during the M/L phase)

Appendix 3-12

Fludioxonil actual dermal and inhalation exposure [µg/day] including correction for field recoveries when required

Operator No	1	2	3	4	5	6	7	8	9	10	11	12
Task	All operations**	All operations**	Bagging	All operations	All operations	Bagging	-	-	Bagging	All operations	-	-
Mixing/loading & bagging [kg a.s. handled per day]	1.085	0.705	0.722	0,800 & 0,722	0,800 & 0,809	0.809	-	-	0.187	0,1 & 0,187	-	-
Duration [min]	171	147	230	249	273	237	-	-	46	51	-	-
Hand Protection	PP	P	U	PP	PP	U	-	-	P	P	-	-
Inner dosimeter total	0.75	1.52	118	7.19	7.2	19.2	-	-	5.09	0.75	-	-
Face/neck wipes	0.345	0.241	2.13	0.787	4.88	0.786	-	-	0.0938	0,0250#	-	-
Hand washes	0.0250#	1.25	1985	19.8	96.7	70.7	-	-	2.26	0.852	-	-
Total dermal exposure	1.095	3.011	2105.13	27.777	108.78	90.686			7.4438	1.602		
Calculated inhalation exposure*	0.0691	0.271	4.04	1.61	1.09	3.16	-	-	0.556	0.0693	-	-

* Calculated inhalation exposure using a standard respiration rate of 14 L/min

**: Mixing/loading was performed using a fast coupling system

#: BLQ value replaced by ½ LOQ

Hand protection: U: unprotected hands P: protected hands PP: partially protected hands (gloves worn mainly or only during the M/L phase)

Appendix 3-13

Imidacloprid actual dermal and inhalation exposure [µg/day] including correction for field recoveries when required

Operator No	1	2	3	4	5	6	7	8	9	10	11	12
Task	-	-	-	-	-	-	Bagging	Bagging	-	-	All operations	All operations
Mixing/loading & bagging [kg a.s. handled per day]	-	-	-	-	-	-	0.315	0.315	-	-	2,80 & 7,366	7,00 & 6,139
Duration [min]	-	-	-	-	-	-	9	9	-	-	197	287
Hand Protection	-	-	-	-	-	-	P	P	-	-	PP	P
Inner dosimeter total	-	-	-	-	-	-	5.41	4.41	-	-	178	20.4
Face/neck wipes	-	-	-	-	-	-	0.258	0.376	-	-	27.6	3.9
Hand washes	-	-	-	-	-	-	14.6	22.9	-	-	331	5.93
Total dermal exposure							20.268	27.686			536.6	30.23
Calculated inhalation exposure*	-	-	-	-	-	-	0.141	0.279	-	-	71.2	0.664

* Calculated inhalation exposure using a standard respiration rate of 14 L/min

Hand protection: U: unprotected hands P: protected hands PP: partially protected hands (gloves worn mainly or only during the M/L phase)

Appendix 3-14

Anthraquinone and imidacloprid actual dermal and inhalation exposure [µg/day]

Operator No	1#	2#	3#	4#	5#	6#	7#	8#	9#	10#	11#	12#	11##	12##
Task	All operations**	All operations**	Bagging	All operations	All operations	Bagging	Bagging	All operations	Bagging	All operations	All operations	All operations	All operations	All operations
Mixing/loading & bagging [kg a.s. handled per day]	11.57	10.27	7.22	8,00 & 7,22	8,00 & 8,09	8.09	10.48	8,99 & 10,48	10.83	5,995 & 10,83	1,5 & 4,022	5,748 & 5,123	2,80 & 7,366	7,00 & 6,139
Duration [min]	186	219	230	249	273	237	378	415	270	300	133	305	197	287
Hand Protection	PP	P	U	PP	PP	U	P	P	P	P	PP	P	PP	P
Inner dosimeter total	22.7	39.7	797	53.8	36.3	132	525	255	368	359	681	71.7	178	20.4
Face/neck wipes	7.17	5.45	37.9	10.7	96.9	10.5	4.65	4.48	10.3	3.39	23	6.52	27.6	3.9
Hand washes	14.5	44.1	1273	357.1	900	686	43.7	151	339	141	704	9.7	331	5.93
Total dermal exposure	44.37	89.25	2107.9	421.6	1033.2	828.5	573.35	410.48	717.3	503.39	1408	87.92	536.6	30.23
Calculated inhalation exposure*	1.3	2.76	48.4	11.1	5.71	27.4	50.7	41.3	62.7	15.4	191	3.5	71.2	0.664

#= anthraqinone data, ##= imidacloprid data

* Calculated inhalation exposure using a standard respiration rate of 14 L/min

** Mixing/loading was performed using a fast coupling system

Hand protection: U: unprotected hands P: protected hands PP: partially protected hands (gloves worn mainly or only during the M/L phase)

Appendix 3-15 Revised SeedTropex model (V15, 2014) Exposure data (long-term exposure)

Cereal Seed in plant				
	M/L	Cal.	Bagging	Cleaning
75th	µg/kg a.i.	µg/kg a.i.	µg/kg a.i.	µg/op
Face	0.83	4.80	2.55	13.92
Hands	79.56	886.40	30.17	2.50
Body	3.87	27.52	5.87	1.93
Inhalation	3.09	8.51	3.01	1.54
Total Int. Dose	7.18	33.02	6.00	2.34

Cereal Seed Mobile	
	75th
	µg/kg a.i.
Face	3.76
Hands	175.04
Body	42.04
Inhalation	0.04
Total Int. Dose	9.40

Seed Sowing		
	Cereal	
	Load	Sow
75th	µg/kg a.i.	µg/kg a.i.
Face	12285.01	139.51
Hands	8396.40	7799.23
Body		1216.59
Inhalation	164.59	180.42
Total Int. Dose	278.11	613.24

Appendix 3-16 Revised SeedTropex model (V15, 2014) Exposure data (acute exposure)

Cereal Seed in plant				
	M/L	Cal.	Bagging	Cleaning
95th	µg/kg a.i.	µg/kg a.i.	µg/kg a.i.	µg/op
Face	4,00	4,80	8,79	32,28
Hands	2736,59	886,40	174,14	52,00
Body	15,68	27,52	39,95	24,44
Inhalation	6,85	8,51	12,80	6,10
Total Int. Dose	30,98	33,02	13,82	10,97

Cereal Seed Mobile	
	95th
	µg/kg a.i.
Face	11,56
Hands	5381,79
Body	226,40
Inhalation	8,51
Total Int. Dose	93,01

Seed Sowing		
	Cereal	
	Load	Sow
95th	µg/kg a.i.	µg/kg a.i.
Face	12285,01	961,56
Hands	18048,35	28001,57
Body		2114,74
Inhalation	361,56	386,27
Total Int. Dose	555,30	1262,96

B.6.6. EXPOSURE AND RISK ASSESSMENT (METHANOL)

The general risk represented by methanol as an impurity of 0.3% in triticonazole irrespective of the formulation can be evaluated by directly comparing the reference values for each compound.

The respective values are:
AOEL/ADI Triticonazole = 0.025 mg/kg bw per dayay
AOEL/ADI Methanol = 6.66 mg/kg bw per dayay

Assuming 100% AOEL usage of triticonazole the maximum exposure to methanol is:
0.025 mg/kg bw per dayay X 0.3 = 0.000075 mg/kg bw per dayay

This is >80 000 fold below the AOEL/ADI/DNEL of methanol. In contrast to triticonazole methanol has a high dermal absorption of 100%. Nonetheless, the high margin of safety clearly demonstrates that exposure to methanol by triticonazole does not pose a risk.

For the representative formulation BAS 595 01 F, a detailed exposure assessment according to SeedTropex is presented below. The exposure (of even unprotected worker) was near zero for seed treatment in plants and mobile, as well as for sowing seeds.

Summary of critical use patterns:

Crop (indoor/field)	Application rate (kg as/100 kg seed)		Spray dilution (L/ha)	Application equipment	Number applications
Cereal seeds	Triticonazole	0.005	Product can be applied undiluted or diluted with water to a maximum ratio of 1:5 product : water	Seed treatment equipment and cereal seed sowing equipment	1
	Methanol	0.000015			

Endpoints for non-dietary risk assessment:

End-Point	Active Substance	Impurity
	Triticonazole	Methanol
Dermal penetration	Concentrate: 1% Dilution: 3%	Concentration: 100% Dilution 100%
AOEL	0.025 mg/kg bw/day	6.66 mg/kg bw/day

Table 6.6 -1: Estimated (unprotected) exposure to methanol from seed treated with BAS 595 01 F (revised SeedTropex model V15)

Seed Treatment information

Product	
Product name	BAS 595 01 F
Active Substance name	Methanol
Formulation type	FS
Active Substance concentration	0,075 g a.s. / L

Application Parameters		
Seed Type	Cereals	
Application dose	2	L form./ ton
Amount a.s. treated / day	0	kg a.s.
Tons of seed processed/day	100	tons
a.s. concentration on seeds	0,15	g/ton
Number of cleaning operations	1	

Sowing Parameters		
Area Treated	20	ha
Kg of seeds/ha	250	kg
Amount of a.s handled	0,00075	kg a.s.

The following parameters have been used:		
AOEL Value	6,6	mg/kg bw/day
Body weight	60	kg
Inhalation ventilation rate	21	L/min.
Dermal penetration M/L/loading	100,00	%
Dermal Penetration Calibration	100,00	%
Dermal penetration Bagging / Sowing	100,00	%
Dermal penetration Cleaning	100,00	%

PPE			
Task	Gloves	Body	Respiration
Mixing/Loading	No	No	No
Calibration	No	No	No
Bagging	No	No	No
Cleaning	No	No	No

Miscelaneouss statistical parameters	
Selection of statistical endpoint	75th percentile
Protections: actual or actual+calculated	Actual + calculated

Exposure

Cereal Seed in plant	Mixing/Loading	Calibration	Bagging	Cleaning	Total	
Total actual dermal exposure	0,030	0,003	0,043	36,904	36,980	µg/kg bw/day
Total inhalation exposure	0,001	0,000	0,001	0,026	0,027	µg/kg bw/day
Total dose absorbed	0,033	0,003	0,056	54,115	54,207	µg/kg bw/day
% AOEL	0,001	0,000	0,001	0,820	0,821	%

Cereal Seed Mobile	Combined	
Total actual dermal exposure	0,23	µg/kg bw/day
Total inhalation exposure	0,00	µg/kg bw/day
Total dose absorbed	0,21	µg/kg bw/day
% AOEL	0,00	%

Cereal Seed Sowing	Loading	Sowing	Total	
Total actual dermal exposure	0,26	0,2793	0,54	µg/kg bw/day
Total inhalation exposure	0,002	0,0023	0,00	µg/kg bw/day
Total dose absorbed	0,1	0,2452	0,36	µg/kg bw/day
% AOEL	0,0	0,0	0,0	%

B.6.7. REFERENCES RELIED ON

The literature search has been extensively described in Volume 3, B6 (active substance). No literature on plant protection products containing triticonazole has been identified.

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCP 7.1.1	[redacted]	1994	Acute oral toxicity in rats - EXP 80472 C016283 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.1	[redacted]	1994	Acute oral toxicity in rats - Amendment No. 1 to the final report dated 25.07.94 - EXP80472 C016284 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.2	[redacted]	1994	Acute dermal toxicity in rats - EXP80472 C016277 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.2	[redacted]	1994	Acute dermal toxicity in rats - Amendment No. 1 to the final report dated 27.7.94 C016278 [redacted] yes	Y	N	-	BASF	DAR (2003)

			Unpublished					
KCP 7.1.3	[redacted]	1994	EXP80472: Acute inhalation toxicity study - Four-hour exposure (nose only) in the rat C016285 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.4	[redacted]	1994	Acute dermal irritation in rabbits - EXP80472 C016281 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.4	[redacted]	1994	Acute dermal irritation in rabbits - Amendment No. 1 to the final report dated 15.07.94 - EXP80472 C016282 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.5	[redacted] J.	1994	EXP 80472: Acute eye irritation in rabbits C016279 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)

KCP 7.1.5	[redacted]	1994	EXP 80472: Acute eye irritation in rabbits - Amendment No. 1 to the final report dated 25.7.94 C044978 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.6	[redacted]	1995	EXP 80472: Skin sensitization test in guinea-pigs (modified BUEHLER test: 9 applications) C016286 [redacted] yes Unpublished	Y	N	-	BASF	DAR (2003)
KCP 7.1.6	[redacted]	2008	BAS 595 01 F - Murine local lymph node assay (LLNA) 2007/1053388 BASF AG, [redacted] yes Unpublished	Y	Y	New data for AIR3 renewal (not considered essential since valid Buehler assay available)	BASF	Submitted for the purpose of renewal (2015)
KCP 7.2.1.2	Wilson A.J.	2009	Fluquinconazole and Prochloraz: Determination of operator exposure during cereal seed treatment with Jockey fungicide in Germany, United Kingdom and France 2009/1049020 Agrochemex Ltd., Manningtree Essex CO11 2NF, United Kingdom yes Unpublished	N	Y	New data for AIR3 renewal	BASF	Submitted for the purpose of renewal (2015)

KCP 7.2.1.2	Pontal P-G., Thouvenin I.	2008	Determination of worker exposure during treatment of cereal seeds by mobile treaters in France 2008/1056997 ADME Bioanalyses, Vergeze, France yes Unpublished	N	Y	New data for AIR3 renewal	BASF	Submitted for the purpose of renewal (2015)
KCP 7.3	Bernard F.	2013	Triticonazole - Radiolabeled Triticonazole in BAS 595 01 F - In vitro study to investigate the dermal penetration through human skin 2013/1323932 Harlan Laboratories Ltd., Itingen, Switzerland yes Unpublished	N	Y	New data for AIR3 renewal	BASF	Submitted for the purpose of renewal (2015)