Conclusion regarding the peer review of the pesticide risk assessment of the active substance

trinexapac

finalised: 14 December 2005

SUMMARY

Trinexapac is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

The Netherlands being the designated rapporteur Member State submitted the DAR on trinexapac in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 7 November 2003. Following a quality check on the DAR, the peer review was initiated on 28 January 2004 by dispatching the DAR for consultation of the Member States and the sole notifier Syngenta Ltd. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in July 2004. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in January, February and March 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 29 September 2005 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as plant growth regulator, as proposed by the applicant, which comprises foliar spraying to cereals, amenity turf and amenity grassland at application rate of 0.2 kg trinexapac-ethyl per hectare in cereals and 0.4 kg in amenity turf and grassland. Trinexapac and trinexapac-ethyl, respectively, can be used only as plant growth regulator.
The representative formulated product for the evaluation was "Moddus 250 EC" ("A-7725 M"), an emulsifiable concentrate (EC), registered in some EU Member States.
Due to the fact that the ethyl ester, a variant of trinexapac, is used in the formulated product, it should be noted that the evaluated data belong to the variant trinexapac-ethyl, unless otherwise specified.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
Sufficient analytical method as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Trinexapac-ethyl is of low acute toxicity. It is not a skin or an eye irritant or a skin sensitiser. There is no evidence of genotoxic or carcinogenic potential. There were no direct effects on reproductive performance or fertility observed. The ADI is 0.32 mg/kg bw/day and the AOEL is 0.34 mg/kg bw/day with a 100-fold safety factor applied. The allocation of the ARfD was not considered necessary due to the low acute toxicity of trinexapac-ethyl. A dermal absorption of 10% was considered for both undiluted and spray preparation. The estimated operator exposure according to the German model and UK-POEM is below the AOEL with and without PPE. No data available for re-entry activities in amenity turf and amenity grassland.

Following application of trinexapac-ethyl to wheat, rice and rape plants by foliar application trinexapac was the major residue found at harvest in straw and in grain or seeds, respectively, accounting for about 90% and 60% of the total residue, respectively. Other metabolites were present at very low levels. It is noted that for one non-rat metabolite CGA 351210, found in rape matrices, no toxicity assessment has been provided; however, rape is not a representative use within the evaluation process for Annex I inclusion of trinexapac. In processing procedures trinexapac-ethyl can be considered as hydrolytically stable whereas trinexapac had degraded by almost 50%. The toxicological relevance of one of the major degradation products, CGA 113745, was not further assessed, since the chronic consumer exposure to trinexapac residues from cereals is low and data on processing are not mandatory in that case. No significant residue levels are expected in rotational crops following application of trinexapac-ethyl according to Good Agricultural Practice (GAP).
Fed to ruminants and poultry, trinexapac-ethyl was intensively metabolised resulting in a comparable pattern to that observed in rat metabolism, in which trinexapac is the major and only residue component of significance. In a feeding study levels of trinexapac in edible animal matrices were all found to be below the limit of quantification (LOQ).
The chronic dietary exposure assessment for consumers based on the representative GAP on cereals indicated that none of the considered consumer subgroups was exposed above 1% of the proposed ADI. Due to the low acute toxicity of trinexapac-ethyl the allocation of an ARfD, and hence an acute consumer risk assessment was not considered necessary.

Soil metabolism of trinexapac-ethyl yields the major metabolite trinexapac, mineralisation to CO_2 is significant accounting for 49% to 58% AR depending on the part of the molecule radiolabelled. Unextracatable residues were relatively low (11-18% AR at 90 days). Trinexapac-ethyl is of very low persistence in soil, trinexapac is of low to moderate persistence. Trinexapac-ethyl and trinexapac

exhibit low to high mobility in soil with adsorption decreasing (i.e. mobility increasing) as soil pH increases.

In the sediment water environment trinexapac-ethyl has low persistence being converted by microbially mediated degradation to trinexapac which exhibits moderate persistence being microbially mineralised to CO_2 (accounting for 59-69% of the applied ring radiolabel after 111 days). In the alkali sediment water systems tested, partitioning to sediment was limited, partitioning to sediment could be higher in natural water systems with lower pH. MS may require additional information to complete aquatic exposure and risk assessments in specific situations where surface water systems adjacent to treated areas are acidic, as sterile hydrolysis studies on trinexapac at pH 5 indicated there might be the potential for two novel breakdown products to be formed under acidic conditions. One of these breakdown products has not been identified. Trinexapac-ethyl is classified as 'not readily biodegradable'. PEC surface water values to be used in the risk assessment for the representative uses from the spray drift route of exposure have been calculated, however the runoff and drainage routes of exposure to surface water bodies have not been assessed. These routes of entry to surface water should be taken into account by MS when these routes of exposure are relevant and the pertinent risk assessments to aquatic organisms should be completed by MS. For the representative uses proposed by the applicant, the potential for contamination of vulnerable groundwater by trinexapac-ethyl and its soil breakdown products above the drinking water limit of 0.1µg/L is considered minimal.

The risk to birds and mammals from uptake of contaminated food for the representative use in cereals is low. The first tier TER values for the long-term risk to birds and mammals are below the Annex VI trigger value indicating a high long term risk to birds and mammals from uptake of contaminated drinking water. Further risk refinement steps are required to address the long term risk from uptake of contaminated drinking water. A high risk to insectivorous birds and mammals from the uptake of contaminated food was identified for the representative use in amenity grass/turf. The Annex VI trigger values were breached for the long term risk to birds and mammals and for the short term risk to birds from uptake of contaminated drinking water for the representative use in amenity grass/turf. Further risk refinement steps are required for the representative use in amenity grass/turf to address the long term risk to insectivorous birds and herbivorous mammals from the uptake of contaminated food and the long term risk to birds and mammals and the short term risk to birds from uptake of contaminated drinking water.
Trinexapac is found in hens and mammals as a metabolite in studies with trinexapac-ethyl and therefore the toxicity of trinexapac is assumed to be covered from the studies with trinexapac-ethyl. The risk of the plant metabolites CGA 275537 and CGA 329773 to birds and mammals is considered to be low. The risk of secondary poisoning is assumed to be low because the log P_{OW} of trinexapac-ethyl is < 3 and trinexapac is more polar than trinexapac-ethyl.
A high risk was identified for non-target arthropods in a first tier risk assessment for the representative use in amenity grass/turf. Higher tier tests were performed showing a low risk to non-target arthropods. For the higher tier risk assessment the RMS used a refined MAF value. The higher

tier risk assessment was discussed at the EPCO Experts` meeting (EPCO 17) in January/February 2005. The meeting agreed to the risk assessment presented by the RMS and concluded on a low risk for non-target arthropods from the representative uses.
No data were available to conclude on the risk to other soil non-target organisms. Since the standard HQ value for *Typhlodromus pyri* and *Aphidius rhopalosiphi* was >2 for the representative use in amenity grass/turf and a DT_{90} of > 100 days was observed in laboratory tests with trinexapac, a confirmatory data requirement to address the risk to other soil non-target organisms is proposed by EFSA. The need for this data was not discussed at an EPCO expert meeting.

The risk to aquatic organisms, bees, earthworms, soil non-target micro-organisms, other non-target organism and biological methods of sewage treatment from the representative uses in cereals and amenity grass/turf is considered to be low.

Key words: trinexapac, trinexapac-ethyl, peer review, risk assessment, pesticide, plant growth regulator

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Trinexapac is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating the Netherlands as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, the Netherlands submitted the report of its initial evaluation of the dossier on trinexapac, hereafter referred to as the draft assessment report, to the EFSA on 7 November 2003. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 28 January 2004 to the Member States and the main notifier Syngenta Ltd. as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 13 July 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by EPCO-Team at the Federal Office for Consumer Protection and Food Safety (BVL) in Braunschweig, Germany, in January – March 2005. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 29 September 2005 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation

evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a peer review report comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received
- the resulting reporting table (rev. 1-1 of 14 July 2004)
- the consultation report

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 29 September 2005)

Given the importance of the draft assessment report including its addendum (compiled version of September 2005 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Trinexapac is the ISO common name for 4-cyclopropyl-(hydroxy)methylene-3,5-dioxocyclohexanecarboxylic acid (IUPAC). Due to the fact that the ethyl ester, a variant of trinexapac, is used in the formulated product, it should be noted that the evaluated data belong to the variant trinexapac-ethyl, unless otherwise specified.

Trinexapac and trinexapac-ethyl, respectively, are unclassified plant growth regulator. Trinexapac-ethyl is taken up via leaves and shoots which results in morphological symptoms such as reduction of crop height or reduced elongation by inhabitation of a certain step in the gibberellin biosynthesis.

The representative formulated product for the evaluation was "Moddus 250 EC" ("A-7725 M"), an emulsifiable concentrate (EC), registered in some EU Member States.

The evaluated representative uses as plant growth regulator as proposed by the applicant comprises foliar spraying to cereals, amenity turf and amenity grassland at application rate of 0.2 kg trinexapac-ethyl per hectare in cereals and 0.4 kg in amenity turf and grassland. Trinexapac-ethyl can be used only as plant growth regulator.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of trinexapac-ethyl as manufactured should not be less than 940 g/kg. At the moment no FAO specification exists.
It should be noted that the proposed specification (max values) for non-relevant impurities are above the values found in the technical material used for toxicological and ecotoxicological tests. Due to an outstanding amended specification or a confirmation that these differences are not of toxicological and ecotoxicological concern, the specification for the technical material with respect to the maximum content of the impurities should be regarded as provisional at the moment

Beside this, the assessment of the data package revealed no particular area of concern.
The main data regarding the identity of trinexapac-ethyl and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of trinexapac-ethyl in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. However, a confirmation of the identity of two significant impurities is outstanding.
Nevertheless, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. trinexapac and its salts in food of plant (cereals, only) and animal origin, soil and water, trinexapac-ethyl in air. The methodology used is HPLC with UV or MS/MS detection. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due the nature of the residues.

The discussion in the expert meeting (EPCO 20, March 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and some issues on analytical methods and physical and chemical data of the trinexapac-ethyl.

2. Mammalian toxicology

Trinexapac was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 18) in February 2005.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Trinexapac-ethyl is almost completely absorbed (>96%) following oral administration. It is extensively metabolised (92%), mainly by hydrolysis to trinexapac. It is barely detectable in fat and kidneys 168 hours after administration. There is no evidence of accumulation; 24 hours after the administration, 91% of trinexapac-ethyl is excreted, mostly in urine.

2.2 ACUTE TOXICITY

The acute toxicity is low, i.e. oral LD_{50} 4210 mg/kg and dermal LD_{50} > 4000 mg/kg, as well as during inhalatory exposure (LC_{50} > 5.3 mg/L air). It is not a skin or an eye irritant nor a skin sensitiser (Maximisation test). **No classification for acute toxicity is required.**

2.3 SHORT TERM TOXICITY

The short term toxicity of trinexapac-ethyl was studied in two oral studies in rats (28-days and 13-weeks), two oral studies in dogs (13-weeks and 1-year) and via dermal route in a 22-day study in rabbits. The major effects consisted in decreased body weight and absolute/relative organ weight. In particular, the decrease of uterus and testes weights in the 1-year oral study in dogs was regarded as an effect of concern. In the DAR the RMS proposed a relevant provisional NOAEL of 1.4 mg/kg bw/day, based on uncertainties on the relevance. In the experts' meeting the effects and relevance on uterus and testes were discussed. The experts agreed that the effect on testes and uterus was not toxicologically relevant because it was within the historical control data and because it did not show a dose response-relationship; moreover, no associated histological effect was recorded. Therefore, the NOAEL in the 1-year dog study was increased to 32 mg/kg bw/day; the NOAEL from the 90-day study in rats is 34 mg/kg bw/day, which is the relevant short term NOAEL. No studies were submitted on repeated inhalation.

2.4 GENOTOXICITY

In the DAR the genotoxic properties of trinexapac-ethyl were studied in a battery of *in vitro* and *in vivo* studies. The overall conclusion is that there is no genotoxic potential for trinexapac-ethyl.

2.5 LONG TERM TOXICITY

One 104-week toxicity study in the rat and one 78-week study in the mouse were submitted in the dossier and evaluated by the RMS.

In the 104-week combined chronic toxicity/carcinogenicity study in rats, males showed an increased incidence of squamous cell carcinoma in the stomach and thyroid follicular adenocarcinoma in the highest dose group, and females showed an increased incidence of urinary bladder papilloma in the highest dose groups. These findings were discussed and considered as incidental by the experts. In the 78-week carcinogenicity study, no toxicologically relevant effects were observed in mice administered doses up to 912 mg/kg bw/d.

In conclusion, the relevant long term NOAEL is 116 mg/kg bw/day from the 104-week study in rats. Trinexapac-ethyl does not show carcinogenic potential.

2.6 REPRODUCTIVE TOXICITY

A two-generation study in the rat is presented in the DAR. There were no direct effects on reproductive performance or fertility.

The parental NOAEL was 60 mg/kg bw/day based on reduced body weight and food consumption. The relevant NOAEL for reproduction was 590 mg/kg bw/day based on reduced body weight gain and reduced survival index in the offsprings.

Two teratogenicity studies (one in rats and one in rabbits) were evaluated. The relevant maternal NOAEL is 60 mg/kg bw/day from the rabbit study, and the foetal/developmental NOAEL, is 360 mg/kg bw/day, based on increased pre-implantation loss and decreased number of live foetuses.

2.7 NEUROTOXICITY

In the 1-year dog study vacuolation of the brain was observed in the highest dose group (727 mg/kg bw/day). No clinical neurological symptoms were reported. The experts linked this effect to an interference with energy metabolism following prolonged exposure to trinexapac-ethyl in dog and evident only at very high doses. No further neurotoxicity testing was deemed necessary, as no neurological lesions or symptoms were reported in other submitted studies.

2.8 FURTHER STUDIES

Metabolites CGA 275537, CGA 313458 and CGA 329773 have been tested and showed to have a low acute oral toxicity (LD_{50} 330-2000 mg/kg bw for CGA 275537 and LD_{50} >2000 mg/kg bw for the others). The Ames test gave negative results for all metabolites. Metabolite CGA 329773 has also been tested in a repeated dose study in rats (NOAEL 1021 mg/kg bw/day).

No toxicity assessment has been provided for metabolite CGA 351210 found in oilseed rape.

No toxicological data is available for metabolite CGA 113745 found in a goat metabolism study (liver, kidney, fat) and in a processing (hydrolysis) study. The applicant states in the Addendum that CGA 113745 has a structure very similar to the manufacturing intermediate CGA 158377, for which the No Effect Level (NOEL) for 28-day study in rat is 100 mg/kg/day and the Ames test negative. Toxicological data for CGA158377 have not been submitted. If for authorisation of uses at MS level processing data become relevant, the toxicological relevance of CGA 158377 and CGA 113745 needs to be clarified.

2.9 MEDICAL DATA

No adverse reactions have been reported in persons involved in field trials and in users of commercial formulations so far.

2.10 ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) and ACUTE REFERENCE DOSE (ARfD)

ADI

The **ADI is 0.32 mg/kg bw/day** based on the NOAEL from the 1-year dog study, with a safety factor of 100.

AOEL

The **AOEL is 0.34 mg/kg bw/day**, based on the NOAEL of 34 mg/kg bw/day from the 90-day study in rat with a safety factor of 100.

ARfD

The allocation of the ARfD for trinexapac-ethyl was not considered necessary due to the low acute toxicity of trinexapac-ethyl.

2.11 DERMAL ABSORPTION

Dermal absorption of trinexapac-ethyl have been assessed through one *in vivo* dermal absorption study in rats and a comparative *in vitro* human/rat study with trinexapac-ethyl formulated as MODDUS 250 EC. A value of 10% for both undiluted preparation and spray dilution was confirmed.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product MODDUS 250 is an EC formulation 250 g trinexapac-ethyl/L, for use in cereals (application rate 0.2 kg as/ha) and in amenity turf and grassland (application rate 0.4 kg as/ha).

Operator exposure

The estimated operator exposure for MODDUS 250 EC is below the AOEL of 0.34 mg/kg bw/day even without PPE for mechanical spraying in cereals, and for manual and mechanical spraying on amenity turf and amenity grassland using the UK-POEM (75th) and the German model (geometric mean) and considering 60 or 70 kg body weight for the UK POEM and the German model, respectively.

Scenario	Model	No PPE	With PPE*
Mechanical spraying cereals	**UK POEM**	69%	8.0%
	German model	7.5%	0.1%
Mechanical spraying on amenity turf and grassland	**UK POEM**	139%	16.0%
	German model	15%	0.4%
Manual spraying on amenity turf and grassland	**UK POEM**	64%	21.3%
	German model	42%	1.0%

* UK-POEM: gloves during mixing/loading and application; German model: gloves during mixing/loading and application, standard protective garment +sturdy footwear, broad-brimmed headgear

Worker exposure

For use in cereals the estimated exposure is assumed to be below the AOEL. The use in amenity turf and amenity grassland could not be evaluated as no models are available for assessing worker exposure in such a scenario.

Bystander exposure

Estimated exposure to bystanders was made according to EUROPOEM II. Exposure values were below the AOEL for mechanical spraying on cereals and for manual and mechanical spraying on amenity turf/grassland.

3. Residues

Trinexapac was discussed at EPCO experts' meeting for residues (EPCO 19) in February 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

Primary crop metabolism studies were conducted with trinexapac-ethyl on wheat, rape and rice. Trinexapac-ethyl is rapidly degraded to very low (rice) or undetectable levels (spring wheat, spring rape) in edible plant parts. The major residue component in edible parts is trinexapac, formed by hydrolysis of the ester bond of trinexapac-ethyl. Trinexapac is representing up to 28% of the total residue in wheat grain, up to 30% in rape oil and meal, and up to 36% in rice grain. Other metabolites are present in relatively low levels, while also a part of the residue is associated with plant matrices. In plant products being potential animal feed, the major residue components are trinexapac (wheat straw), CGA 275537 (rice straw), and CGA 351210, free and conjugated (rape stalks). A part of the residue is also found to be associated with plant matrices (glucose, lipids, cellulose, pectin, and lignin). The metabolites CGA 275537 and CGA 351210 are neither found in the rat nor in livestock animals. Metabolite CGA 275537 has been tested and was not regarded to be of toxicological concern (see 2.8). But no toxicity assessment has been provided for metabolite CGA 351210, which was found in rape matrices (seeds, oil, meal, pods, stalks), partially at significant levels. However, this is not further elaborated since rape is not a representative use within the evaluation process for Annex I inclusion of trinexapac, but may be reconsidered by Member States when it comes to national authorisation of uses on oil seed crops.

The proposed metabolic pathway of trinexapac-ethyl in plants includes hydrolysis of the ester bond to trinexapac. Further degradation proceeds via stepwise oxidation/decarboxylation after cleavage of the 6-membered ring yielding saturated and unsaturated tricarboxylated acids such as tricarballylic acid (CGA 275537) and trans-aconitic acid (CGA 312753), which is an intermediate of the citric acid cycle (Krebs cycle). From the intermediates of the citric acid cycle and their breakdown products, sugars, fatty acids and certain amino acids are formed by de-novo synthesis. In wheat the ring

cleavage occurs also on the parent molecule yielding the mono-ethylester of the aconitic acid. In rape trinexapac is reduced to 2-(cyclopropyl-hydroxy-methylene)-5-hydroxymethyl-cyclohexane-1,3-dione (CGA 351210), and subsequent conjugation with sugars occurs. Trinexapac is by far the predominating residue component in edible plant parts of cereals, whereas the applied trinexapac-ethyl is rapidly degraded to undetectable levels. Hence, it is proposed to define the residue in cereals as trinexapac and its salts [4-(Cyclopropyl-alpha-hydroxy-methylene-3,5-dioxocyclohexane-carboxylic acid and anionic form] for monitoring and risk assessment purposes.
A sufficient number of supervised residue trials on cereals in accordance with the critical GAP was available from Northern and Southern Europe. Residue trials were conducted with trinexapac-ethyl on barley, oats, wheat and triticale. Basically, trinexapac was the residues determined, but in few trials trinexapac-ethyl was also analysed. Application on cereals is intended early in the growing season and therefore extrapolation from the available trials to the whole group of cereals was considered possible. Residues of trinexapac up to 0.2 mg/kg were found in cereal grain and up to 0.14 mg/kg in straw.

In processing procedures such as boiling, brewing, baking, sterilization and pasteurisation, trinexapac-ethyl can be considered as hydrolytically stable with negligible degradation. In contrast, studies with trinexapac under hydrolysis conditions indicated that at the end of incubation, trinexapac had degraded and represented 51-59% of the total radioactivity. Degradation products identified were CGA 313458 (16-21%) and CGA 113745 (9.6-12%), which haven't been found in rat metabolism. CGA 313458 was tested and considered of no toxicological concern (see 2.8). For the other compound, RMS concluded that the toxicological endpoints of CGA 158377 provided by the applicant may also reflect those of CGA 113745, since the primary metabolic step in the metabolism of CGA 158377 is likely to be hydrolysis of the ethyl ester bond yielding CGA 113745. However, the complete toxicology package for CGA 158377 has not been submitted (see 2.8). Based on the representative uses for Annex I inclusion processing studies are not mandatory, since the TMDI is well below 10% ADI (see 3.3). Therefore further data can currently not be considered essential. If for authorisation of uses on MS level processing data become relevant the toxicological profile of CGA 113745 and/or CGA 158377 will have to be addressed.
In processing studies with wheat and barley grain from residue trials it appeared, that most of the residue (trinexapac) in wheat grain is found to be transferred to the bran fraction, to whole-meal flour and subsequently to whole-grain bread. Concentration of the residue is only observed in the bran fraction (about 4-fold). The processing of barley grain into beer results in a reduction of residue levels. However, these studies may need to be reassessed subject to the relevance of CGA 113745.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

In rotational crops, residue levels were at or below the LOQ and too low for identification. Hence, no significant residue levels are to be expected in rotational crops following application of trinexapac-ethyl according to GAP.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism of trinexapac-ethyl was studied in lactating goats and laying hens. However, it is noted that trinexapac, and also CGA 351210 (a further degradation product of trinexapac), are the major residue components in livestock feed. As such, the livestock metabolism studies with trinexapac-ethyl might be considered less relevant in first instance. But due to the fast and extensive metabolism of trinexapac-ethyl to trinexapac in animals, the results gained from studies with trinexapac-ethyl are considered applicable for the evaluation.

After oral dosing with highly exaggerated doses of trinexapac-ethyl, highest residue concentrations are found in kidneys of both species. Relatively low residue levels are observed in milk and eggs. Residue concentrations reach plateau levels in milk after about 2 to 3 days and in eggs after about 2 days. Trinexapac is the major residue component identified in milk, meat and offal from ruminants, accounting for about 66-97% TRR. In one of the goat studies also metabolite CGA 113745 was found in liver, kidney and fat (6-16% TRR), however, absolute levels are low (<0.4 mg/kg) considering the exaggerated dose administered to the animals (*ca* 300 N) and would be negligible at the estimated highest likely feeding rate in practice (N).
In poultry meat, offal, and egg yolk, again, trinexapac is the major residue component representing about 60% TRR, 10-80% TRR, and 28% TRR, respectively. The exception is egg white, in which trinexapac-ethyl is dominating (44% TRR), although being present at very low levels.

The metabolic pathway of the trinexapac-ethyl in livestock comprises of hydrolysis of the ester bond to the formation of trinexapac. CGA 113745 was the only other metabolite identified in goat milk and tissues. The observed metabolic pathway of trinexapac-ethyl in livestock is comparable to the rat, in which trinexapac is the major and only residue component of significance. Therefore it is proposed to define the residue in animal products as trinexapac and its salts for monitoring and risk assessment purposes.
Livestock feeding studies performed with trinexapac indicate that following treatment at N rate no significant residue levels of trinexapac are expected. However, MRLs for food of animal origin have been proposed by RMS. (see 3.4)

3.3. CONSUMER RISK ASSESSMENT

The chronic dietary risk assessment for consumers is based on the Theoretical Maximum Daily Intake (TMDI) calculation with consumption data from the WHO/GEMS Food European diet and the Dutch model (RIKILT-DLO, the Netherlands). In the calculations the respective MRLs are used. The contribution to the ADI of 0.32 mg/kg bw is less then 1% for both of the considered consumer subgroups of adults and 1-6 years old children.
Based on the toxicological characteristics of trinexapac-ethyl the allocation of an ARfD is not needed, and consequently no assessment of the acute risk to consumers.

3.4. PROPOSED MRLS

Cereals	Barley, oats, wheat, rye, triticale	0.3 mg/kg
Animal products	Milk	0.01*mg/kg
	Eggs	0.02* mg/kg
	Meat and offal (poultry, mammal)	0.02* mg/kg
		* LOD

No Codex MRLs have been established or proposed yet and need to be considered.

4. Environmental fate and behaviour

Issues raised during the peer review, including a statement provided by the applicant on potential breakdown products that might be formed under natural conditions in acidic sediment water systems, were discussed in a scientific meeting between Member State experts in January – February 2005 (EPCO 16).

In the original DAR trinexapac was denoted as trinexapac-acid. In this conclusion only the name trinexapac is used for this compound.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

In the reliable aerobic laboratory soil biodegradation studies (4 different soils) that were dosed with trinexapac-ethyl radio-labelled in either the hydroxymethylene, carbonyl or ring groups, trinexapac-ethyl was rapidly degraded to trinexapac, which accounted for 93-98%AR after 24 hours. Trinexapac was subsequently mineralised to CO_2. Other extracted resolved labelled breakdown products accounted for <9%AR at all sampling times, except for the carbonyl label for a sandy loam soil (day 10 sample), when the origin of the TLC plate (polar fraction, probably multi component) accounted for 11% AR. Mineralisation measured as volatile CO_2 was 58%AR (carboxymethylene label), 56%AR (ring label) and 49%AR (carbonyl label) after 90 days. These values for radioactivity not extracted by methanol/water/oxalic acid and oxalic acid/dimethylformamide were 6.8%AR, 18%AR and 11%AR respectively again after 90 days.

Under sterile soil conditions the conversion of trinexapac-ethyl to trinexapac was significantly reduced, indicating the rapid conversion is mediated by microbial activity. This is consistent with the results of aqueous hydrolysis experiments carried out under acidic and neutral conditions.

Under anaerobic conditions (studies dosed with ring or carbonyl labelled trinexapac-ethyl), trinexapac was also the major transformation product, with formation rates of *ca.* 58%AR at the first day 0 sampling time and representing a maximum of 69% AR at 30 days. Mineralisation and formation of unextracted residues was significantly reduced compared to aerobic conditions. Cumulative volatiles

reached 3% of AR after 63 days. Unextracted residues were 3 to 8% of AR after 63 days. 22-25% of AR was trinexapac in the overlying water in the study after 63 days. Under anaerobic conditions formation of trinexapac from trinexapac-ethyl will still occur but subsequent degradation of trinexapac is reduced compared to that observed under aerobic conditions.

The potential for photolytic breakdown of labelled trinexapac-ethyl at the soil surface was tested in a sandy loam soil under artificial light. Degradation was faster in the dark control samples than in the irradiated samples, possibly due to the lower soil moisture content caused by heat from the light source. No novel breakdown products were identified in irradiated samples. Photolysis at the soil surface is therefore not expected to be a significant process contributing to the breakdown of trinexapac-ethyl or trinexapac.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

In the one soil tested where results were considered reliable, single first order aerobic laboratory DT_{50} for the degradation of trinexapac-ethyl normalised to 20°C were 0.31-0.34 days. $^{14}CO_2$ production was used by the RMS to estimate the single first order aerobic laboratory DT_{50} of trinexapac (to overcome deficiencies in the extraction methodologies in some laboratory studies). It should be noted that this is not a generally accepted method, but can be used in this case as only one significant metabolite (trinexapac) was shown to be contributing to CO_2 formation. The degradation rates estimated in the different laboratory experiments are summarised in Table 4.1.

Table 4.1 Single first order DT50 estimates calculated from results of laboratory aerobic soil degradation studies

Study	Substance	Soil	Dose [mg as/kg]	Dose rate [kg as/ha]	T [°C]	pH	DT_{50} [d]	DT_{50} 20 °C [d]	
C	[^{14}C-ring]-trinexapac-ethyl	sandy loam	10	7.5	25	7.5	0.23	0.34	average 0.31
C	[^{14}C-carbonyl] trinexapac-ethyl	sandy loam	10	7.5	25	7.5	0.19	0.28	
D	1,2,6-^{14}C- trinexapac-ethyl	sandy loam	10	7.5	25	7.5	0.13	0.19	average 0.34
D	1,2,6-^{14}C- trinexapac-ethyl	sandy loam	10	7.5	25	7.5	0.34	0.48	
A	trinexapac[1]	loam	2.78	2.08	20	7.2		7.0 [4]	
A	trinexapac[1]	sandy loam	2.78	2.08	20	7.4		8.8 [4]	
A	trinexapac[1]	loamy sand	2.78	2.08	20	5.6		10.3 [4]	

Study	Substance	Soil	Dose [mg as/kg]	Dose rate [kg as/ha]	T [°C]	pH	DT_{50} [d]	DT_{50} 20 °C [d]	
B	trinexapac[3]	silt loam	0.53	0.4	20	7.4		5.3 [4]	
B	trinexapac[3]	silt loam	0.11	0.08	20	7.4		2.5 [4]	
B	trinexapac[3]	silt loam	0.53	0.4	10	7.4	6.3 [4]		
C	trinexapac[3]	sandy loam	10	7.5	25	7.5	20.5	30.6	average 35.1
C	trinexapac[2]	sandy loam	10	7.5	25	7.5	26.5	39.5	
D	trinexapac[3]	sandy loam	10	7.5	25	7.5	25.6	38.1	

1: applied as ^{14}C-hydroxymethylene labelled trinexapac-ethyl
2: applied as ^{14}C-carbonyl-labelled trinexapac-ethyl
3: applied as ^{14}C-ring-labelled trinexapac-ethyl
4: estimated from CO_2 formation

The average DT_{50}s at 20 °C were 0.335 days for trinexapac-ethyl (average of 0.31 and 0.34 days) and 11.7 days for trinexapac (average of 7.0, 8.8, 10.3, 5.3, 2.5 and 36.5; DT_{50}-values of Study c and d, 35.1 and 38.1, are averaged to one DT_{50} of 36.5 days because the same soil is used under the same conditions).

According to the data requirements, information on the rate of degradation in another 3 soils should be required for trinexapac-ethyl. However the rapporteur considered that 'as trinexapac-ethyl is a precursor that rapidly transforms to trinexapac, conversion might be expected to be similarly fast in different soil types'. In view of this, the rapporteur proposed a DT_{50} of 1 day for trinexapac-ethyl was used as worst case estimate and further information from experiments with additional soils dosed with trinexapac-ethyl were not necessary. No Member State expert disagreed with this proposal. The EFSA also accepts the use of a 1 day DT_{50} as being a reasonable conservative estimate but it may not necessarily represent a worst case. However in this case, as sufficient DT_{50} data are available for trinexapac and because the DT_{50}s quoted for trinexapac, are in fact DT_{50}s for all mineralised components (so includes trinexapac-ethyl), the EFSA supports the use of an estimated trinexapac-ethyl DT_{50} of 1 day to calculate the exposure concentrations used for risk assessment.

Under anaerobic conditions the rate of transformation from trinexapac-ethyl to trinexapac was rapid (trinexapac was 58%AR at the day 0, sampling time), subsequent degradation of trinexapac was limited, meaningful DT50 could not be estimated due to the limited number of samples taken and the absence of any clear pattern of decline for trinexapac from these samples.

Field studies have been carried out in Switzerland, Germany and France. All studies suffered from some deficiencies in design or reporting of findings. From one study in Germany at 3 different trial sites, indicative single first order DT_{50} values for of 6.9, 16 and 21days could be obtained for the dissipation of trinexapac under field conditions. Because of the deficiencies identified in these field studies, results of laboratory studies were used in subsequent exposure assessments. Field dissipation

studies are not a formal requirement for this substance as laboratory first order DT50 values were less than the trigger defined in the annex II data requirements of 60 days.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

In laboratory batch adsorption studies the trinexapac-ethyl K_{foc} values determined were : 629 L/kg, 1/n=0.92 (pH5.9 clay), 284 L/kg, 1/n=1.01 (pH6.5 sand) 143 L/kg, 1/n=0.92 (pH6.7 loam) 60 L/kg, 1/n=0.92 (pH7.5 sandy loam). These values for trinexapac were 581 L/kg, 1/n=0.92 (pH5.9 clay), 609 L/kg, 1/n=0.85 (pH6.5 sand) 328 L/kg, 1/n=0.9 (pH6.7 loam) 145 L/kg, 1/n=0.9 (pH7.5 sandy loam). Adsorption for both compounds would appear to be pH-dependent (lowest adsorption at high pH). In view of the pKa of trinexapac-ethyl and trinexapac, adsorption experiments should have been performed with soils of pH >7. Therefore, the lowest K_{foc}-values from the pH7.5 soil of 60 L/kg (trinexapac-ethyl) and 145 L/kg (trinexapac) were used for exposure assessment.

Laboratory soil column leaching studies were performed with aged residues of trinexapac-ethyl in two soils (loamy sand, organic matter 2%, pH 7.2 and silty loam, organic matter 3.6%, pH 7.7). K_{oc} could not be derived from this study, but minimal leaching of trinexapac-ethyl, trinexapac or other metabolites was observed (radioactivity in leachate was 0.1-0.4% of that applied to the soil columns before leaching).

A long-term accumulation and leaching study was performed in which soil water (sampled using suction cup samplers) at 2 and 2.5 m depth was analysed for trinexapac over 4 years when trinexapac-ethyl was applied in May at 125 g as/ha (**lower than the representative uses applied for**) per year to wheat or barley crops growing on a silt loam soil (2.5-3% organic matter, pH 7.7-7.9) at Vouvray Switzerland. Groundwater samples contained no residues (>0.05µg/L) of trinexapac, except for two occasions in the 4th year when 0.13-0.14 µg/L was found on the day of application and 0.06-0.07 µg/L after 14 days from samplers at 2.5m depth. At the same sampling times soil water concentrations from samplers at 2m depth were <0.05µg/L. These findings probably occurred as a result of preferential flow processes that are subject to significant spatial heterogeneity. Even considering these positive detections at individual sampling times at some suction cup samplers, annual average soil water concentrations would have been less than 0.1µg/L.

In another two year field leaching experiment trinexapac-ethyl was applied at a rate of 125 g as/ha (**lower than the representative uses applied for**) per year in May, to wheat growing on a loamy sand soil (1.8% organic matter, pH topsoil 7.6 below 30cm>8) at Vouvray Switzerland. Trinexapac was not detected in soil water (sampled using suction cup samplers) at any time during the 497-day sampling period above the detection limit of 0.05 µg/L at 0.8 and 1.2 m depths.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis

Three hydrolysis studies were performed. The results are presented in Table 4.2.

Table 4.2 Results of the hydrolysis studies

Test substance	Dose [µg/L]	pH	Experiment temperature [°C]	DT_{50} 20°C [d] Single first order	Major metabolite	Formation rate [% of AR]
^{14}C-labelled trinexapac-ethyl	10	5	25	∞		-
		7	25	∞		-
		9	25	11	trinexapac	88.2 (30 d)
^{14}C-labelled trinexapac-ethyl	10	5	25	767	trinexapac	18 (179 d)
					monoethyl ester of	13 (179 d)
		7	25	1167	tricarballylic acid	16 (179 d)
					trinexapac	
^{14}C-trinexapac	700	4	50	47		
		5	50	71		
		7	50	450		
		9	50	∞		
		4	20	79	2-(4-cyclopropyl-2,4-dioxobutyl)-succinic acid	31 (91 d)
						25 (91d)
		4	44	23	unknown	
		5	20	74	2-(4-cyclopropyl-2,4-dioxobutyl)-succinic acid	22 (91 d)
						35 (91 d)
		5	44	22	unknown	

Three studies on photodegradation in water were performed.

In the first study, ^{14}C-labelled trinexapac-ethyl was irradiated with artificial light (290-880 nm) at a nominal concentration of 2 mg/L. The single first order DT_{50} of trinexapac-ethyl was 21.3 equivalent days of midsummer sunlight at 40°N and 20°C. Minor metabolites were trinexapac (formed at 5.3% of AR at day 10), 2-(4-cyclopropyl-2,4-dioxobutyl)-succinic acid (formed at 6.5% of AR at day 15) and three other unidentified metabolites (formed at 8.9, 9.7 and 9.4% of AR after 15 days).

In a second study, samples with trinexapac-ethyl were irradiated with artificial light (290-360 nm). The single first order DT_{50} value, calculated with the program GC-SOLAR, was 8.5 equivalent days of sunlight at 50°N (mean of a year), determined at pH 7 and 22°C .

In a third study, trinexapac solutions were irradiated with artificial light (290-360). The single first order DT_{50} value, calculated with the program GC-SOLAR, was 20.2 equivalent days of sunlight at 50°N (mean of a year), determined at pH 7 and 22°C.

Biodegradability of trinexapac-ethyl was tested in a ready biodegradability study with a sewage sludge inoculum. Trinexapac-ethyl was classified as not readily biodegradable.

Degradation in two laboratory water-sediment systems was studied (20°C): one with Rhine water (pH 8.2) and sand sediment (1.8% organic matter), and another with pond water (pH 8.5) and sandy clay loam sediment (2.7% organic matter). The systems were dosed with ^{14}C-ring labelled trinexapac-ethyl. For trinexapac-ethyl, the single first order DT_{50}, water were 3.4 and 4.9 days (average 4.2 days) and the single first order DT_{50}, whole system were 3.8 and 5.2 days (average 4.5 days). Trinexapac was formed in both systems, the maximum formation rate in water was 48 and 64% in the pond and river systems, respectively. The single first order DT_{50}, water for trinexapac were 10.8 and 19.1 days (average 15.0 days) and the single first order DT_{50}, whole system were 9.9 and 17.8 days (average 13.9 days). Another three minor breakdown products were resolved by chromatography but not identified. The sum of these three components accounted for a maximum of 9% AR. At all sampling times trinexapac-ethyl and trinexapac in sediment accounted for < 7%AR. Partitioning to sediment might be greater than this under more acidic test conditions, due to the pH dependence of adsorption discussed at section 4.1.3. Mineralisation was maximally 73% of AR after 83 days in the river system and 59% of AR after 111 days in the pond system. Sediment residues not extracted by acetonitrile/acetic acid and Soxhlet with methanol were maximally 26 and 39% of AR after 55 days in the river and pond systems respectively.

The exposure assessment to surface water (calculation of predicted environmental concentrations (PEC) in surface water) has been appropriately completed for the spray drift route of entry assuming single first order DT_{50} surface water of 4.9 days for trinexapac-ethyl and 19.1 days for trinexapac (longest DT_{50} from dark laboratory sediment water studies). $PEC_{sediment}$ were not calculated and are not required to complete the risk assessment, due to the low toxicity to aquatic invertebrates (see section 5.2). The runoff and drainage routes of entry to surface water have not been considered in the available exposure and risk assessment. For the representative uses evaluated these routes of entry to surface water cannot be excluded. These routes of entry to surface water should be considered by Member States when granting product authorisations.

The sterile hydrolysis studies where trinexapac was dosed have indicated that under acidic conditions in aqueous systems (study conditions were pH 5, 20°C) the major metabolite 2-(4-cyclopropyl2,4-dioxobutyl)-succinic acid and an unidentified breakdown product may be formed. (These were >10%AR from 35 to 91 days in this sterile study). There is no experimental evidence that these hydrolysis products formed under acidic sterile conditions would not be formed in major amounts under acidic natural conditions where micro-organisms are responsible for degradation (both the available natural sediment water systems studied were alkaline). Information from the applicant regarding this question was included in the addendum to the DAR dated January 2005. This issue was discussed at the experts' meeting. The experts concluded that satisfactory aquatic exposure assessments have been completed with the available data for neutral or alkaline surface water systems, but that based on the available data there was the possibility that the available risk

assessment may not fully cover more acidic surface water systems. Acidic surface water bodies adjacent to agricultural fields are not common across the EU and are restricted to specific areas (for example. where there are peaty soils). The coincidence of use in acidic situations and amenity grassland may be reasonably prevalent in some Member States. Therefore in Member States where these conditions occur, it would be appropriate for additional data and risk assessments to be requested.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

PECgroundwater values were calculated using FOCUSPEARL. The nine available FOCUS-scenarios were used to simulate use on spring cereals, winter cereals and grassland. Application to the soil surface was simulated for a single annual application of 0.2 kg as/ha in cereals on April 1st. Five applications each year of 0.4 kg as/ha with a 30 day interval were simulated for grassland on April 1st, May 1st, June 1st, July 1st and August 1st. A fraction reaching the soil of 50% for cereals and 10% for grass was assumed as recommended by FOCUS. The first order DT_{50} value for biodegradation in soil of 1 day at 20 °C was used for trinexapac-ethyl. Sorption of trinexapac-ethyl is dependent on pH, with K_{fom}s ranging from 35 L/kg at pH 7.5 to 370 L/kg at pH 5.9. To cover the worst case the lowest K_{fom} of 35 L/kg (1/n=0.9 default) was used as input, assuming that this value represents a worst case at all pH levels.

PECgroundwater values for the major soil metabolite trinexapac were calculated applying the same method. The average laboratory first order DT_{50} for biodegradation of trinexapac in soil of 11.7 days at 20 °C was used. K_{fom} values for the metabolite trinexapac were again dependant on pH. They ranged from 85 L/kg at pH 7.5 to 358 L/kg at pH 6.5. To cover the worst case lowest K_{fom} of 86 L/kg (1/n=0.9 default) was used. The 'application rate' of the metabolite was calculated from the application rates of trinexapac-ethyl, corrected for the highest formation rate observed in the aerobic degradation studies of 98%, and the relative molar mass of 0.89.

The predicted annual average concentrations of trinexapac-ethyl and trinexapac in leachate leaving the top 1m soil layer calculated by PEARL, as defined by FOCUS as representing shallow vulnerable groundwater were <0.001 µg/L in all scenarios for both cereal crops and amenity grassland.

As already discussed at section 4.1.3, information is available from field leaching studies that does not contradict the outcome of the FOCUS groundwater modelling that was carried out to reflect the representative uses selected by the applicant. However it is important to note that the application rate used in these field leaching studies (125g a.s./ha/year) was not high enough to enable these experiments to support any of the representative uses selected by the applicant (where application rates are 200-2000g a.s./ha/year).

The available information indicates that following good agricultural practice for the representative uses evaluated, the potential for contamination of vulnerable groundwater by trinexapac-ethyl and trinexapac is minimal.

4.3. FATE AND BEHAVIOUR IN AIR

Trinexapac-ethyl has a vapour pressure of 2.16×10^{-3} Pa, and a Henry's law constant of 5.4×10^{-4} Pa•m^3•mol^{-1}, or in dimensionless form $2.15 \bullet 10^{-5}$. Based on the experimental data submitted it is considered that significant volatilisation of trinexapac-ethyl is unlikely to occur from soil. From leaves, measured volatilisation amounted to 10-15% of that applied within 24 hours. The atmospheric indirect photolytic oxidation half-life for trinexapac-ethyl was estimated by the Atkinson method of calculation to be 0.05-0.17 days (1.29 –4.08 h hours) and 0.134-0.162 d (3.2-3.9 h) for trinexapac. The trinexapac-ethyl that volatilises from plant surfaces, would therefore not be expected to be subject to long range transport in the atmosphere.

5. Ecotoxicology

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk assessment was conducted according to the latest Guidance Document on Birds and Mammals (SANCO/4145/2000) and resulted in TERs above the relevant Annex VI trigger values for the acute, short-term and long-term risk to birds and mammals for the representative use in cereals (early and late growth stages). The Annex VI trigger value of 5 for the long-term risk was not met for the representative use in amenity grass and turf in a first tier risk assessment for insectivorous birds and for herbivorous mammals. The refined long term risk assessment for insectivorous birds and herbivorous mammals from the notifier was discussed at the EPCO experts' meeting (EPCO 17) in January/February 2005. The refinement of long term risk to insectivorous birds was based on the assumption that grassland and turf are comparable to very early growth stages of cereals where large insects predominate and thus allowing the application of the lower RUD value for large insects. This assumption was not supported by data. The meeting agreed to the assessment of the RMS that it is not justified to use the lower RUD value for large insects since grassland is a much more developed ecosystem compared to arable land with lots of bare ground in early growth stages of cereals and therefore no reason to assume that small insects would not occur in grassland. The refined risk assessment for herbivorous mammals was considered as not acceptable by the RMS because of the following reasons: The DT_{50} of trinexapac-ethyl used for the refinement of MAF and f_{twa} is based on studies which were either not included in the dossier or not accepted because essential raw data were not reported. The DT_{50} for the metabolite trinexapac-acid was not estimated and not used in the refined chronic exposure calculation. The assessment of the RMS was confirmed by the meeting. Therefore a high chronic risk to insectivorous birds and to herbivorous mammals from uptake of contaminated food cannot be excluded for the representative use in amenity grass and turf based on a first tier risk assessment.

The risk to birds and mammals from uptake of contaminated drinking water was calculated by the RMS based on PEC surface water concentrations. Therefore EFSA provided TER calculations in an addendum based on the 5 fold dilution of the sprayed solution according to the "Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC"

(Sanco/4145/2000 of 25. September 2002). The acute and short-term risk to birds and the acute risk to mammals for the representative use in cereals is considered to be low. The first tier TER values for the long-term risk to birds and mammals is below the Annex VI trigger value indicating a high long term risk to birds and mammals from uptake of contaminated drinking water. A refined risk assessment is necessary to address the long term risk to birds and mammals from the representative use in cereals.

For the representative use in amenity grassland the TER calculations resulted in values which were above the Annex VI trigger values for the acute risk. The TER values for the long term risk to birds and mammals were below the Annex VI trigger value of 5 and the TER for the short term risk to birds was below the Annex VI trigger value of 10 when the formulation is applied with the minimum amount of water (200 L/ha). Therefore a high short term risk for birds and a high long term risk to birds and mammals from uptake of contaminated drinking water are shown in a first tier risk assessment for the representative use in amenity grass and turf.

Further risk refinement steps are required for the representative use in amenity grass/turf to address the long term risk to insectivorous birds and herbivorous mammals from the uptake of contaminated food and the long term risk to birds and mammals and the short term risk to birds from uptake of contaminated drinking water.

Trinexapac (CGA-179500) was the major metabolite in soil, water and plants. Trinexapac is found in hens and mammals as a metabolite in studies with the parent trinexapac-ethyl (CGA-163935). Therefore it is concluded that the toxicity of trinexapac is covered from the studies with trinexapac-ethyl. The risk of secondary poisoning of trinexapac is considered to be low since the log P_{OW} of trinexapac-ethyl is < 3 and trinexapac is more polar than trinexapac-ethyl.

A high risk from contaminated drinking water was shown from a first tier risk assessment based on worst case assumptions (e.g. the total daily water demand is taken from leaf axils or puddles which are contaminated by the sprayed solutions). Some MSs are of the opinion that long-term exposure to contaminated drinking water can be excluded and hence regard the long-term risk from uptake of contaminated drinking water as low. However, no common agreement among MSs exists yet on the potential long-term risk from contaminated drinking water. It is planned to discuss the risk to birds and mammals from uptake of contaminated drinking water as a general point in an EPCO expert meeting.

The metabolites CGA 275537, CGA 313458 and CGA 329773 were present in plants at very low levels. Acute toxicity data on mammals were available and a risk assessment was conducted for the metabolites CGA 275537 and CGA 329773. No risk assessment was conducted for the metabolite CGA 313458 because it was not present in grass or wheat. The acute TER values were above the relevant Annex VI trigger value of 10 indicating a low acute risk from the metabolites CGA 275537 and CGA 329773 to mammals from the intended use in cereals and amenity grass/turf. Because of the

low acute toxicity of the metabolites and because exposure to the metabolites will be less than that of trinexapac-ethyl, the long term risk from CGA 275537 and CGA 329773 is assumed to be low. No toxicity data with the metabolites CGA 275537 and CGA 329773 are available for birds. The RMS considered the risk from CGA 275537 and CGA 329773 to birds to be low. This assumption was based on the observation that the toxicity of trinexapac-ethyl for mammals is comparable to that for birds. Therefore it was deemed acceptable to extrapolate the conclusion of the risk assessment for plant metabolites for mammals to birds. The risk assessment for the plant metabolites was discussed at the EPCO experts` meeting. The EPCO experts` meeting agreed on the risk assessment for the plant metabolites presented by the RMS.

5.2. RISK TO AQUATIC ORGANISMS

Trinexapac-ethyl was tested in acute studies with fish (*Oncorhynchus mykiss, Lepomis macrochirus, Cyprinus carpio, Ictalurus punctatus*) and aquatic invertebrates (*Daphnia magna*). Chronic studies with trinexapac-ethyl were conducted with fish and algae (*Pseudokirchnerilla subcapitata, Anabaena flos-aquae)* and higher aquatic plants (*Lemna gibba*). Acute data on fish and *Daphnia magna* were also available for the formulation and trinexapac. Chronic studies with the formulation and trinexapac were conducted with algae and *Lemna gibba*. A chronic test with *Daphnia magna* was conducted with the formulation but not with trinexapac. However the acute toxicity of trinexapac (48 h EC_{50} >100 mg/L) to daphnids is low and the TER values for the acute risk to daphnids are far above the Annex VI trigger value. Therefore it is assumed that the chronic risk from trinexapac to aquatic invertebrates is low and no chronic studies with *Daphnia magna* are required. No chronic data with the formulation and trinexapac were available for fish. Since the acute toxicity of trinexapac to fish was less than that of trinexapac-ethyl and the TER values for the acute risk are far above the Annex VI trigger values it is assumed that the chronic risk to fish from trinexapac is low. All TER values for the tested species were calculated to be well above the relevant Annex VI trigger values. Therefore the risk to aquatic organisms from the representative uses in cereals and amenity grass/turf is considered to be low.

The bioconcentration factor for trinexapac-ethyl was determined to be 6 in a bioaccumulation test with *Lepomis macrochirus* (whole body at steady state). The BCF of 6 is below the relevant Annex VI trigger value of 100 for not readily biodegradable substances. Therefore the risk from bioconcentration of trinexapac-ethyl is considered to be low. Since trinexapac is more polar than trinexapac-ethyl it is considered as unlikely that the BCF of trinexapac would exceed the Annex VI trigger value.

Trinexapac-ethyl and trinexapac degraded rapidly in the water phase of the water-sediment system. Although trinexapac-ethyl, trinexapac nor any other metabolite was found in the sediment in amounts of >10 %AR in the available sediment water studies, in acidic aquatic systems partitioning to sediment might be expected to be greater (as adsorption is increased at lower pH, see section 4.1.3). However testing with sediment dwelling organisms was not considered necessary due to the low toxicity to daphnia (48 h EC50 > 100 mg trinexapac/L, 21 d NOEC = 2.4 mg trinexapac-ethyl /L), so the risk to sediment dwelling organisms is considered to be low.

5.3. RISK TO BEES

The acute oral and contact toxicity was tested with trinexapac-ethyl and the formulation. The HQ values calculated for the representative uses in cereals and amenity grass/turf were well below the Annex VI trigger value of 50 indicating al low risk to honeybees.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Laboratory tests were conducted on sprayed sand with *Aleochara bilineata, Poecilus cupreus* and on glass plates with *Coccinella septempunctata* at dose levels of 0.4, 0.2 and 0.016 kg a.s./ha. Effects of >30 % were observed for *Coccinella septempunctata*. Additionally a risk assessment according to ESCORT2 was conducted. The LR50 values were determined as 0.144 kg a.s./ha and 0.197 kg a.s./ha for *Aphidius rhopalosiphi* and *Typhlodromus pyri*. The corresponding HQ values for the off-field risk were below the Annex VI trigger value of 2 for both representative uses. The HQ value of 2 was exceeded for both species for the in-field risk from the representative use in amenity grass/turf. On the basis of the first-tier testing a high risk was shown for *Coccinella septempunctata* and a high in-field risk was shown for *Aphidius rhopalosiphi* and *Typhlodromus pyri* from the representative use in amenity grass/turf. Higher tier tests (extended laboratory studies) were performed with *Aphidius rhopalosiphi, Typhlodromus pyri, Chrysoperla carnea* and *Coccinella septempunctata*. No effects of > 50% were observed up to the dose rate of 0.4 kg a.s./ha. The highest tested dose in the tests with *Typhlodromus pyri* and *Aphidius rhopalosiphi* were equivalent to 1.6 kg a.s./ha and 4.05 kg a.s./ha. No effects of > 50% were observed. The tested dose rates are considered to be sufficient based on a multiple application factor (MAF) of 1.14. The default MAF value of 3 given in ESCORT2 is based on a ratio of DT_{50} : application interval of 2.3 : 1. This would mean that with a spray interval of 30 days the DT_{50} in plants would be 69 days. The RMS argued that this is unrealistic and the MAF was calculated as in the birds and mammals risk assessment based on a default DT_{50} value of 10 leading to a MAF of 1.14. The dose applied in the extended lab study with *Coccinella septempunctata* was to low (0.4 kg a.s./ha instead of 0.4 kg a.s./ha x 1.14). The EPCO expert meeting agreed that the dose rate was slightly too low but the effects seen at this dose were <30 % and therefore the risk to *Coccinella septempunctata* was considered to be low.

5.5. RISK TO EARTHWORMS

The acute toxicity of trinexapac-ethyl, trinexapac and the formulation were tested with earthworms. The test with the technical trinexapac-ethyl was assessed as not valid and therefore the toxicity data with the formulated trinexapac-ethyl were used in the risk assessment. The TER values for trinexapac and formulated trinexapac-ethyl were two orders of magnitude above the relevant Annex VI trigger value of 10. This indicates a low acute risk to earthworms from the representative use in cereals and amenity grass/turf. The DT_{90} value for trinexapac-ethyl in soil was extrapolated from the laboratory studies to be <1 day, therefore no chronic testing is required for trinexapac-ethyl. No DT_{90} value is given for trinexapac-acid. The unreliable indicative DT_{50} for trinexapac-acid from field studies were in the range of 6.9 – 21 days (DT_{90} 23-70 days) and the longest DT_{50} value from the lab studies was 36.5 days and the DT_{90} was 121 days. According to the Guidance Document on Terrestrial

Ecotoxicology a case by case decision should be made on the necessity of chronic testing if the DT_{90} is between 100 and 365 days and/or the number of applications is between 3 and 6. Taking into account the very low acute risk (TER > 10000 for amenity grass/turf) chronic testing with trinexapac-acid is considered as not necessary.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

No data on the risk to other soil non-target organisms were available. According to the Guidance Document on Terrestrial Ecotoxicology (17 Oct. 2002) testing is required if the DT_{90} of the active substance or its metabolites in soil is between 100 and 365 days and the standard HQ value for non target arthropods is >2. The DT_{90} of trinexapac-ethyl was extrapolated from laboratory studies to be less than 1 day. However, the DT_{90} range for trinexapac from the relied on laboratory studies was 8.3-121 days. The field studies (assessed by the RMS as unreliable indicative values) are in the range of 23 – 70 days. Therefore it cannot be excluded that the DT_{90} could be above 100 days under field conditions. The standard HQ values for *Typhlodromus pyri* and *Aphidius rhopalosiphi* were >2 for the representative use in amenity grass/turf. Therefore EFSA proposes a confirmatory data requirement to address the risk to other soil non-target organisms from the use in amenity grass/turf.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects on soil micro-organisms were tested in carbon-mineralisation and nitrification studies with trinexapac-ethyl and the formulation (A7725M EC 250). Trinexapac-ethyl technical was tested at dose rates equivalent to 0.86 and 8.6 kg trinexapac-ethyl/ha and the formulated trinexapac-ethyl was tested at dose rates equivalent to 0.4 and 4 kg trinexapac-ethyl/ha. No effects exceeding the critical Annex VI trigger level of ±25 % were observed in the tests with trinexapac-ethyl. Maximal effects of > ±25% were observed on the first day of the carbon mineralization test and after 8 days in the nitrification test. No effects exceeding the relevant trigger value of ±25 % were detected at the end of testing after 57 days (carbon mineralization) and 28 days (nitrification). Therefore the risk to soil non-target micro-organisms from the representative uses in cereals and amenity grass/turf is considered to be low. The RMS provided in the addendum (Jan. 2005) an argumentation with regard to testing of trinexapac with soil non-target micro-organisms. Trinexapac was the major degradation product in the aerobic soil degradation studies with formation rates of max. 98 % after 1 day (25 °C). Therefore it is highly unlikely that trinexapac would not have been formed in the soil-micro-organism study and a separate study with trinexapac is considered as not necessary. The EPCO experts meeting agreed to the argument of the RMS.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Three studies with trinexapac-ethyl and two with the formulation were conducted to detect effects on non target plants (soybean, lettuce, carrot, tomato, cucumber, cabbage, oat, ryegrass, corn and onion). New TER calculations were presented in the addendum of Jan. 2005, taking into account the effect of multiple applications in amenity grass/turf and the ecological relevance of radicle elongation. A worst case exposure rate of 5 x 0.4 kg trinexapac-ethyl/ha and spray drift at a distance of 1m (90^{th} percentile

2.77%) were used for the TER calculations. The resulting TERs for growth and emergence (EC_{50} >0.405 kg trinexapac-ethyl/ha) were above the Annex VI trigger value of 5 indicating a low risk for non-target plants from the representative uses in cereals and amenity grass/turf. An argumentation was presented in the addendum why the parameter radicle elongation (EC_{50} <0.02 kg trinexapac-ethyl/ha) was considered as not ecotoxicologically relevant and consequently not used in the risk assessment. This argumentation and the risk assessment in the addendum were discussed in the EPCO experts` meeting. The meeting agreed that the risk to non-target plants is low with regard to the representative uses in cereals and amenity grass/turf.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No inhibitory effects of trinexapac-ethyl were observed in the test with activated sewage sludge at concentrations ranging from 1 to 100 mg/L. Therefore the risk to biological methods of sewage treatment plants is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: trinexapac-ethyl and trinexapac and its salts

Definition for monitoring: trinexapac and its salts

Water

Ground water

Definitions for risk assessment: trinexapac-ethyl and trinexapac and its salts

Definition for monitoring: trinexapac and its salts

Surface water

Definitions for risk assessment: water phase trinexapac-ethyl and trinexapac and its salts

sediment phase trinexapac and its salts

Definition for monitoring: trinexapac and its salts

Air

Definition for risk assessment: trinexapac-ethyl

Definition for monitoring: trinexapac-ethyl

Food of plant origin

Definitions for risk assessment: trinexapac and its salts (cereals only)

Definitions for monitoring: trinexapac and its salts (cereals only)

Food of animal origin

Definitions for risk assessment: trinexapac and its salts

Definitions for monitoring: trinexapac and its salts

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Trinexapac-ethyl	Very low persistent (DT_{50lab} (20 ºC) < 1d)	See 5.5, 5.6 and 5.7
Trinexapac	Low to moderate persistent (DT_{50lab} (20 º C) = 2.5 – 39.5 d)	The risk of trinexapac to earthworms is low

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth FOCUS for the representative uses	Pesticidal activity	Toxicological activity	Ecotoxicological activity
Trinexapac-ethyl	High to low mobility (pH dependent, higher mobility at higher pH)	FOCUS modelling: No	Yes	Yes	See 5.2
Trinexapac	High to low mobility (pH dependent, higher mobility at higher pH)	FOCUS modelling: No	Yes	Yes	Trinexapac is less toxic to aquatic organisms compared to trinexapac-ethyl except aquatic plants. The risk from trinexapac to aquatic organisms is low.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Trinexapac-ethyl (water phase only)	See 5.2
Trinexapac (water phase and sediment phase)	Trinexapac is less toxic to aquatic organisms compared to trinexapac-ethyl except aquatic plants. The risk from trinexapac to aquatic organisms is low.

Air

Compound (name and/or code)	Toxicology
Trinexapac-ethyl	Not acutely toxic via inhalation. No data available for repeated exposures.

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Data to confirm the identity of the impurities CGA281145 and CGA264326 revealed by chemical analysis must be provided (date of submission unknown, data gap identified by RMS in the DAR. The submitted new study was not accepted by RMS and the experts' meeting, refer to chapter 1).
- A refined risk assessment for birds and mammals (according to SANCO/4145/2000) is required for the representative use in amenity grass/turf (date of submission is unknown, data requirement identified by the RMS in the DAR, the submitted refined risk assessment was not accepted in the experts' meeting, refer to chapter 5.1).
- A refined risk assessment is required to address the long term risk to birds and mammals from uptake of contaminated drinking water for the representative use in cereals and to address the short-term and long-term risk to birds and the long-term risk to mammals in amenity grass/turf (proposed by EFSA, not peer reviewed, date of submission is unknown, refer to point 5.1).
- A confirmatory data requirement to address the risk to other soil non-target organisms from the representative use in amenity grass/turf is proposed by EFSA. This data gap was not discussed at an experts` meeting (date of submission is unknown, refer to point 5.6).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as plant growth regulator, as proposed by the applicant, which comprises foliar spraying to cereals, amenity turf and amenity grassland at application rate of 0.2 kg trinexapac-ethyl per hectare in cereals and 0.4 kg in amenity turf and grassland. Trinexapac and trinexapac-ethyl, respectively, can be used only as plant growth regulator.

Due to the fact that the ethyl ester, a variant of trinexapac, is used in the formulated product, it should be noted that the evaluated data belong to the variant trinexapac-ethyl, unless otherwise specified.

The representative formulated product for the evaluation was "Moddus 250 EC" ("A-7725 M"), an emulsifiable concentrate (EC), registered in some EU Member States.

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Sufficient analytical method as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

The information on mammalian toxicology indicate trinexapac-ethyl is rapidly and nearly completed absorbed. Main metabolites identified were trinexapac, CGA 275537, CGA 313458 and CGA

329773. The acute toxicity during oral, dermal and inhalation exposure is low. No studies have been submitted for inhalatory exposure. It is not a skin or an eye irritant or a skin sensitizer. Main effects observed during short term exposure were reduced body weight and food consumption; the relevant oral NOAEL is 34 mg/kg bw/day from the 90-day rat study. There is no genotoxic or carcinogenic potential. The incidence of neoplastic lesions in the stomach, urinary bladder and thyroid in rat, was considered incidental and not treatment-related.

There were no direct effects on reproductive performance or fertility observed.

Metabolites CGA 275537, CGA 313458 and CGA 329773 have a low acute oral toxicity and they are negative at the Ames test. No toxicological data is available for metabolite CGA 113745 found in a goat metabolism study and in the hydrolysis study. However, the toxicological studies with CGA 158377 are thought to reflect the properties of CGA 113745 but have still to be submitted and to be evaluated.

The ADI is 0.32 mg/kg bw/day based on the NOAEL from the 1-year study in dog; the AOEL is 0.34 mg/kg bw/day, based on the NOAEL of 34 mg/kg bw/day from the 90-day rat study, with a SF of 100.

The allocation of the ARfD was considered not necessary due to the low acute toxicity of treinexapac-ethyl. A dermal absorption of 10% was considered for both undiluted and spray preparation. The estimated operator exposure according to the German model and UK-POEM is below the AOEL with and without PPE. No data available for re-entry activities in amenity turf and amenity grassland.

Following application of trinexapac-ethyl to wheat, rice and rape plants by foliar application trinexapac was the major residue found at harvest in straw and in grain or seeds, respectively, accounting for about 90% and 60% of the total residue, respectively. Other metabolites were present at very low levels. It is noted that for one non-rat metabolite CGA 351210, found in rape matrices, no toxicity assessment has been provided; however, rape is not a representative use within the evaluation process for Annex I inclusion of trinexapac. In processing procedures trinexapac-ethyl can be considered as hydrolytically stable whereas trinexapac had degraded by almost 50%. The toxicological relevance of one of the major degradation products, CGA 113745, was not further assessed, since the chronic consumer exposure to trinexapac residues is low and data on processing are not mandatory in that case. No significant residue levels are expected in rotational crops following application of trinexapac-ethyl according to Good Agricultural Practice (GAP).

Fed to ruminants and poultry, trinexapac-ethyl was intensively metabolised resulting in a comparable pattern to that observed in rat metabolism, in which trinexapac is the major and only residue component of significance. In a feeding study levels of trinexapac in edible animal matrices were all found to be below the limit of quantification (LOQ).

The chronic dietary exposure assessment for consumers based on the representative GAP on cereals indicated that none of the considered consumer subgroups was exposed above 1% of the proposed ADI. Due to the low acute toxicity of trinexapac-ethyl the allocation of an ARfD, and hence an acute consumer risk assessment was not considered necessary.

The information on fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment that covers a large proportion of the EU where the representative uses on cereals and amenity grassland occur. Member States may need to require further information to address the nature of residues that might occur in acidic surface water bodies, and if the presence of novel breakdown products under these conditions is confirmed, further information to complete an aquatic risk assessment. For the representative uses proposed by the applicant, the potential for contamination of vulnerable groundwater by trinexapac-ethyl and its soil breakdown products above the drinking water limit of 0.1µg/L is considered minimal.

The risk to birds and mammals from uptake of contaminated food is low for the representative use in cereals. The TER values for the long-term risk to birds and mammals is below the Annex VI trigger value indicating a high long term risk to birds and mammals from uptake of contaminated drinking water. A refined higher tier risk assessment is necessary to address the long term risk to birds and mammals from the representative use in cereals. A high risk to insectivorous birds and mammals from the uptake of contaminated food was identified for the representative use in amenity grass/turf. Further risk refinement steps are required for the representative use in amenity grass/turf to address the long term risk to insectivorous birds and herbivorous mammals from the uptake of contaminated food and the long term risk to birds and mammals and the short term risk to birds from uptake of contaminated drinking water.
No data were available to conclude on the risk to other soil non-target organisms. Since the standard HQ value for *Typhlodromus pyri* and *Aphidius rhopalosiphi* was >2 for the representative use in amenity grass/turf and a DT_{90} of > 100 days was observed in laboratory tests with trinexapac, a confirmatory data requirement to address the risk to other soil non-target organisms is proposed by EFSA. This data requirement was not discussed at an EPCO Expert meeting.
The risk to aquatic organisms, bees, non-target arthropods, earthworms, soil non-target micro-organisms, other non-target organism and biological methods of sewage treatment from the representative uses in cereals and amenity grass/turf is considered to be low.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- None

Critical areas of concern

- At the moment a final specification for the max content of non-relevant impurities cannot be set.
- Re-entry for workers and public in amenity turf and amenity grassland to be considered at a Member State level.
- A high risk to insectivorous birds and mammals from the uptake of contaminated food was identified for the representative use in amenity grass/turf. Further risk refinement steps are required for the representative use in amenity grass/turf to address the long term risk to

insectivorous birds and herbivorous mammals from the uptake of contaminated food and the long term risk to birds and mammals and the short term risk to birds from uptake of contaminated drinking water.

- No data were available to conclude on the risk to other soil non-target organisms. Since the standard HQ value for *Typhlodromus pyri* and *Aphidius rhopalosiphi* was >2 for the representative use in amenity grass/turf and a DT_{90} of > 100 days was observed in laboratory tests with trinexapac a confirmatory data requirement to address the risk to other soil non-target organisms is proposed by EFSA. This data requirement was not discussed at an EPCO Expert meeting.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(Abbreviations used in this list are explained in appendix 2)

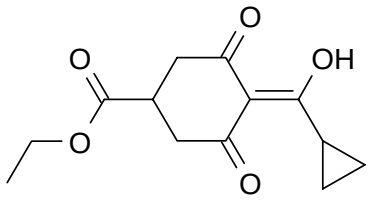
Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Trinexapac (pa ISO) Trinexapac-ethyl is a variant of the active substance trinexapac, all data relied on the variant unless it is otherwise specified
Function (e.g. fungicide)	plant growth regulator
Rapporteur Member State	The Netherlands
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	4-(cyclopropyl-hydroxymethylene)-3,5-dioxo-cyclohexanecarboxylic acid ethyl ester
Chemical name (CA) ‡	4-(cyclopropyl-hydroxymethylene)-3,5-dioxo-cyclohexanecarboxylic acid ethyl ester
CIPAC No ‡	732.202 (Trinexapac-ethyl) 732 (Trinexapac)
CAS No ‡	95266-40-3 (Trinexapac-ethyl) 104273-73-6 (Trinexapac)
EEC No (EINECS or ELINCS) ‡	not available
FAO Specification ‡ (including year of publication)	not available
Minimum purity of the active substance as manufactured ‡ (g/kg)	940g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	none
Molecular formula ‡	$C_{13}H_{16}O_5$
Molecular mass ‡	252.3

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	36.1 - 36.6 °C (996 g/kg)
Boiling point (state purity) ‡	Thermal decomposition starts at about 310 °C boiling point at 4.2 Pa is 99.8 °C (996 g/kg)
Temperature of decomposition	Thermal decomposition starts at about 310 °C
Appearance (state purity) ‡	Red-brown solidified melt (968 g/kg) White powder (996 g/kg)
Relative density (state purity) ‡	Density: 1.31 g/cm3 at 22 °C (996 g/kg)
Surface tension	σ = 55.5 mN/m at 90% of the saturation conc. and 20 °C
Vapour pressure (in Pa, state temperature) ‡	$2.16 \cdot 10^{-3}$ Pa at 25 °C
Henry's law constant (Pa m^3 mol^{-1}) ‡	$5.4 \cdot 10^{-4}$ Pa · m^3 / mol
Solubility in water ‡ (g/L or mg/L, state temperature)	All values at 25 °C: (all 993 g/kg) 1.1 g/L at pH 3.5 distilled water 2.8 g/L at pH 4.9 buffer solution 10.2 g/L at pH 5.5 buffer solution 21.1 g/L at pH 8.2 buffer solution
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	At 25 °C: acetone > 500 g / L methanol > 500 g / L *n*-octanol 420 g / L toluene > 500 g / L dichloromethane > 500 g / L ethyl acetate > 500 g / L hexane 45 g / L
Partition co-efficient (log POW) ‡ (state pH and temperature)	1.5 at pH 5, 25 °C -0.29 at pH 6.9, 25 °C -2.1 at pH 8.9, 25 °C (all 996 g/kg)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 5 $t_{0.5}$ = 485 to 562 days at 25 °C pH 7 $t_{0.5}$ = 828 to 908 days at 25 °C pH 9 $t_{0.5}$ = 8.1 days at 25 °C
Dissociation constant ‡	pKa = 4.57 at 20 °C

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	Molar extinctions coefficients: neutral 240.2 nm 9335 l / mol · cm^{-1} 277.4 nm 13976 l / mol · cm^{-1} acidic 240.0 nm 11712 l / mol · cm^{-1} 280.4 nm 12368 l / mol · cm^{-1} basic 270.8 nm 21320 l / mol · cm^{-1}
Photostability (DT50) ‡ (aqueous, sunlight, state pH)	Xenon arc light source Buffer solution pH 7 and 20°C: $t_{0.5}$ = 6.5 days
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	$\phi = 1.00 \cdot 10^{-3}$ at pH 7 (anionic form) $\phi = 8.32 \cdot 10^{-3}$ at pH 2.3 (undissociated form)
Flammability ‡	Trinexapac-ethyl is not considered highly flammable
Explosive properties ‡	Trinexapac-ethyl is not considered an explosive

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

List of representative uses evaluated*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Cereals	Northern and Southern MS	MODDUS 250 EC	F	Prevention of lodging	EC	250 g/L	foliar spray	BBCH 49 (North) BBCH 30-39 (South)	1	--	0.05-0.1	200 - 400	0.2		
Amenity turf and amenity grass-land	Northern and Southern MS	MODDUS 250 EC	F	Increased stress tolerances	EC	250 g/L	foliar spray		5	30 d	0.04-0.2	200 - 1000	0.4		Applied on actively growing turf [1]

[1] The risk assessment has revealed a risk in section 5.

Remarks:				
	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)	(i)	g/kg or g/L
	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)	(j)	Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.2: Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (principle of method)	HPLC UV detector Column: Nucleosil C18
Impurities in technical as (principle of method)	HPLC: UV detector. Column Nucleosil 100 C18 (12 organic by-products) GC: FID detector. Column: wide-bore fused silica (1 organic by-product and a solvent) Potentiometric Titration (1 organic by-product)
Plant protection product (principle of method)	HPLC: UV detector. Column: Nucleosil C18

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Metabolite trinexapac (CGA 179500) is the only relevant residue in plants. Method (REM 137.13) for trinexapac (CGA 179500): Samples are extracted by homogenisation with methanol:water:phosphate buffer (pH7) (30:56:14 v/v/v). Extracts are centrifuged and aliquots are subsequently diluted with ultra-pure water. An Oasis™ HLB solid phase extraction (SPE) procedure is then carried out to facilitate sample clean up. Final determination is by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). LOQ: 0.01 mg/kg (apple, potato, whaet grain, oil seed rape) Method on parent available: HPLC- UV three column switching with an RP 18 and two PRP1 columns. LOQ 0.02 mg/kg grain 0.04 straw mg/kg REM 137.01

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Metabolite trinexapac (CGA 179500) is the only relevant residue in animal. Method (REM 137.14) for trinexapac (CGA 179500): Animal tissue and egg samples are extracted by shaking with water:methanol (80:20 v/v) containing 0.33% 1 M sodium hydroxide solution. Milk is extracted by shaking with water:methanol (98:2 v/v) containing 0.2% 1 M sodium hydroxide solution. Extracts are centrifuged and aliquots are diluted with ultra-pure water. An Oasis™ HLB solid phase extraction (SPE) procedure is then carried out. Final determination is by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). LOQ: 0.01 mg/kg for eggs, muscle, kidney, liver and fat, and 0.005 mg/kg for milk.
Soil (principle of method and LOQ)	Method (RAM 436/01) for trinexapac-ethyl: Extraction with methanol/phosphate buffer mixture and analysis by HPLC with triple quadrupole mass spectrometry detection (LC-MS/MS). LOQ: 0.01 mg/kg Method (RAM 437/01) for trinexapac (CGA 179500): Extraction with water under reflux, and analysis by HPLC with triple quadrupole mass spectrometry detection (LC-MS/MS). LOQ: 0.01 mg/kg
Water (principle of method and LOQ)	Method (RAM 438/01) for trinexapac-ethyl and trinexapac (CGA 179500): specific clean up, and analysis by LC-MS/MS LOQ: 0.1 µg /L for trinexapac-ethyl and CGA 179500 in river water, groundwater and drinking water.
Air (principle of method and LOQ)	Trinexapac-ethyl: Retention on an absorbing matrix, elution and analysis by high performance liquid chromatography with UV-detection (REM 137.07) LOQ: 20 µg/m^3
Body fluids and tissues (principle of method and LOQ)	no analytical method for the determination of residues in body fluids and tissue is required.

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	none

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)

Rate and extent of absorption ‡	Oral: at least 96%, irrespective of dose and sex, based on radiolabel recovered from urine, cage wash, carcass and tissues 168 after administration. Twenty-four hours after administration absorption was at least 91%, based on radiolabel recovered from urine.
Distribution ‡	Barely detectable in fat (1 and 166 mg/kg bw dose groups) and kidneys (high dose group only) 168 h after administration.
Potential for accumulation ‡	No evidence of accumulation.
Rate and extent of excretion ‡	91% in 24 h, ca. 95% in 168 h; mostly in urine
Metabolism in animals ‡	Extensively metabolised, mainly hydrolysis to trinexapac (92% of urinary radiolabel after low dose administration)
Toxicologically significant compounds ‡ (animals, plants and environment)	Trinexapac-ethyl, CGA 113745

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	4210 mg/kg bw
Rat LD50 dermal ‡	> 4000 mg/kg bw
Rat LC50 inhalation ‡	> 5.3 mg/L
Skin irritation ‡	Not irritating
Eye irritation ‡	Not irritating
Skin sensitization ‡ (test method used and result)	Not sensitising to skin (Maximisation test)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Decreased body weight / decrease of absolute and relative organ weight
Lowest relevant oral NOAEL / NOEL ‡	1-yr dog: 32 mg/kg bw/day 90-d rat: 34 mg/kg bw/day
Lowest relevant dermal NOAEL / NOEL ‡	1000 mg/kg bw/d (highest dose tested)
Lowest relevant inhalation NOAEL / NOEL ‡	No data – not required

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Reduced body weight, neoplastic lesions in urinary bladder
Lowest relevant NOAEL / NOEL ‡	104-w rat: 116 mg/kg bw/d
Carcinogenicity ‡	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Reduced body weight gain and reduced survival index of pups at parental toxic doses
Lowest relevant reproductive NOAEL / NOEL ‡	Parental: 60 mg/kg bw/day Reproductive: 590 mg/kg bw/d
Developmental target / critical effect ‡	Increased pre-implantation loss, decreased number of live foetuses at maternal toxic doses (rabbit)
Lowest relevant developmental NOAEL / NOEL ‡	Parental: 60 mg/kg bw/day Developmental 360 mg/kg bw/d

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

acute neurotoxicity NOAEL	No data – not required
semi-chronic neurotoxicity NOAEL	Vacuolation of the brain (1-yr dog, at 20000 mg/kg food (727 mg/kg bw/d)) – No concern from other studies.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Other toxicological studies ‡ (Annex IIA, point 5.8)

Metabolites	CGA275537 LD_50 oral rat >330 mg/kg bw <2000 mg/kg bw Ames test negative CGA329773 LD_{50} oral rat >2000 mg/kg bw Ames test negative 28 d oral rat: NOAEL 12000 ppm (1021 mg/kg bw/d) CGA313458 LD_{50} oral rat >2000 mg/kg bw Ames test negative

Medical data ‡ (Annex IIA, point 5.9)

Records are kept on file; no adverse effects reported so far.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.32 mg/kg bw/d	one-year oral toxicity dog	100
AOEL ‡	0.34 mg/kg bw/d	13-w oral toxicity rat	100
ARfD ‡ (acute reference dose)	allocation not necessary		

Dermal absorption (Annex IIIA, point 7.3)

Moddus 250 EC	10% for both undiluted preparation and spray dilution, based on *in vivo* dermal absorption study with rats and comparative (rat-human) *in vitro* dermal absorption study

Acceptable exposure scenarios (including method of calculation)

Operator	Exposure below the AOEL with and without PPE for all intended uses (up to 70% with German model and UK-POEM), except for mechanical spraying on amenity turf – UK POEM (139% of the AOEL)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Workers	Exposure below the AOEL in cereals. No data available for amenity turf and amenity grassland
Bystanders	Exposure below the AOEL (<1%)

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	none

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.4: Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	cereals (wheat and rice), oil seeds/pulses (rape)
Rotational crops	lettuce, wheat, sugar beet, corn
Plant residue definition for monitoring	Trinexapac (CGA 179500)
Plant residue definition for risk assessment	Trinexapac (CGA 179500)
Conversion factor (monitoring to risk assessment)	None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Lactating goats, laying hens
Animal residue definition for monitoring	Trinexapac (CGA 179500)
Animal residue definition for risk assessment	Trinexapac (CGA 179500)
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

.....	No significant residue levels are expected

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

.....	Trinexapac (CGA 179500) is stable for two years in cereals at –18°C.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes	Poultry*: yes	Pig: yes
Muscle	< 0.02	< 0.02	
Liver	< 0.02	< 0.02	
Kidney	< 0.02	< 0.02	
Fat	< 0.02	< 0.02	
Milk	< 0.01		
Eggs		< 0.02	

* No livestock feeding study available. No measurable residues (above LOQ) are expected based on extrapolation of the data from the poultry metabolism study and the TMDI level in poultry feed.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL (grain)	STMR (grain) (b)
Barley grain Barley straw	N	3 x <0.02, 0.02, 0.03, 0.06, 2 x 0.07, 2 x 0.08, 0.09, 0.10, 0.11, 0.13, 0.14 2 x 0.02, <0.04, 2 x 0.05, 2 x 0.06, 0.08, 0.12, 0.13, 0.14	Extrapolation possible to the whole crop group of cereals	0.3	0.07
Oat grain Oat straw	N	0.03, 0.04 2 x <0.04	Data set South EU not different from data set North EU and are combined for MRL setting		
Wheat grain Wheat straw	N	0.05, 0.20 2 x <0.04			
Barley grain Barley straw	S	<0.02, 0.02, 0.06, 0.10, 0.18, 0.20 3 x <0.02, 0.05, 0.06, 0.12			

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.32 mg/kg bw/day
TMDI (European Diet) (% ADI)	0.0013 mg/kg bw/day (0.4% ADI)
TMDI (NL Diet) (% ADI)	adults: 0.00087 mg/kg bw/day (0.27% ADI) children (1-6 y): 0.0018 mg/kg bw/day (0.58% ADI)
NEDI (% ADI)	not applicable
Factors included in NEDI	not applicable
ARfD	not required
Acute exposure (% ARfD)	not applicable

Processing studies, nature of residue (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Type of study	High temperature hydrolysis of trinexapac (CGA-179500) [25 minutes, pH 4, 90°C; 60 minutes, pH 5, 100°C; 20 minutes, pH 6, 120°C]: CGA-179500 51-59% AR, degradation products CGA 313458 (16-21% AR) and CGA 113745 (9.6-12% AR).

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/processed crop	Number of studies	Transfer factor	% Transference *
barley grain to:	8	-	
- malt		0-0.8	not indicated
- wort		0-0.1	
- beer		0-<0.3	
wheat grain to:	1	-	
- bran (scoured total bran)		3.8	67
- flour (type 550)		0.3	24
- wholemeal flour		1.0	99
- whole grain bread		0.6	89

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

cereals:	0.3 mg/kg
meat and offal:	0.02* mg/kg
eggs:	0.02* mg/kg
milk:	0.01* mg/kg

*) LOQ

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.5: Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	56% after 90 d (^{14}C-ring-label) 49% after 90 d (^{14}C-carbonyl-label) 58% after 90 d (1,2,6-^{14}C-label)
Non-extractable residues after 100 days ‡	18% after 90 d (^{14}C-ring-label) 11% after 90 d (^{14}C-carbonyl-label) 6.8% after 90 d (1,2,6-^{14}C-label)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	trinexapac (CGA 179500): range 93-98% of AR maximum 98% of AR after 1 d (25 °C)

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡	non-extractable residue: 6.0-8.0% of AR after 0-63 d cumulative volatiles 3% of AR after 63 d trinexapac: 58 - 87% of AR in soil after 0- 29d, 22-25% of AR in water after 63 d
Soil photolysis ‡	non-extractable residue: 7.0% of AR after 4 h mineralisation: 10% maximum after 21 days trinexapac: 66% of AR after 6 h

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Method of calculation	non-linear regression of first-order kinetics
Laboratory studies ‡ (range or median, with n value, with r^2 value)	**trinexapac-ethyl** $DT_{50, lab}$ (20°C, aerobic): 0.31, 0.34 d (r^2 0.95-0.99; 1 soil) average $DT_{50, lab}$ (20°C, aerobic): 0.33 d (1 soil) **trinexapac** (applied as parent) $DT_{50,lab}$ (20°C, aerobic): 7.0, 8.8, 10.3, 5.3, 2.5 (r^2 0.83-0.94; 2 labels; 4 soils) $DT_{50, lab}$ (20°C, aerobic): 30.6, 39.5 d (r^2 0.95-0.99; 2 labels; 1 soil), 38.1 d (r^2 0.96; 1 label; 1 soil); average 36.5 d (sandy loam) overall mean $DT_{50, lab}$ (20°C, aerobic): 11.7 d (5 soils) **trinexapac-ethyl** $DT_{90, lab}$ (20°C, aerobic): <1 d (extrapolated) Trinexapac $DT_{90, lab}$ (20°C, aerobic 8.3-121 d (extrapolated)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

	trinexapac-ethyl $DT_{50, lab}$ (10°C, aerobic): not available **trinexapac** $DT_{50, lab}$ (10°C, aerobic): 6.3 d (r^2 0.83; 1 soil)
	degradation in the saturated zone ‡:
Field studies ‡ (state location, range or median with n value)	**trinexapac** $DT_{50, field}$: Motterwitz, Germany: 21 d (r^2 0.80) Tabarz, Germany:: 6.9 d (r^2 0.80) Koblenz, Germany: 16 d (r^2 0.91) indicative values
	$DT_{90, field}$: indicative values 23-70 d (extrapolated)
Soil accumulation and plateau concentration ‡	not available, not required

Rate of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation	trinexapac-ethyl $DT_{50, lab}$ (25°C, anaerobic): not available, only 3 time points measured
Soil photolysis	trinexapac-ethyl DT_{50} 2.8 d under light, 0.67 d in dark (20 °C) in view of fast biodegradation, contribution of photolysis to overall dissipation is not relevant

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡
K_d ‡

trinexapac-ethyl

K_F [L/kg]	1/n	pH	K_{oc} [L/kg]	K_{om} [L/kg]
17.8	0.92	5.9	629	370
1.5	1.01	6.5	289	170
0.67	0.92	6.7	143	84
0.66	0.92	7.5	60	35

Trinexapac

K_F [L/kg]	1/n	pH	K_{oc} [L/kg]	K_{om} [L/kg]
16.4	0.92	5.9	581	342
3.22	0.85	6.5	609	358
1.54	0.90	6.7	328	193
1.61	0.90	7.5	145	85

pH dependence ‡ (yes / no) (if yes type of dependence)	yes, decreased sorption at increasing pH both trinexapac-ethyl and trinexapac

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	no data available
Aged residues leaching ‡	No leaching of trinexapac-ethyl nor trinexapac
Lysimeter/ field leaching studies ‡	Vouvry, Switzerland; results from field leaching study 0.125 kg as/ha in 1993 and 1994; wheat residues of trinexapac-were <0.05 µg/L Soil water sampled at 0.8-1.2m depth

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	**trinexapac-ethyl** F_{soil}: 50% for cereals, 10% for amenity grass and turf 5 cm soil incorporation soil density 1.5 kg/L DT_{50} 1 d **trinexapac** F_{soil}: 50% for cereals, 10% for amenity grass and turf 5 cm soil incorporation soil density 1.5 kg/L DT_{50} 36.5 d
Application rate	**trinexapac-ethyl** 1 time 0.2 kg as/ha 5 times 0.4 kg as/ha at an interval of 30 d **trinexapac** application rates for trinexapac-ethyl corrected for max. formation rate (98%) and relative molar mass (0.89)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

PEC_S (mg/kg)

Days after last application	Single application		Multiple application (5x, interval 30 days)	
	actual	time weighted average	actual	time weighted average
trinexapac-ethyl, cereals				
0	0.133	-		
1	0.067	0.096		
2	0.033	0.072		
4	0.008	0.045		
7	0.001	0.027		
14	$8.1 \cdot 10^{-6}$	0.014		
28	$5.0 \cdot 10^{-10}$	0.007		
trinexapac-ethyl, amenity grass and turf				
0	0.053	-	0.073	-
1	0.027	0.038	0.071	0.038
2	0.013	0.029	0.069	0.029
4	0.003	0.018	0.064	0.018
7	0.000	0.011	0.058	0.011
14	$3.3 \cdot 10^{-6}$	0.005	$3.3 \cdot 10^{-6}$	0.005
28	$2.0 \cdot 10^{-10}$	0.003	$2.0 \cdot 10^{-10}$	0.003
trinexapac, cereals				
0	0.116	-		
1	0.114	0.115		
2	0.112	0.114		
4	0.107	0.112		
7	0.101	0.109		
14	0.089	0.102		
28	0.068	0.090		
56	0.040	0.071		

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

PEC_S (mg/kg)

Days after last application	Single application		Multiple application (5x, interval 30 days)	
	actual	time weighted average	actual	time weighted average
Trinexapac, amenity grass and turf				
0	0.046		0.1	
1	0.046	0.046	0.098	0.099
2	0.045	0.046	0.096	0.098
4	0.043	0.045	0.093	0.096
7	0.041	0.043	0.088	0.094
14	0.036	0.041	0.077	0.088
28	0.027	0.036	0.058	0.077
56	0.016	0.028	0.034	0.061

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	**trinexapac-ethyl** pH 5 (20°C): no significant decay pH 7 (20°C): no significant decay pH 9 (20°C): DT_{50} 10.9 d trinexapac 88% at pH 9 after 30 d pH 5 (25°C): DT_{50} 767 d pH 7 (25°C): DT_{50} 1157 d trinexapac 18% at pH 5 after 179 d mono-ethyl ester of tricarboxylic acid 12.5% at pH 5 after 179 d **trinexapac** pH 4 (20°C): DT_{50} 79 d pH 5 (20°C): DT_{50} 74 d 2-(4-cyclopropyl-2,4-dioxobutyl)-succinic acid 31% at pH 4 and 22% at pH 5 after 91 d unknown 25% at pH 4 and 35% at pH 5 after 91 d
Photolytic degradation of active substance and relevant metabolites ‡	**trinexapac-ethyl** 20°C, pH 7, artificial sunlight >290 nm, 40°N: DT_{50} 21 d, quantum yield $1.86 \cdot 10^{-3}$ moles/Einstein 22°C, pH 7, artificial sunlight >290 nm, 50°N: DT_{50} 8.5 d, quantum yield $1.0 \cdot 10^{-3}$ moles/Einstein 22°C, pH 7, artificial sunlight >290 nm, 50°N: DT_{50} 20 d, quantum yield $3.65 \cdot 10^{-4}$ moles/Einstein no metabolites >10% of AR
Readily biodegradable (yes/no)	No
Degradation in water/sediment	Non linear regression first order kinetics sand pH 8.2, sandy clay loam pH 8.5

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

- DT_{50} water (aerobic; 20 ˚C):	**trinexapac-ethyl** sand: 3.4 d and sandy clay loam: 4.9; average 4.2 d **trinexapac**(applied as parent): sand: 10.8 d and sandy clay loam: 19.1; average 15.0 d
- DT_{90} water(aerobic; 20 ˚C):	**trinexapac-ethyl** 11.2 d and 16.2 d (extrapolated from DT_{50} value assuming first order exponential decay with factor = 3.3) **trinexapac (applied as parent)** 35.6 d and 63.0 d (extrapolated from DT_{50} value assuming first order exponential decaywith factor = 3.3)
-DT_{50} sediment(aerobic; 20 ˚C):	**trinexapac-ethyl** sand: 5.3 d and sandy clay loam: 0.86; average 3.1 d
- DT_{90} sediment(aerobic; 20 ˚C):	**trinexapac-ethyl** 17.5 d and 2.8 d (extrapolated from DT_{50} value assuming first order exponential decay with factor 3.3)
- DT_{50} whole system(aerobic; 20 ˚C):	**trinexapac-ethyl** sand: 3.8 d and sandy clay loam: 5.2; average 4.5 d trinexapac (applied as parent): sand: 9.9 d and sandy clay loam: 17.8; average 13.9 d
- DT_{90} whole system(aerobic; 20 ˚C):	**trinexapac-ethyl** 12.5 d and 17.2 d (extrapolated from DT_{50} value assuming first order exponential decay with factor 3.3) **trinexapac (applied as parent)** 32.7 d and 58.7 d (extrapolated from DT_{50} value assuming first order exponential decay with factor 3.3)
Mineralisation	sand: 73% of AR after 83 d sandy clay loam: 59% of AR after 111 d
Non-extractable residues	sand: 26% of AR after 55 d sandy clay loam: 39% of AR after 55 d
Distribution in water / sediment systems (active substance)	dissipation of trinexapac-ethyl from the systems is dominated by degradation in water and sediment. sediment extractable residue of trinexapac-ethyl was 4.4 and 6.0% of AR

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Distribution in water / sediment systems (metabolites)	metabolites >10% of AR in water phase: trinexapac: 64% of AR in sand; 48% of AR in sandy clay loam after 14 d dissipation of trinexapac from the systems is dominated by degradation in the water phase and sediment. Maximum sediment extractable residue of trinexapac was 3.8 and 6.9% of AR

PEC (surface water) (Annex IIIA, point 9.2.3)

Parent

Method of calculation	static water body, 30 cm depth sorption, advection and sedimentation set to zero **trinexapac-ethyl** DT50, water: 4.9 d **trinexapac** DT50, water: 19.1 d
Application rate	**trinexapac-ethyl** 1 time 0.2 kg as/ha 5 times 0.4 kg as/ha at an interval of 30 d **trinexapac** application rates for trinexapac corrected for max. formation rate in water (64%) and relative molar mass (0.89)
Main routes of entry	spray drift, basic drift values for field crops Guidance Document on Aquatic Ecotoxicology[3], 1 and 5 applications, 1 m distance

PEC_{SW} (µg/L)

Days after last application	Single application		Multiple application	
	actual	time weighted average	actual	time weighted average
trinexapac-ethyl, cereals at 1 m, drift %: 2.77. 0.2 kg as/ha				
0	1.85			
4		1.41		
7		1.17		
21		0.59		
28		0.46		
trinexapac-ethyl, amenity grass and turf at 1m, drift %: 2.77. 5 times 0.4 kg as/ha				

[3] Sanco/3268/2001 rev. 4 (final) 17-10-2002, drift values in Annex to previous draft (Working Document 8075/VI/97, revision 8, dd. 27-06-2001)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

PEC_{SW} (µg/L)

Days after last application	Single application		Multiple application	
	actual	time weighted average	actual	time weighted average
0	3.69		3.75	
4		2.82		2.86
7		2.34		2.38
21		1.18		1.20
28		0.92		0.93
trinexapac, cereals				
0	1.05			
4		0.98		
7		0.93		
21		0.74		
28		0.66		
trinexapac, amenity grass and turf				
0	2.11		3.16	
4		1.96		2.94
7		1.86		2.79
21		1.47		2.21
28		1.32		1.98

PEC_{SED} (sediment)

Method of calculation	Not calculated
Application rate	-
Main routes of entry	-

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

PEC_{GW} (groundwater) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Experimental: No leaching (>0.05µg/L) in a long-term accumulation experiment after four years of use of 0.125 kg as/ha per year. sampling depth .2-2.5m, silt loam om 2.5-3%, pH 7.7 No leaching (>0.05µg/L) of trinexapac in two year field leaching (suction) experiment after application of 0.125 kg as/ha per year sampling depth 0.8-1.2m loamy sand om 1.8%, pH 7.6 Modelling: PEARL[4] with FOCUS-scenarios[5] for Northern and Southern Europe **trinexapac-ethyl** DT_{50} for soil biodegradation: 1 d K_{om}: 35 L/kg 1/n=0.9 (default) **trinexapac** DT_{50} for soil biodegradation: 11.7 d K_{om}: 85 L/kg 1/n=0.9 (default)
Application rate	**trinexapac-ethyl** 1 time 0.2 kg as/ha on April 1st, F_{soil} 50% 5 times 0.4 kg as/ha starting on April 1st with an interval of 1 month, F_{soil} 10% **trinexapac** application rates for trinexapac-ethyl corrected for max. formation rate (98%) and relative molar mass (0.89)

PEC_{GW} (µg/L)

Maximum concentration	-
Average annual concentration	trinexapac-ethyl <0.001 trinexapac <0.001

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	No data
Quantum yield of direct phototransformation	No data

[4] Leistra, M., Van der Linden, A.M.A., Boesten, J.J.T.I., Tiktak, A. Van den Berg, F. 2000. PEARL model for pesticide behaviour and emissions in soil-plant systems. Description of the processes. Wageningen/Bilthoven, Alterra/National Institute of Public Health and the Environment (RIVM), Report Alterra 013, RIVM 711401009. URL: http://www.alterra.nl/models/pearl/home.htm

[5] FOCUS. 2000. Focus groundwater scenarios in the EU review of active substances. Report of the FOCUS Groundwater Scenarios Workgroup. EC Document reference sANCO/321/2000, rev. 2.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Photochemical oxidative degradation in air ‡	Calculation according to Atkinson method: trinexapac-ethyl: DT_{50}:0.17 d (C_{OH} $5 \cdot 10^5$ cm^{-3}) Trinexapac-ethyl: DT_{50} 1.29-10.8 hrs (AOPWIN 1.85, 12 hrs day) Trinexapac: DT_{50} 0.134-0.162 d (C_{OH} $5 \cdot 10^5$ cm^{-3})
Volatilization ‡	from plant surfaces: at least 10-15% after 24 h from soil: no volatilisation after 10 d

PEC (air)

Method of calculation	No data

$PEC_{(a)}$

Maximum concentration	No data

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**Definition for risk assessment** **soil** trinexapac-ethyl and trinexapac and its salts **groundwater** trinexapac-ethyl and trinexapac and its salts **surface water** trinexapac-ethyl and trinexapac and its salts **sediment** trinexapac and its salts **air** trinexapac-ethyl **Definition for monitoring** All compartments except air trinexapac and its salts Air trinexapac-ethyl

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	-
Surface water (indicate location and type of study)	-
Ground water (indicate location and type of study)	-
Air (indicate location and type of study)	-

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R53 because not readily biodegradable

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.6: Effects on non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals ‡	LD_{50} = 4210 mg/kg bw
Acute toxicity to birds ‡	NOAEL = 60 mg/kg bw·d (teratogenicity rabbit)
Dietary toxicity to birds ‡	LD_{50} >2000 mg/kg bw (mallard duck)
Reproductive toxicity to birds ‡	LC_{50} >5200 mg/kg fd (mallard duck, bobwhite quail) LC_{50} >991 mg/kg bw·d (bobwhite quail)
	NOEC ≥ 600 mg/kg fd, ≥ 53.3 mg/kg bw·d (bobwhite quail, ♀)

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Mammals
exposure via water: maximum PECsw small mammal, 10 g bw, DWI 1.57 ml/d
exposure via food (acute and long-term)
small insectivorous mammal, 10 g bw, residues on insects, 0.2 kg as/ha, no degradation
small herbivorous mammal, 25 g bw, 1 time 0.2 kg/ha early cereals, 5 times 0.4 kg as/ha grass (interval 30 d, DT_{50} 10 d)

Birds
exposure via water: maximum PECSW small bird, 10 g bw, DWI 2.7 mL/d
exposure via food (acute, short-term and long-term):
small insectivorous bird, 10 g bw residues on insects, 0.2 or 0.4 kg as/ha, no degradation
large herbivorous bird, 3000 g bw, 1 time 0.2 kg as/ha (cereals), 5 times 0.4 kg as/ha grass (interval 30 d, DT_{50} 10 d)

Type of application	Route of exposure	Time scale	Toxicity endpoint	ETE	TER	Annex VI trigger
mammals						
cereals	surface water	acute	LD_{50} 42.1 mg/mammal	$2.90.10^{-6}$	$1.5.10^{7}$	10
amenity grass and turf	surface water	acute	LD_{50} 42.1 mg/mammal	$5.88.10^{-6}$	$7.2.10^{6}$	10
cereals early	crop	acute	LD_{50} 4210 mg/kg bw.d	39.5	107	10
cereals late	insects	acute	LD_{50} 4210 mg/kg bw.d	1.76	2387	10
amenity grass and turf	crop	acute	LD_{50} 4210 mg/kg bw.d	111	38	10
cereals early	crop	long-term	NOAEL 60 mg/kg bw.d	11.2	5.4	5
cereals late	insects	long-term	NOAEL 60 mg/kg bw.d	0.64	93	5

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Type of application	Route of exposure	Time scale	Toxicity endpoint	ETE	TER	Annex VI trigger
amenity grass and turf	crop	long-term	NOAEL 60 mg/kg bw.d	25.5	2.4	5
birds						
cereals	surface water	acute	LD_{50} >20 mg/bird	$5.00 \cdot 10^{-6}$ mg/bird	$>4.0 \cdot 10^{6}$	10
	surface water	short-term	LC_{50} >5200 mg/kg fd	$1.85 \cdot 10^{-3}$ mg/L	$>2.8 \cdot 10^{6}$	10
amenity grass and turf	surface water	acute	LD_{50} >20 mg/bird	$1.00 \cdot 10^{-5}$ mg/bird	$>2.0 \cdot 10^{6}$	10
	surface water	short-term	LC_{50} > 5200 mg/kg fd	$3.75 \cdot 10^{-3}$ mg/L	$>1.4 \cdot 10^{6}$	10
cereals early	insects	acute	LD_{50} >2000 mg/kg bw·d	10.8 mg/kg bw·d	>185	10
	crop	acute	LD_{50} >2000 mg/kg bw·d	12.5 mg/kg bw·d	>160	10
cereals late	insects	acute	LD_{50} >2000 mg/kg bw·d	10.8 mg/kg bw·d	>185	10
amenity grass and turf	insects	acute	LD_{50} >2000 mg/kg bw·d	21.6 mg/kg bw·d	> 93	10
	crop	acute	LD_{50} >2000 mg/kg bw·d	35.0 mg/kg bw·d	> 57	10
cereals early	insects	short-term	LC_{50} > 991 mg/kg bw·d	6.0 mg/kg bw·d	>164	10
	crop	short-term	LC_{50} > 991 mg/kg bw·d	6.7 mg/kg bw·d	>148	10
cereals late	insects	short-term	LC_{50} > 991 mg/kg bw·d	6.0 mg/kg bw·d	>164	10
amenity grass and turf	insects	short-term	LC_{50} > 991 mg/kg bw·d	12.1 mg/kg bw·d	> 82	10
	crop	short-term	LC_{50} > 991 mg/kg bw·d	15.2 mg/kg bw·d	> 65	10
cereals early	insects	long-term	NOEL ≥ 53.3 mg/kg bw·d	6.0 mg/kg bw·d	≥ 8.8	5
	crop	long-term	NOEL ≥ 53.3 mg/kg bw·d	3.5 mg/kg bw·d	≥ 15	5
cereals late	insects	long-term	NOEC ≥ 53.3 mg/kg bw·d	6.0 mg/kg bw·d	≥ 8.8	5
amenity grass and turf	insects	long-term	NOEC ≥ 53.3 mg/kg bw·d	12.1 mg/kg bw·d	≥ 4.4	5
	crop	long-term	NOEC ≥ 53.3 mg/kg bw·d	8.1 mg/kg bw·d	≥ 6.6	5

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale	Endpoint	Toxicity (mg as/L)
Laboratory tests				
trinexapac-ethyl				
Ictalurus punctatus	trinexapac-ethyl tech.	96 h	mortality, LC_{50}	35
Oncorhynchus mykiss	A 7725 M (250 EC)	96 h	mortality, LC_{50}	6
Pimephales promelas	trinexapac-ethyl tech.	35 d	ELS, NOEC	0.41
Daphnia magna	trinexapac-ethyl tech.	48 h	immobility, EC_{50}	>142.5
Daphnia magna	A 7725 M (250 EC)	48 h	immobility, EC_{50}	0.73
Daphnia magna	trinexapac-ethyl tech.	21 d	reproduction, mortality, growth F0, NOEC	2.4
Daphnia magna	A 7725 M (250 EC)	21 d	reproduction, mortality, NOEC	0.25
Anabaena flos-aquae	trinexapac-ethyl tech.	96 h	growth rate, E_rC_{50}	25.7
Anabaena flos-aquae	A 7725 M (250 EC)	96 h	biomass, E_bC_{50}	1.4
Lemna gibba	trinexapac-ethyl tech.	7 d	biomass, E_bC_{50}	8.8
Lemna gibba	A 7725 M (250 EC)	7 d	biomass, E_bC_{50}	5.5
trinexapac				
Cyprinus carpio *Oncorhynchus mykiss*	trinexapac tech.	96 h	mortality, LC_{50}	>100
Daphnia magna	trinexapac tech.	48 h	immobility, EC_{50}	>100
Anabaena flos-aquae	trinexapac tech.	96 h	biomass, E_bC_{50} growth rate, E_rC_{50}	17.5
Lemna gibba	trinexapac tech.	7 d	biomass, E_bC_{50}	1.5
Microcosm or mesocosm tests: not provided				

* In the DAR the metabolite ‘trinexapac’ is named ‘trinexapac-acid’

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Type of application	Application rate (kg as/ha), Number of applications	max. PEC_{SW} (mg/L)	Organism	Time-scale	TER	Annex VI Trigger
trinexapac-ethyl						
cereals	0.2, 1	$1.85 \cdot 10^{-3}$ (PEC_0)	*Daphnia magna*	acute	77027[a]	100
			Daphnia magna	acute	395[b]	100
			Ictalurus punctatus	acute	18919[a]	100
			Oncorhynchus mykiss	acute	3243[b]	100
			Anabaena flos-aquae	long-term	13892[a]	10
			Anabaena flos-aquae	long-term	757[b]	10
			Lemna gibba	long-term	4757[a,b]	10
			Lemna gibba	long-term	2432[b]	10
			Daphnia magna	long-term	1297[a]	10
			Daphnia magna	long-term	135[b]	10
			Pimephales promelas	long- term	222[a]	10
trinexapac-ethyl						
amenity grass and turf	0.4, 5	$3.75 \cdot 10^{-3}$ (PEC_0)	*Daphnia magna*	acute	38000[a]	100
			Daphnia magna	acute	195[b]	100
			Ictalurus punctatus	acute	9333[a]	100
			Oncorhynchus mykiss	acute	1600[b]	100
			Anabaena flos-aquae	long-term	6853[a]	10
			Anabaena flos-aquae	long-term	373[b]	10
			Pimephales promelas	long-term	109	10
			Daphnia magna	long-term	640[a]	10
			Daphnia magna	long-term	67[b]	10
			Lemna gibba	long-term	2346[a,]	10
			Lemna gibba	long-term	1200[b]	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Type of application	Application rate (kg as/ha), Number of applications	max. PEC_{SW} (mg/L)	Organism	Time-scale	TER	Annex VI Trigger
trinexapac						
cereals	0.114[c], 1	$1.05 \cdot 10^{-3}$ (PEC_0)	*Daphnia magna*	acute	>95238	100
			Cyprinus carpio Oncorhynchus mykiss	acute	>95238	100
			Anabaena flos-aquae	long-term	16667	10
			Lemna gibba	long-term	1429	10
amenity grass and turf	0.114[c], 1	$1.05 \cdot 10^{-3}$ (PEC_0)	*Daphnia magna*	acute	>47393	100
			Cyprinus carpio Oncorhynchus mykiss	acute	>47393	100
			Anabaena flos-aquae	long-term	8294	10
			Lemna gibba	long-term	711	10
amenity grass and turf	0.228[c], 5	$3.16 \cdot 10^{-3}$ (PEC_0)	*Daphnia magna*	acute	>31646	100
			Cyprinus carpio Oncorhynchus mykiss	acute	>31646	100
			Anabaena flos-aquae	long-term	5538	10
			Lemna gibba	long-term	475	10

* In the DAR the metabolite 'trinexapac' is named 'trinexapac-acid'
[a]: based on toxicity trinexapac-ethyl techn.
[b]: based on toxicity trinexapac-ethyl 250 EC
[c]: application rate of trinexapac-ethyl, corrected for formation rate (64%) and relative molar mass (0.89)

Bioconcentration

Bioconcentration factor (BCF) ‡	6 L/kg wwt
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	1.4 d not available
Level of residues (%) in organisms after the 14 day depuration phase	below detection limit

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Acute oral toxicity ‡	LD_{50} >108 µg as/bee (MODDUS 250 EC)
Acute contact toxicity ‡	LD_{50} = 69.6 µg as/bee (MODDUS 250 EC)

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.2	cereals	oral	<1.86	50
		contact	2.87	50
0.4	amenity grass and turf	oral	<3.71	50
		contact	5.75	50

Field or semi-field tests:
no data, not considered necessary

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Species	Stage	Test Substance	Substrate	Dose (g as/ha)	Endpoint	Adverse effect * (%)	Trigger
Laboratory tests							
T. pyri	protonymphs	250 EC	glass	38-600	LR_{50}	197 g as/ha	
A. rhopalosiphi	adults	250 EC	glass	50-800	LR_{50}	114 g as/ha	
O. insidiosus	nymphs	250 EC	glass	150	mortality reproduction	-2 +5	30
C. septempunctata	larvae	250 EC	glass	16	mortality	**76**	30
				200	mortality	**48**	30
				400	mortality	**64**	30
A. bilineata	adults	250 EC	sand	16	reproduction	5.7	30
				200	reproduction	5.8	30
				400	reproduction	13	30

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Species	Stage	Test Substance	Substrate	Dose (g as/ha)	Endpoint	Adverse effect * (%)	Trigger
P. cupreus	adults	250 EC	sand	16	mortality food consumption	3.3 +1.4	30
				200	mortality food consumption	0 +1.4	30
				400	mortality food consumption	0 +1.4	30

Species	Stage	Test Substance	Substrate	Dose (g as/ha)	Endpoint	Adverse effect * (%)	Trigger
Laboratory tests (extended)							
T. pyri	protonymphs	250 EC	leaves	100-1600	LR_{50}	>1600 g as/ha	
				100	mortality	-3.8	50
				200	mortality	0	50
				400	mortality reproduction	14 4.9	50
				800	mortality reproduction	3.9 3.8	50
				1600	mortality reproduction	16 +11	50
A. rhopalosiphi	adults	250 EC	leaves	50-4050	LR_{50}	>4050 g as/ha	
				50	mortality reproduction	0 +23	50
				150	mortality reproduction	0 2.9	50
				450	mortality reproduction	0 +20	50
				1350	mortality reproduction	0 5.4	50
				4050	mortality reproduction	13 25	50

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Species	Stage	Test Substance	Substrate	Dose (g as/ha)	Endpoint	Adverse effect * (%)	Trigger
C. carnea	larvae	250 EC	leaves	28-400	LR_{50}	>400 g as/ha	
				28	mortality reproduction	2.3 +21	50
				200	mortality reproduction	9.1 10	50
				400	mortality reproduction	-2.3 +25	50
C. septem-punctata	larvae	250 EC	leaves	28-400	LR_{50}	>400 g as/ha	
				28	mortality reproduction	10 18	50
				200	mortality reproduction	27 +14	50
				400	mortality reproduction	27 6	50
Field or semi-field tests: no data available, not considered necessary							

* Adverse effect:
x % effect on mortality = x % increase of mortality compared to control
y % effect on a sublethal parameter = y % decrease of sublethal parameter compared to control
When effects are favourable for the test organisms, a + sign is used for the sublethal effectpercentages (i.e. increase compared to control) and a – sign for mortality effectpercentages (i.e. decrease compared to control).

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡	LC_{50} >250 mg as/kg dry soil (MODDUS 250 EC) trinexapac LC_{50} >1000 mg/kg dry soil
Reproductive toxicity ‡	no data available, not considered necessary

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

based on initial PEC_S
cereals: 1 application of 0.2 kg as/ha, F_{soil} 80%; amenity grass and turf: 5 applications of 0.4 kg as/ha, F_{soil} 50%
DT_{50} 1 d (ethyl) and 13 d (acid); 5 cm depth incorporation, soil bulk density 1.5 kg/L

Substance	Crop	PEC_S (mg/kg)	TER	Annex VI Trigger
MODDUS 250 EC	cereals	0.133	>1880	10
MODDUS 250 EC	amenity grass and turf	0.073	> 3425	10
trinexapac *	cereals	0.116	>8621	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Substance	Crop	PEC_S (mg/kg)	TER	Annex VI Trigger
trinexapac *	amenity grass and turf	0.1	> 10000	10

* In the DAR the metabolite 'trinexapac' is named 'trinexapac-acid'

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralization ‡	<25% effect after 28-57 d on nitrification at 0.53-8.6 mg as/kg <25% effect after 28 d on N-mineralisation at 0.53-8.6 mg as/kg
Carbon mineralization ‡	<25% effect after 28-57 d on respiration at 0.53-8.6 mg as/kg

Effects on other non-target organisms (flora and fauna) believed to be at risk (Annex IIA 8.6)

Phytotoxicity tests are performed with the technical substance (760 and 840 g as/ha) and formulation (125-405 g as/ha). Phytotoxicity occurred in a post-emergence application with the formulation. Pea was most sensitive with a NOEC of 0.051 kg as/ha. This indicates that the formulation is more phytotoxic than the technical substance. Weight is most sensitive parameter, lowest NOEC is 0.024 kg as/ha for cucumber, lowest NOEC for plant height is 0.048 kg as/ha for cabbage and oat. EC_{50} for emergence and growth were higher than the highest dose in all cases (>0.76 kg as/ha for applications with the technical substance and >0.405 kg as/ha for the formulation). In a germination experiment, radicle elongation was observed. The effect was inversely related to dose, with significant effects of 413 to 213% at rates of 0.02 to 0.38 kg as/ha. No effect was seen at 0.76 kg as/ha.

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N: Dangerous to the environment R52/R53: Harmful to aquatic organisms, may cause long-term effects in the aquatic environment S60: This material and its container must be disposed of as hazardous waste S61: Avoid release to the environment

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median

LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year