The Chemical Company

DOSSIER FOR THE EVALUATION OF THE ACTIVE SUBSTANCE

Picolinafen (BAS 700 H)

Data requirement according to Regulation (EU) No. 544/2011 and (EU) No. 545/2011 of 10 June 2011 (formerly Annex II and III of Directive 91/414/EEC)
using OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substance
(Dossier Guidance)
and Commission Regulation (EC) No 1141/2010 of 7 December 2010 (AIR procedure)

Document M-II

Summary and evaluation (Tier II)

Section 1

Identity, physical and chemical properties and further information

BASF DocID 2012/1208875

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On behalf of:

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Date: 30 August 2012

1 Identity of the active substance

List of Contents

According to Article 1(c) of Regulation (EU) No. 1141/2010 the supplementary dossier includes data and risk assessments which were not part of the original dossier and which are necessary to reflect changes. Reasoning for each test or study as required by Art 1(d)/(e) of the Regulation is given in the reference list of the dossier.

1.1 Applicant (name, address, contact, phone and fax numbers)

1.1.1 Legal entity

BASF Agro B.V. Arnhem (NL) - Wädenswill Branch
Moosarcherstrasse 2
Postfach 69
CH – 8820 Wädenswill/Au
Switzerland

1.1.2 Affiliates or representatives

BASF Belgium Coordination Center Comm. V.,
Drève Richelle, 161 E/F
B-1410 Waterloo
Belgium

Contact person: [redacted]
Tel. [redacted]
Fax.
E-mail: xxxxxxxxxxxxxxxx

1.1.3 Alternate

[redacted]

Contact person: [redacted]
Tel No.: [redacted]
Fax No.: [redacted]
E-mail: [redacted]

1.2 Manufacturer(s) (name, address, contact, phone and fax numbers)

This confidential information is provided in Document JM II.

1.3 ISO common name proposed or accepted, and synonyms

ISO Common Name: Picolinafen

1.4 Chemical name

IUPAC nomenclature:	4'-Fluoro-6-[(α,α,α,-trifluoro-m-tolyl)oxy]picolinanilide
CA nomenclature:	N-(4-Fluorophenyl)-6-[3-(trifluoromethyl)phenoxy]-2-pyridinecarboxamide

1.5 Manufacturer's codes, names and patent status

1.5.1 Manufacturer's code number(s), incl. countries and periods where used

Shell: WL 161616
Cyanamid: AC 900001, AC 900,001, CL 900001, CL 900,001
BASF: BAS 700 H

1.5.2 Trade name(s)

This is not a requirement under Directive 91/414/EEC / Reg. (EC) No. 1107/2009.

1.5.3 Patent status

This is not a requirement under Directive 91/414/EEC / Reg. (EC) No. 1107/2009.

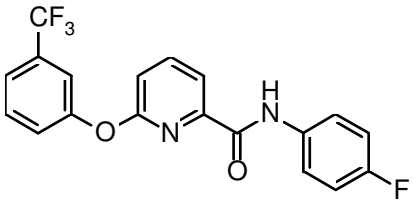
1.6 Existing CAS, CIPAC, EINECS and ELINCS numbers

CAS No.: 137641-05-5
EINECS No.: not assigned
CIPAC No. 639

1.7 Molecular formula, molecular mass and structural formula

Molecular formula: $C_{19}H_{12}F_4N_2O_2$
Molecular mass: 376.3

Structural formula of picolinafen:



1.8 Method of manufacture

1.8.1 Method of manufacture for each plant

This confidential information is contained in Document JM II.

1.8.2 Description of starting materials

This confidential information is contained in Document JM II.

1.9 Specification of purity of the active substance

1.9.1 Minimum and/or nominal content (g/kg) of pure active substance

Minimum content of pure active substance: 980 g/kg

1.9.2 Certified limits of the active substances

This confidential information is contained in Document JM II.

1.9.3 Control product specification form/confidential statement of formula

This confidential information is contained in Document JM II.

1.10 Identity, content and structure of isomers, impurities and additives

1.10.1 Inactive isomers

This confidential information is contained in Document JM II.

1.10.2 Impurities and additives

This confidential information is contained in Document JM II.

1.11 Batch analysis data

1.11.1 Analytical profile of batches

This confidential information is given in Document JM II.

1.11.2 Results of analyses of batches used in toxicological testing

This confidential information is given in Document JM II.

1.12 Other/special studies

There are no other/special studies.

2 Physical and chemical properties of the active substance

Annex Point IIA	Guideline and method	Test material purity and Specification	Findings	Comments	GLP Y/N	Author, Year
Melting point and boiling point (2.1)						
Melting point, freezing point or solidification point, purified a.s. (2.1.1)				Refer to the DAR, September 2000.		
Boiling point of purified active substance (2.1.2)				Refer to the DAR, September 2000.		
Temperature at which decomposition or sublimation occurs (2.1.3)				Refer to the DAR, September 2000.		
Relative density of purified active substance (2.2)				Refer to the DAR, September 2000.		
Vapour pressure and volatility (2.3)						
Vapour pressure of purified active substance (2.3.1)				Refer to the DAR, September 2000.		

Annex Point IIA	Guideline and method	Test material purity and Specification	Findings	Comments	GLP Y/N	Author, Year
Henry's law constant (2.3.2)				Refer to the DAR, dated September 2000.		
Appearance (2.4)						
Description of the physical state and colour, pur and techn. a.s. (2.4.1)				Refer to the DAR, September 2000.		
Description of the odour - purified and technical active substance (2.4.2)				Refer to the DAR, September 2000.		
Spectra and molecular extinction at relevant wavelengths (2.5)						
Spectra for purified active substance (2.5.1)						
UV/VIS (2.5.1.1)				Refer to the DAR, September 2000.		
IR (2.5.1.2)				Refer to the DAR, September 2000.		
NMR (2.5.1.3)				Refer to the DAR, September 2000.		
MS (2.5.1.4)				Refer to the DAR, September 2000.		

Annex Point IIA	Guideline and method	Test material purity and Specification	Findings	Comments	GLP Y/N	Author, Year
Wavelengths at which UV/VIS molecular extinction occurs, max > 290 nm (2.5.1.5)				Refer to the DAR, September 2000.		
optical purity (2.5.1.6)				Refer to the DAR, September 2000.		
Spectra for impurities (2.5.2)						
UV/VIS (2.5.2.1)				Refer to the DAR, September 2000.		
IR (2.5.2.2)				Refer to the DAR, September 2000.		
NMR (2.5.2.3)				Refer to the DAR, September 2000.		
MS (2.5.2.4)				Refer to the DAR, September 2000.		
Solubility of purified active substance in water (pH 4-10) (2.6)				Refer to the DAR, September 2000.		
Solubility in organic solvents at 15 to 25°C (2.7)				Refer to the DAR, September 2000.		
Partition coefficient (2.8)						
n-Octanol/water partition coefficient (2.8.1)				Refer to the DAR, September 2000.		

Annex Point IIA	Guideline and method	Test material purity and Specification	Findings	Comments	GLP Y/N	Author, Year
Effect of pH (4 to 10) on the n-octanol/water partition coefficient (2.8.2)				Refer to the DAR, September 2000.		
Hydrolysis and photolysis (2.9)						
Hydrolysis rate at pH 4, 7 and 9 under sterile and dark conditions (2.9.1)				Refer to the DAR, September 2000.		
Direct phototransformation in sterile water using artificial light (2.9.2)				Refer to the DAR, September 2000.		
Quantum yield of direct phototransformation (2.9.3)				Refer to the DAR, September 2000.		
Lifetime in the top layer of aqueous systems (calculated and real) (2.9.4)				Refer to the DAR, September 2000.		
Dissociation in water of purified active substance (2.9.5)				Refer to the DAR, September 2000.		

Annex Point IIA	Guideline and method	Test material purity and Specification	Findings	Comments	GLP Y/N	Author, Year
Estimated photochemical oxidative degradation (2.10)				Refer to the DAR, September 2000.		
Flammability including auto-flammability (2.11)						
Flammability of the active substance as manufactured (2.11.1)				Refer to the DAR, September 2000.		
Auto-flammability of the active substance as manufactured (2.11.2)				Refer to the DAR, September 2000.		
Flash point of the active substance as manufactured (2.12)				Refer to the DAR, September 2000.		
Explosive properties of the active substance as manufactured (2.13)				Refer to the DAR, September 2000.		
Surface tension of the active substance as manufactured (2.14)				Refer to the DAR, September 2000.		

Annex Point IIA	Guideline and method	Test material purity and Specification	Findings	Comments	GLP Y/N	Author, Year
Oxidizing properties of the active substance as manufactured (2.15)				Refer to the DAR, September 2000.		
pH (2.16)				Refer to the DAR, September 2000.		
Stability (2.17)				Refer to the DAR, September 2000.		
Storage stability (2.17.1)				Refer to the DAR, September 2000.		
Stability (temperature, metals) (2.17.2)				Refer to the DAR, September 2000.		
Other/special studies (2.18)				Refer to the DAR, September 2000.		

3 Further Information on the active substance

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3.1 Function e.g. fungicide

Herbicide

3.2 Effects on harmful organisms e.g. contact action

3.2.1 Nature of the effects on harmful organisms

Picolinafen is an active substance which belongs to the chemical group of Aryloxypicolinamides.

Picolinafen has been shown to inhibit the enzyme, phytoene desaturase, which is an enzyme in the carotenoid biosynthesis pathway of plants. Inhibition of this enzyme leads to a disruption of the synthesis of carotenoid pigments. Carotenoid pigments serve to protect chlorophyll from harmful photo-oxidation caused by high light levels.

A reduction of the chlorophyll protecting carotenoids and xanthophylls leads to degradation of chlorophyll by photo-oxidation. This results in a bleaching effect (lack of chlorophyll) on the foliage of sensitive species. This mode of action is also sometimes known as CBI (Carotenoid Biosynthesis Inhibition).

3.2.2 Translocation in plants

After its application susceptible weed species readily absorb picolinafen by foliage and translocate it through the plant to newly emerging shoots and leafs, most probably in the xylem. Although root uptake occurs, the subsequent translocation to shoots is limited. In the field the target weed species show symptoms as bleaching or whitening of leaf tissue.

3.3 Fields of use e.g. forestry

Picolinafen is used as an agriculture herbicide in cereals to control broad-leaved weeds post-emergence of the crop.

3.4 Harmful organisms controlled and crops / products protected or treated

3.4.1 Details of existing and intended uses

Picolinafen containing products are used in agriculture as pre- and post-emergence herbicides, applied either before or after crop and weeds have emerged. The area of use covers basically all cereal crops (wheat, barley, rye, triticale) for the control of broadleaved weeds.

The representative Good Agricultural Practice (GAP) consists of 1 (one) application to winter sown cereals post-emergence (BBCH 11 – 29) with a maximum application rate of 100 g a.s./ha. Application is by conventional tractor mounted sprayer using water volumes ranging from 200 – 400 litres water/ha. The GAP for renewal is identical to the GAP previously assessed for Annex I inclusion of picolinafen.

3.4.2 Details of harmful organisms against which protection is afforded

BAS 700 03 H controls important dicotyledonous weed species such as *Capsella bursa-pastoris, Galium aparine, Lamium amplexicaule, Lamium purpureum, Myosotis arvense, Raphanus raphanistrum, Senecio vulgaris, Sinapis arvensis, Stellaria media, Veronica agrestis, Veronica arvensis, Veronica hederaefolia, Veronica persica,* and *Viola arvensis* when applied in autumn or spring.

3.4.3 Effects achieved e.g. sprout suppression

Control of broadleaved weeds through disruption of the synthesis of carotenoid pigments. This results in bleaching or whitening of leaf tissue and eventual die off of susceptible weeds.

3.5 Mode of action

3.5.1 Mode of action, mechanism(s) and pathway(s) involved

Picolinafen has been shown to inhibit the enzyme, phytoene desaturase, which is an enzyme in the carotenoid biosynthesis pathway of plants. Inhibition of this enzyme leads to a disruption of the synthesis of carotenoid pigments. Carotenoid pigments serve to protect chlorophyll from harmful photo-oxidation caused by high light levels.

A reduction of the chlorophyll protecting carotenoids and xanthophylls leads to degradation of chlorophyll by photo-oxidation. This results in a bleaching effect (lack of chlorophyll) on the foliage of sensitive species.

3.5.2 Details of active metabolites and degradation products

There are no active metabolites or degradation products.

3.5.3 Formation of active metabolites and degradation products

There are no active metabolites or degradation products.

3.6 Possible development of resistance or cross-resistance

Picolinafen belongs to the Herbicide-Resistance Action Committee (HRAC) classification (F1) of inhibitors of carotenoid biosynthesis at the phytoene desaturase step (PDS).

Picolinafen is more often used in tank mixtures with herbicides with other modes of action in order to complete the spectrum of activity. Therefore the possible development of weed resistance will be negligible.

3.7 A material safety data sheet for the active substance

Report: II A 3.7/1
anonymous 2012(a)
Safety data sheet - Picolinafen
BASF DocID 2012/1219501 - dRR
Guidelines: EEC 1907/2006
GLP: No, not subject to GLP regulations

1. Identification of the substance/mixture and of the company/undertaking

Product identifier

PICOLINAFEN TECHNICAL

Relevant identified uses of the substance or mixture and uses advised against

Relevant identified uses: crop protection active ingredient

Details of the supplier of the safety data sheet

Company:
BASF SE
67056 Ludwigshafen
GERMANY
Operating Division Crop Protection

Telephone: +49 621 60-27777
E-mail address: Produktinformation-Pflanzenschutz@basf.com

Emergency telephone number

International emergency number:
Telephone: +49 180 2273-112

2. Hazards Identification

Label elements

According to Regulation (EC) No 1272/2008 [CLP]

Pictogram:

Signal Word:
Warning

Hazard Statement:

H400	Very toxic to aquatic life.
H410	Very toxic to aquatic life with long lasting effects.

Precautionary Statements (Prevention):

P273	Avoid release to the environment.

Precautionary Statements (Response):

P391	Collect spillage.

Precautionary Statements (Disposal):

P501	Dispose of contents/container to hazardous or special waste collection point.

According to Directive 67/548/EEC or 1999/45/EC

EEC Directives

Hazard symbol(s)

N	Dangerous for the environment.

R-phrase(s)

R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

S-phrase(s)

S61	Avoid release to the environment. Refer to special instructions/safety data sheets.

Hazard determining component(s) for labelling: PICOLINAFEN

Classification of the substance or mixture

According to Regulation (EC) No 1272/2008 [CLP]

Acute hazards to the aquatic environment: Cat. 1
Chronic hazards to the aquatic environment: Cat. 1

According to Directive 67/548/EEC or 1999/45/EC

Possible Hazards:
Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Other hazards

Assessment PBT / vPvB:
Not fulfilling PBT (persistent/bioaccumulative/toxic) criteria..
Not fulfilling vPvB (very persistent/very bioaccummulative) criteria..

3. Composition/Information on Ingredients

Substances

Chemical nature

Product for the production of: crop protection product

picolinafen (Content (W/W): >= 97 %)
CAS Number: 137641-05-5

4. First-Aid Measures

Description of first aid measures

Avoid contact with the skin, eyes and clothing. Remove contaminated clothing. First aid personnel should pay attention to their own safety. If danger of loss of consciousness, place patient in recovery position and transport accordingly. Apply artificial respiration if necessary. If difficulties occur: Obtain medical attention. Show container, label and/or safety data sheet to physician.

On skin contact:
After contact with skin, wash immediately with plenty of water and soap. If irritation develops, seek medical attention.

On contact with eyes:
Immediately wash affected eyes for at least 15 minutes under running water with eyelids held open, consult an eye specialist.

On ingestion:
Rinse mouth immediately and then drink plenty of water, seek medical attention. Do not induce vomiting unless told to by a poison control center or doctor. Never induce vomiting or give anything by mouth if the victim is unconscious or having convulsions.

Most important symptoms and effects, both acute and delayed

Symptoms: No significant reaction of the human body to the product known.

Indication of any immediate medical attention and special treatment needed

Treatment: Treat according to symptoms (decontamination, vital functions), no known specific antidote.

5. Fire-Fighting Measures

Extinguishing media

Suitable extinguishing media:
water spray, foam, dry powder

Unsuitable extinguishing media for safety reasons:
Unknown

Special hazards arising from the substance or mixture

carbon monoxide, hydrogen fluoride, nitrogen oxides

The product is combustible. The substances/groups of substances mentioned can be released if the product is involved in a fire.

Advice for fire-fighters
Special protective equipment:
Wear self-contained breathing apparatus and chemical-protective clothing.

Further information:
Dispose of fire debris and contaminated extinguishing water in accordance with official regulations. Collect contaminated extinguishing water separately, do not allow to reach sewage or effluent systems. In case of fire and/or explosion do not breathe fumes. Keep containers cool by spraying with water if exposed to fire.

6. Accidental Release Measures

Personal precautions, protective equipment and emergency procedures
Use personal protective clothing. Avoid contact with the skin, eyes and clothing.

Environmental precautions
Do not discharge into the subsoil/soil. Do not discharge into drains/surface waters/groundwater.

Methods and material for containment and cleaning up
For small amounts: Contain with dust binding material and dispose of.
For large amounts: Sweep/shovel up.
Avoid raising dust. Cleaning operations should be carried out only while wearing breathing apparatus. Dispose of absorbed material in accordance with regulations. Collect waste in suitable containers, which can be labeled and sealed. Clean contaminated floors and objects thoroughly with water and detergents, observing environmental regulations.

Reference to other sections
Information regarding exposure controls/personal protection and disposal considerations can be found in section 8 and 13.

7. Handling and Storage

Precautions for safe handling
No special measures necessary if stored and handled correctly. Ensure thorough ventilation of stores and work areas.

Protection against fire and explosion:
The product is combustible. Dust can form an explosive mixture with air. Prevent electrostatic charge - sources of ignition should be kept well clear - fire extinguishers should be kept handy.

Conditions for safe storage, including any incompatibilities
Segregate from foods and animal feeds.
Further information on storage conditions: Keep away from heat. Protect against moisture. Protect from direct sunlight.

Storage stability:
Storage duration: 60 Months

Protect from temperatures above: 40 °C

Changes in the properties of the product may occur if substance/product is stored above indicated temperature for extended periods of time.

Specific end use(s)
For the relevant identified use(s) listed in Section 1 the advice mentioned in this section 7 is to be observed.

8. Exposure Controls/Personal Protection

Control parameters

Components with workplace control parameters

No occupational exposure limits known.

Exposure controls

Personal protective equipment

Respiratory protection:
Breathing protection if breathable aerosols/dust are formed. Breathing protection if dusts are formed. Wear respiratory protection if ventilation is inadequate. Particle filter with medium efficiency for solid and liquid particles (e.g. EN 143 or 149, Type P2 or FFP2)

Hand protection:
Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber (0.5 mm), butyl rubber (0.7 mm) and other

Eye protection:
Safety glasses with side-shields (frame goggles) (e.g. EN 166)

Body protection:
Body protection must be chosen depending on activity and possible exposure, e.g. apron, protecting boots, chemical-protection suit (according to EN 14605 in case of splashes or EN ISO 13982 in case of dust).

General safety and hygiene measures
Handle in accordance with good industrial hygiene and safety practice. Avoid contact with the skin, eyes and clothing. Wearing of closed work clothing is recommended. Remove contaminated clothing. Store work clothing separately. Keep away from food, drink and animal feeding stuffs. No eating, drinking, smoking or tobacco use at the place of work. Hands and/or face should be washed before breaks and at the end of the shift.

9. Physical and Chemical Properties

Information on basic physical and chemical properties

Form:	powder
Colour:	off-white
Odour:	musty
Odour threshold:	not determined

pH value:	3.7 - 3.8 (water, 20 °C) (saturated solution)	
Melting point:	107.2 - 107.6 °C (1,013 hPa)	(Directive 92/69/EEC, A.1)
Boiling point:	approx. 230 °C The substance / product decomposes therefore not determined.	(Directive 92/69/EEC, A.2)
Flash point:	> 180 °C	(Directive 92/69/EEC, A.9, closed cup)
Evaporation rate:	< 0.01 (20 °C)	
Flammability:	not highly flammable	(Directive 92/69/EEC, A.10)
Lower explosion limit:	not determined	
Upper explosion limit:	not determined	
Vapour pressure:	> 0.0000001 Pa (20 °C)	(OECD Guideline 104)
Relative density:	1.42 (20 °C)	(Directive 92/69/EEC, A.3)
Relative vapour density (air):	negligible	
Solubility in water:	0.039 mg/l (20 °C)	(OECD Guideline 105)
Solubility (quantitative) solvent(s):	acetone 557 g/l (20 °C)	
Solubility (quantitative) solvent(s):	methanol 30.4 g/l (20 °C)	
Partitioning coefficient n-octanol/water (log Kow):	4.7 (20 °C; pH value: 7)	(Directive 92/69/EEC, A.8)
Self ignition:	not self-igniting	(Method: Directive 92/69/EEC, A.16)
Thermal decomposition:	No decomposition if stored and handled as prescribed/indicated.	
Viscosity, dynamic:	not applicable	
Viscosity, kinematic:	not applicable	
Explosion hazard:	not explosive	(Directive 92/69/EEC, A.14)
Fire promoting properties:	not fire-propagating	(Directive 92/69/EEC, A.17)

Other information

Bulk density:	240 kg/m3 (20 °C)	
pKA:	The substance does not dissociate.	(OECD Guideline 112)
Surface tension:	72.3 mN/m (20 °C; 0.00004 g/l)	(Directive 92/69/EEC, A.5)
Grain size distribution:	No data available.	
Molar mass:	376.3 g/mol	

10. Stability and Reactivity

Reactivity
No hazardous reactions if stored and handled as prescribed/indicated.

Corrosion to metals:	Corrosive effects to metal are not anticipated. Not corrosive to: mild steel	
Formation of flammable gases:	Information on hazardous decomosition products:	Forms no flammable gases in the presence of water.

Chemical stability

The product is stable if stored and handled as prescribed/indicated.

Possibility of hazardous reactions
No hazardous reactions if stored and handled as prescribed/indicated.

Conditions to avoid
Avoid all sources of ignition: heat, sparks, open flame. Avoid extreme temperatures. Avoid prolonged exposure to extreme heat. Avoid contamination. Avoid electro-static discharge. Avoid prolonged storage.

Incompatible materials

Substances to avoid:
No substances known that should be avoided.

Hazardous decomposition products

Hazardous decomposition products:
No hazardous decomposition products if stored and handled as prescribed/indicated.

11. Toxicological Information

Information on toxicological effects

Acute toxicity

Assessment of acute toxicity:
Virtually nontoxic after a single ingestion. Virtually nontoxic after a single skin contact. Virtually nontoxic by inhalation.

Experimental/calculated data:
LD50 rat (oral): > 5,000 mg/kg (OECD Guideline 401)

LC50 rat (by inhalation): > 5.9 mg/l 4 h (OECD Guideline 403)
No mortality was observed.

LD50 rat (dermal): > 4,000 mg/kg (OECD Guideline 402)
No mortality was observed.

Irritation

Assessment of irritating effects:
Not irritating to the skin. Not irritating to the eyes.

Experimental/calculated data:
Skin corrosion/irritation rabbit: non-irritant (OECD Guideline 404)

Serious eye damage/irritation rabbit: non-irritant (OECD Guideline 405)

Respiratory/Skin sensitization

Assessment of sensitization:
There is no evidence of a skin-sensitizing potential.

Experimental/calculated data:
Guinea pig maximization test guinea pig: Non-sensitizing. (OECD Guideline 406)

Germ cell mutagenicity

Assessment of mutagenicity:
No mutagenic effect was found in various tests with microorganisms and mammalian cell culture. The substance was not mutagenic in a test with mammals.

Carcinogenicity

Assessment of carcinogenicity:
In long-term studies in rats and mice in which the substance was given by feed, a carcinogenic effect was not observed.

Reproductive toxicity

Assessment of reproduction toxicity:
The results of animal studies gave no indication of a fertility impairing effect.

Developmental toxicity

Assessment of teratogenicity:
Animal studies gave no indication of a developmental toxic effect at doses that were not toxic to the parental animals.

Specific target organ toxicity (single exposure)

Assessment of STOT single:
The available information is not sufficient for evaluation.

Repeated dose toxicity and Specific target organ toxicity (repeated exposure)

Assessment of repeated dose toxicity:
Repeated exposure to large quantities may affect certain organs.

Aspiration hazard

No aspiration hazard expected.

Other relevant toxicity information

Misuse can be harmful to health.

12. Ecological Information

Toxicity

Toxicity to fish:
LC50 (96 h) > 0.68 mg/l, Oncorhynchus mykiss

Aquatic invertebrates:
EC50 (48 h) > 0.45 mg/l, Daphnia magna

Aquatic plants:
EC50 (72 h) 0.000025 mg/l, algae

Microorganisms/Effect on activated sludge:
No data available concerning toxicity for bacteria.

Soil living organisms:
No data available.

Terrestrial plants:
EC50 5 - 10 g a.s./ha,

Persistence and degradability

Assessment biodegradation and elimination (H2O):
Not readily biodegradable (by OECD criteria).

Bioaccumulative potential

Bioaccumulation potential:
Because of the n-octanol/water distribution coefficient (log Pow) accumulation in organisms is possible.

Mobility in soil (and other compartments if available)

Assessment transport between environmental compartments:
No data available.

Results of PBT and vPvB assessment

Not fulfilling PBT (persistent/bioaccumulative/toxic) criteria..

Not fulfilling vPvB (very persistent/very bioaccummulative) criteria..

Other adverse effects

The substance is not listed in Annex I of Regulation (EC) 2037/2000 on substances that deplete the ozone layer.

13. Disposal Considerations

Waste treatment methods

Do not discharge into drains/surface waters/groundwater.
Must be disposed of or incinerated in accordance with local regulations.

Contaminated packaging:
Contaminated packaging should be emptied as far as possible and disposed of in the same manner as the substance/product.

14. Transport Information

Land transport

ADR

Hazard class:	9
Packing group:	III
ID number:	UN 3077
Hazard label:	9, EHSM
Proper shipping name:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains PICOLINAFEN 97%)

RID

Hazard class:	9
Packing group:	III
ID number:	UN 3077
Hazard label:	9, EHSM
Proper shipping name:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains PICOLINAFEN 97%)

Inland waterway transport

ADNR

Hazard class:	9
Packing group:	III
ID number:	UN 3077
Hazard label:	9, EHSM
Proper shipping name:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains PICOLINAFEN 97%)

Sea transport
IMDG

Hazard class:	9
Packing group:	III
ID number:	UN 3077
Hazard label:	9, EHSM
Marine pollutant:	YES
Proper shipping name:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains PICOLINAFEN 97%)

Air transport
IATA/ICAO

Hazard class:	9
Packing group:	III
ID number:	UN 3077
Hazard label:	9, EHSM
Proper shipping name:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (contains PICOLINAFEN 97%)

15. Regulatory Information

Safety, health and environmental regulations/legislation specific for the substance or mixture

Chemical Safety Assessment

A chemical safety assessment acc. to art. 14 of Regulation (EC) No 1907/2006 is not required, because art. 15 of the same regulation applies.

16. Other Information

Vertical lines in the left hand margin indicate an amendment from the previous version.

The data contained in this safety data sheet are based on our current knowledge and experience and describe the product only with regard to safety requirements. The data do not describe the product's properties (product specification). Neither should any agreed property nor the suitability of the product for any specific purpose be deduced from the data contained in the safety data sheet. It is the responsibility of the recipient of the product to ensure any proprietary rights and existing laws and legislation are observed.

3.8 Procedures for destruction and decontamination

3.8.1 Pyrolytic behaviour under controlled conditions at 800°C

Not required as the halogen content of picolinafen is less than 60%.

3.8.2 Detailed instructions for safe disposal

Unwanted amounts of picolinafen can be destroyed best by combustion in a licensed incinerator, in accordance with local regulations.

Contaminated packs and/or equipment that cannot be cleaned by washing with water should be disposed of in the same manner as the product.

3.8.3 Methods other than controlled incineration for disposal

No alternative to incineration for disposal of active ingredient has been identified.

3.9 Procedures for decontamination of water in case of an accident

There are no readily available methods for decontamination of water. Precautions must be taken to avoid contamination as advised on the MSDS (see point 3.7 – BASF DocID 2012/1219501).

3.10 Other/special studies

None

9 Proposals for classification and labelling of the a.s.

The following is proposed in accordance with Directive 99/45/EC in combination with the latest classification and labelling guidance under Directive 67/548/EEC (i.e. in the 18th ATP published as Directive 93/21/EEC):

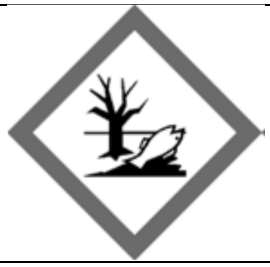
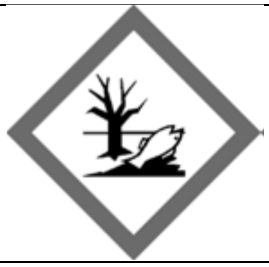
Picolinafen:

Hazard Symbol:	**N**	
Indication of danger:	**-**	
Risk Phrases:	**R50/53**	Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.
Safety Phrases:	**S 35**	This material and its container must be disposed of in a safe way.
	S61	Avoid release to the environment. Refer to special instructions/safety data sheet.

BAS 700 03H:

Hazard Symbol:	**N**	
Indication of danger:	**-**	
Risk Phrases:	**R50/53**	Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.
Safety Phrases:	**S 35**	This material and its container must be disposed of in a safe way.
	S61	Avoid release to the environment. Refer to special instructions/safety data sheet.

The following is proposed in accordance with Regulation (EC) No 1272/2008:

	Picolinafen	**BAS 700 03H**
GHS pictogram		
Signal word	Warning	Warning
Hazard statement	H410: Very toxic to aquatic life with long lasting effects	H410: Very toxic to aquatic life with long lasting effects
Precautionary Statement Prevention	P273	P273
Precautionary Statement Response	P391	P391
Precautionary Statement Storage	-	-
Precautionary Statement Disposal	P501	P501

The Chemical Company

DOSSIER FOR THE EVALUATION OF THE ACTIVE SUBSTANCE

Picolinafen (BAS 700 H)

Data requirement according to Regulation (EU) No. 544/2011 and (EU) No. 545/2011
of 10 June 2011 (formerly Annex II and III of Directive 91/414/EEC)
using OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substance (Dossier Guidance)
and Commission Regulation (EC) No 1141/2010 of 7 December 2010 (AIR procedure)

Document M-II

Summary and evaluation (Tier II)

Section 2

Analytical methods

BASF DocID 2012/1208876

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Date: 30 August 2012

4 Analytical Methods and Validation

List of Contents

4.1 Analytical standards and samples

4.1.1 Analytical standards for pure active substance

Samples will be provided on request.

4.1.2 Samples of the active substance as manufactured

Samples will be provided on request.

4.1.3 Analytical standards for relevant metabolites and other components

Samples will be provided on request.

4.1.4 Samples of reference substances for relevant impurities

Samples will be provided on request.

4.2 Methods for the analysis of the active substance as manufactured

4.2.1 Methods for the analysis of the active substance as manufactured

Refer to the DAR, dated September 2000.

4.2.2 Applicability of existing CIPAC methods

Refer to the DAR, dated September 2000.

4.2.3 Description of analytical methods for the determination of impurities

Refer to the DAR, dated September 2000.

4.2.4 Description of analytical methods for the determination of additives

Refer to the DAR, dated September 2000.

4.2.5 Enforcement analytical methodology

Refer to the DAR, dated September 2000.

4.2.6 Inter-Laboratory analytical methodology validation

Refer to the DAR, dated September 2000.

4.2.7 Storage stability of working solutions in analytical methodology

Refer to the DAR, dated September 2000.

4.3 Description of analytical methods for the determination of residues

New methods of analysis are provided for the determination of residues (Point 4.3). The provision of new data is justified on the grounds that new analytical methods are required for a number of crop groups and animal products to allow compliance with existing or proposed MRL's. Furthermore, the methods assessed in the original review for picolinafen were not validated to the standards given in the most recent guidance documents (SANCO/825/00 rev.8.1, 16th November 2010 and SANCO/3029/99 rev.4 11th July 2000 for pre- and post-registration methods). Validation of previously assessed methods would now be inadequate in a number of important respects and new requirements have since become mandatory. The methods of analysis summarised below are intended to fully replace the methods assessed in the original review.

Report:	II A 4.3/1 Class T., Merdian N. 2010(a) Picolinafen: Development and validation of a multi-residue enforcement method for the determination and confirmation of Picolinafen (BAS 700 H) in four crop types BASF DocID 2010/1209768
Guidelines:	EEC 91/414 Annex II (Part A Section 4.2); SANCO/825/00 rev. 7 (17 March 2004)
GLP:	Yes (laboratory certified by Umweltministerium Baden-Wuerttemberg, Stuttgart)

Principle of the method

Samples of homogenised matrix (10 g for tomato/whole orange, 5 g for barley grain, 2.5 g for rapeseed) are weighed into a 50 mL centrifuge tube and subjected to the QuEChERS multi-residue method. Water (10 mL) is added to the barley grain and rape seed samples. All samples are extracted with acetonitrile (10 mL) with shaking for 1 minute. The contents of a dispersive SPE (dSPE) citrate extraction tube are added to each sample and these are shaken for 1 minute, followed by centrifugation at > 3000 rpm for 5 minutes. The fat/oil present in the whole orange and rape seed samples are frozen out for 1 hour, followed by centrifugation at > 3000 rpm for 2 minutes. An aliquot (6 mL) of the acetonitrile layer is transferred to a dispersive SPE PSA SPE clean up tube and Bakerbond C18 (4 g) is added to the orange and rape seed samples. All samples are shaken for 30 seconds and centrifuged at > 3000 rpm for 5 minutes. The fat/oil present in the whole orange and rape seed samples are frozen out for 1 hour, followed by centrifugation at > 3000 rpm for 2 minutes. An aliquot (0.05 mL) of the supernatant is transferred to a vial, diluted to 1 mL with 1/1, v/v, acetonitrile/water containing 0.1% formic acid and analysed by high performance liquid chromatography with tandem mass specific detection (HPLC-MS/MS) in positive electrospray mode, using a Phenomenex Luna C18 column (150 mm x 2 mm, 3 µm) with gradient elution and mobile phases of 0.1% formic acid in water and 0.1% formic acid in methanol. Quantification was performed using external standards. The ion transition m/z 377 → 238 ion is used for quantification and the ion transition m/z 377 → 145 is used for confirmation.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention time of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using seven concentrations of picolinafen external standard across the range of 0.05 to 10 ng/mL. The results are presented in Table 4.3/1 below. No significant matrix effects were observed for any of the matrices.

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.3/2 and Table 4.3/3 below.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.3/2
and Table 4.3/3 below.

Limit of Quantification (LOQ)
The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 0.01 mg/kg for all matrices.

Conclusion
The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 7.

Table 4.3/1 Linearity Data

Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
377 → 238	0.05 – 10	0.9991	1.18×10^6	2.23×10^4
377 → 145	0.05 – 10	0.9988	4.42×10^5	265

Table 4.3/2 Precision and Accuracy Data (Ion Transition 377 → 238)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Tomato	0.01	5	101	3
	0.10	5	100	3
	All levels	10	101	3
Orange	0.01	5	110	1
	0.10	5	102	2
	All levels	10	106	4
Barley Grain	0.01	5	76	3
	0.10	5	73	1
	All levels	10	74	3
Rape Seed	0.01	5	73	3
	0.10	5	72	1
	All levels	10	72	2

Table 4.3/3 Precision and Accuracy Data (Ion Transition 377 → 145)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Tomato	0.01	5	104	2
	0.10	5	99	2
	All levels	10	102	3
Orange	0.01	5	109	3
	0.10	5	101	3
	All levels	10	105	5
Barley Grain	0.01	5	79	2
	0.10	5	71	1
	All levels	10	75	6
Rape Seed	0.01	5	72	1
	0.10	5	72	1
	All levels	10	72	1

Report: II A 4.3/2
Schlewitz P. 2011(h)
Independent laboratory validation of an analytical method for the analysis of Picolinafen residues in crops (barley grain, tomatoes, oilseed rape, orange)
BASF DocID 2011/1018557

Guidelines: SANCO/3029/99 rev. 4 (11 July 2000); SANCO/2009/10684; SANCO/825/00 rev. 8.1 (16 November 2010); EEC 96/46; EEC 91/414

GLP: Yes
(laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Principle of the method
As described in IIA 4.3/1.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention time of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using seven concentrations of picolinafen external standard across the range of 0.08 to 3.03 ng/mL for barley grain, 0.04 to 1.52 ng/mL for oilseed rape seeds and 0.17 to 6.06 ng/mL for tomatoes and oranges. Typical results are presented in Table 4.3/4 below. No significant matrix effects were observed..

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.3/5 and Table 4.3/6 below.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.3/5
and Table 4.3/6 below.

Limit of Quantification (LOQ)
The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 0.01 mg/kg for all matrices.

Conclusion
The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.

Table 4.3/4 Linearity Data

Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
377 → 238	0.08 – 3.03	0.9992	5.63×10^{-5}	0.01
377 → 145	0.08 – 3.03	0.9995	1.66×10^{-4}	0.02

Table 4.3/5 **Precision and Accuracy Data (Ion Transition 377 → 238)**

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Barley Grain	0.01	5	80.7	8.2
	0.10	5	73.8	5.9
	All levels	10	77.2	8.3
Tomato	0.01	5	90.1	2.4
	0.10	5	79.8	2.5
	All levels	10	85.0	6.8
Oilseed Rape Seed	0.01	5	86.3	3.8
	0.10	5	82.9	2.0
	All levels	10	84.6	3.6
Whole Orange	0.01	5	92.9	3.2
	0.10	5	96.1	1.7
	All levels	10	94.5	3.0

Table 4.3/6 **Precision and Accuracy Data (Ion Transition 377 → 145)**

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Barley Grain	0.01	5	81.4	4.1
Tomato	0.01	5	102.8	3.6
Oilseed Rape Seed	0.01	5	86.6	8.2
Whole Orange	0.01	5	102.1	4.0

Report: II A 4.3/3
Class T., Przybylek A. 2010(c)
Picolinafen: Development and validation of a multi-residue enforcement method for the determination and confirmation of Picolinafen (BAS 700 H) and its metabolite CL153815 in six types of animal food stuff
BASF DocID 2010/1209769

Guidelines: EEC 91/414 Annex II 4.2; SANCO/825/00 rev. 7 (17 March 2004)

GLP: Yes
(laboratory certified by Umweltministerium Baden-Wuerttemberg, Stuttgart)

Principle of the method
Milk - samples of homogenised matrix (10 g) are weighed into a 50 mL centrifuge tube and subjected to the QuEChERS multi-residue method. The samples are extracted with acetonitrile (10 mL) with vigorous shaking for approximately 1 minute. The contents of a dispersive SPE (dSPE) citrate extraction tube are added and the samples are shaken for approximately 1 minute, followed by centrifugation at 3000 rpm for 5 minutes. The samples are frozen out for approximately 2 hours.

Meat, Liver, Kidney, Egg - samples of homogenised matrix (5 g) are weighed into a 50 mL centrifuge tube and subjected to the QuEChERS multi-residue method. Water (5 mL) is added to each sample. The egg samples are shaken briefly and extracted with acetonitrile (10 mL) with shaking for 1 minute. The meat, liver and kidney samples are extracted with acetonitrile (10 mL) by homogenisation with Ultra Turrax for 2 minutes and the tool is washed with water (2mL). The contents of a dispersive SPE (dSPE) citrate extraction tube are added to each sample and these are shaken for 1 minute, followed by centrifugation at 3000 rpm for 5 minutes. The fat present in the samples is frozen out for approximately 2 hours.

Fat - samples of homogenised matrix (2.5 g) are weighed into a 50 mL centrifuge tube and subjected to the QuEChERS multi-residue method. Acetonitrile (10 mL) is added, the samples are warmed briefly in a water bath, then extracted with vigorous shaking for approximately 1 minute. Water (5 mL) is added and the samples are shaken and briefly warmed to reduce fat clumping. The contents of a dispersive SPE (dSPE) citrate extraction tube are added to each sample and these are shaken for approximately 1 minute, followed by centrifugation at 3000 rpm for 5 minutes. The samples are frozen out for approximately 2 hours.

All samples - an aliquot (0.067 mL for fat, 0.05 mL for all other samples) of the supernatant is transferred to a vial, diluted to 1 mL with 1/1, v/v, acetonitrile/water containing 0.1% formic acid and analysed for content of picolinafen and metabolite CL153815 by high performance liquid chromatography with tandem mass specific detection (HPLC-MS/MS) in positive electrospray mode, using a Phenomenex Luna C18 column (150 mm x 2 mm, 3 µm) with gradient elution and mobile phases of 0.1% formic acid in water and 0.1% formic acid in methanol. Quantification was performed using external standards. The picolinafen ion transition m/z 377 → 238 ion is used for quantification and the ion transition m/z 377 → 145 is used for confirmation. The CL153815 ion transition m/z 284 → 238 ion is used for quantification and the ion transition m/z 284 → 145 is used for confirmation.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention times of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using nine concentrations of external standard across the range of 0.025 to 10 ng/mL for each analyte. The results are presented in Table 4.3/7 below. No significant matrix effects were observed for any of the matrices.

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix and analyte. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.3/8, Table 4.3/9, Table 4.3/10 and Table 4.3/11.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix and analyte. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.3/8, Table 4.3/9, Table 4.3/10, Table 4.3/11.

Limit of Quantification (LOQ)
The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 0.01 mg/kg for each analyte in all matrices.

Conclusion
The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 7.

Table 4.3/7 Linearity Data

Analyte	Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
Picolinafen	377 → 238	0.025 – 10	0.9990	1.22×10^6	-1.5×10^3
	377 → 145	0.025 – 10	0.9994	4.14×10^5	-3.1×10^3
CL153815	284 → 238	0.025 – 10	0.9994	2.46×10^6	-7.7×10^3
	284 → 145	0.025 – 10	0.9999	1.07×10^6	-7.6×10^3

Table 4.3/8 Precision and Accuracy Data (Picolinafen Ion Transition 377 → 238)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Milk	0.01	5	95	5
	0.10	5	96	4
	All levels	10	95	4
Egg	0.01	5	93	2
	0.10	5	92	3
	All levels	10	93	2
Meat (bovine)	0.01	5	98	3
	0.10	5	97	6
	All levels	10	98	4
Liver (bovine)	0.01	5	94	3
	0.10	5	99	4
	All levels	10	96	4
Kidney (bovine)	0.01	5	96	4
	0.10	5	86	4
	All levels	10	91	7
Fat (bovine)	0.01	5	84	1
	0.10	5	85	6
	All levels	10	85	4

Table 4.3/9 Precision and Accuracy Data (Picolinafen Ion Transition 377 → 145)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Milk	0.01	5	96	5
	0.10	5	95	3
	All levels	10	96	4
Egg	0.01	5	100	3
	0.10	5	93	2
	All levels	10	97	5
Meat (bovine)	0.01	5	104	3
	0.10	5	99	5
	All levels	10	101	5
Liver (bovine)	0.01	5	101	1
	0.10	5	98	4
	All levels	10	100	3
Kidney (bovine)	0.01	5	95	2
	0.10	5	83	4
	All levels	10	89	8
Fat (bovine)	0.01	5	82	3
	0.10	5	86	5
	All levels	10	84	5

Table 4.3/10 Precision and Accuracy Data (CL153815 Ion Transition 284 → 238)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Milk	0.01	5	74	5
	0.10	5	95	3
	All levels	10	84	13
Egg	0.01	5	70	1
	0.10	5	90	2
	All levels	10	80	13
Meat (bovine)	0.01	5	71	1
	0.10	5	85	3
	All levels	10	78	10
Liver (bovine)	0.01	5	72	1
	0.10	5	90	3
	All levels	10	81	12
Kidney (bovine)	0.01	5	73	3
	0.10	5	89	2
	All levels	10	81	10
Fat (bovine)	0.01	5	79	3
	0.10	5	103	4
	All levels	10	91	14

Table 4.3/11 Precision and Accuracy Data (CL153815 Ion Transition 284 → 145)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Milk	0.01	5	73	5
	0.10	5	94	4
	All levels	10	83	14
Egg	0.01	5	70	1
	0.10	5	87	2
	All levels	10	79	11
Meat (bovine)	0.01	5	71	2
	0.10	5	82	3
	All levels	10	77	8
Liver (bovine)	0.01	5	71	1
	0.10	5	85	3
	All levels	10	78	10
Kidney (bovine)	0.01	5	73	2
	0.10	5	83	3
	All levels	10	78	7
Fat (bovine)	0.01	5	79	2
	0.10	5	99	5
	All levels	10	89	12

Report: II A 4.3/4
Schlewitz P. 2011(i)
Independent laboratory validation of an analytical method for the analysis of Picolinafen and its metabolite residues in six types of animal food stuff (eggs, milk, fat, liver, kidney and meat)
BASF DocID 2011/1018558

Guidelines: SANCO/825/00 rev. 8.1 (16 November 2010); EEC 91/414; EEC 96/46; SANCO/3029/99 rev. 4 (11 July 2000); SANCO/2009/10684

GLP: Yes
(laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Principle of the method
As described in IIA 4.3/3.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention times of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using nine concentrations of external standard across the range of 0.025 to 10 ng/mL for each analyte. The results are presented in Table 4.3/12 below. No significant matrix effects were observed for any of the matrices.

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix and analyte. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.3/13, Table 4.3/14 , Table 4.3/15 and Table 4.3/16 below.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ for each matrix and analyte. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.3/13, Table 4.3/14, Table 4.3/15 and Table 4.3/16 below.

Limit of Quantification (LOQ)
The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 0.01 mg/kg for each analyte in all matrices.

Conclusion
The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.

Table 4.3/12 Linearity Data

Analyte	Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
Picolinafen	377 → 238	0.025 – 10	0.9907	2.05×10^{-5}	-0.15
	377 → 145	0.025 – 10	0.9903	6.11×10^{-5}	-0.13
CL153815	284 → 238	0.025 – 10	0.9991	1.51×10^{-5}	-0.03
	284 → 145	0.025 – 10	0.9991	4.80×10^{-5}	-0.03

Table 4.3/13 Precision and Accuracy Data (Picolinafen Ion Transition 377 → 238)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Egg	0.01	5	99.6	3.6
	0.10	5	100.5	1.2
	All levels	10	100.0	2.6
Milk	0.01	5	83.9	8.0
	0.10	5	87.9	3.9
	All levels	10	85.9	6.3
Fat (bovine)	0.01	5	73.9	3.2
	0.10	5	75.5	1.9
	All levels	10	74.7	2.7
Liver (bovine)	0.01	5	82.1	3.8
	0.10	5	84.5	2.8
	All levels	10	83.3	3.5
Kidney (bovine)	0.01	5	101.0	1.9
	0.10	5	102.4	3.2
	All levels	10	101.7	2.6
Meat (bovine)	0.01	5	103.4	4.3
	0.10	5	103.0	3.9
	All levels	10	103.2	3.9

Table 4.3/14 Precision and Accuracy Data (Picolinafen Ion Transition 377 → 145)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Egg	0.01	5	96.2	7.4
Milk	0.01	5	92.6	9.3
Fat (bovine)	0.01	5	71.5	2.2
Liver (bovine)	0.01	5	82.9	6.3
Kidney (bovine)	0.01	5	97.0	3.7
Meat (bovine)	0.01	5	102.2	6.9

Table 4.3/15 Precision and Accuracy Data (CL153815 Ion Transition 284 → 238)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Egg	0.01	5	79.5	3.0
	0.10	5	95.0	1.5
	All levels	10	87.2	9.6
Milk	0.01	5	77.1	5.1
	0.10	5	92.8	0.8
	All levels	10	84.9	10.3
Fat (bovine)	0.01	5	73.7	4.5
	0.10	5	100.6	3.6
	All levels	10	87.2	16.7
Liver (bovine)	0.01	5	76.5	1.9
	0.10	5	87.9	1.7
	All levels	10	82.2	7.5
Kidney (bovine)	0.01	5	89.0	3.2
	0.10	5	103.6	3.1
	All levels	10	96.3	8.5
Meat (bovine)	0.01	5	82.1	2.9
	0.10	5	96.5	4.6
	All levels	10	89.3	9.3

Table 4.3/16 Precision and Accuracy Data (CL153815 Ion Transition 284 → 145)

Matrix	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Egg	0.01	5	78.2	1.5
Milk	0.01	5	79.0	4.7
Fat (bovine)	0.01	5	80.8	3.7
Liver (bovine)	0.01	5	81.6	1.0
Kidney (bovine)	0.01	5	72.9	2.4
Meat (bovine)	0.01	5	88.1	2.0

4.4 Description of methods for analysis of soil (parent and metabolites)

New methods of analysis are provided for the determination of residues in soil (Point 4.4). The provision of new data is justified on the grounds that the methods assessed in the original review for picolinafen were not validated to the standards given in the most recent guidance documents (SANCO/825/00 rev.8.1, 16th November 2010 and SANCO/3029/99 rev.4 11th July 2000 for pre- and post-registration methods). Validation of previously assessed methods would now be inadequate in a number of important respects and new requirements have since become mandatory. The methods of analysis summarised below are intended to fully replace the methods assessed in the original review.

Report:	II A 4.4/1 Schlewitz P. 2011(c) Validation of the analytical method for the determination of Picolinafen residues in soil BASF DocID 2011/1018559
Guidelines:	SANCO/825/00 rev. 8.1 (16 November 2010); EEC 91/414; EEC 96/46; SANCO/3029/99 rev. 4 (11 July 2000)
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Principle of the method (DFG S19 multi-residue method)
Soil samples (10 g) are homogenised with water (25 mL) and acetone (50 mL) for 10 minutes using a magnetic stirrer. Celite 545 (10 g) is added and the samples are swirled for 10 seconds. The mixture is vacuum filtered (low vacuum) avoiding the filter cake becoming completely dry and the filter cake is then rinsed with acetone (10 mL). The filtrate is transferred to separating funnel with sodium chloride (5 g) and shaken vigorously for 5 minutes. Dichloromethane is added (25 mL), the flask is shaken for 5 minutes and the phases are allowed to separate for 10 minutes. The aqueous phase is re-extracted with dichloromethane (20 mL) and the aqueous phase is discarded. Anhydrous sodium sulphate (10 g) is added to the combined organic phases and the solution is shaken periodically for 5 minutes. The solution is filtered through a paper filter (15 cm) and anhydrous sodium sulphate (3 cm). The filtrate is collected in a 500 mL round bottomed flask and the filter paper is rinsed with dichloromethane (2 x 20 mL). The combined filtrates are concentrated to a volume of 2 mL on a rotary evaporator and remaining solvent is removed under a stream of nitrogen. The residue is reconstituted in hexane (2 mL) and transferred onto a SPE silica gel cartridge for clean up. The flask is rinsed with 65/35, v/v, hexane/toluene (6 mL) and this is added to the cartridge. The flask is further rinsed with toluene (6 mL) and this is added to the cartridge. The cartridge is eluted with 95/5, v/v, toluene/acetone (10 mL). The eluate is evaporated to dryness under a stream of nitrogen, reconstituted in ethanol (10 mL) and analysed by ultra high performance liquid chromatography with tandem mass specific detection (UPLC-MS/MS) in positive electrospray mode, using a Waters Luna C18 column (100 mm x 4.6 mm, 1.7 µm) with gradient elution and mobile phases of 0.1% formic acid in water and 0.1% formic acid in acetonitrile. Quantification was performed using external standards. The ion transition m/z 377.1 → 238.0 ion is used for quantification and the ion transition m/z 377.1 → 145.0 is used for confirmation.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention time of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using seven concentrations of picolinafen external standard across the range of 3.3 to 121.2 ng/mL. The results are presented in Table 4.4/1 below.

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.4/2 below.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.4/2 below.

Limit of Quantification (LOQ)
The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 0.01 mg/kg in soil.

Conclusion
The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.

Table 4.4/1 Linearity Data

Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
377.1 → 238	3.3 – 121.2	0.9991	2.60×10^{-4}	0.38
377.1 → 145	3.3 – 121.2	0.9990	7.55×10^{-4}	0.34

Table 4.4/2 Precision and Accuracy Data

Matrix	Ion Transition (m/z)	Fortification Level (mg/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
Soil	377.1 → 238	0.01	5	79.4	7.8
		0.10	5	79.8	4.3
		All levels	10	79.6	5.9
	377.1 → 145	0.01	5	79.3	7.9

4.5 Description of methods of analysis of water (parent and metabolites)

New methods of analysis are provided for the determination of residues in water (Point 4.5). The provision of new data is justified on the grounds that the methods assessed in the original review for picolinafen were not validated to the standards given in the most recent guidance documents (SANCO/825/00 rev.8.1, 16th November 2010 and SANCO/3029/99 rev.4 11th July 2000 for pre- and post-registration methods). Validation of previously assessed methods would now be inadequate in a number of important respects and new requirements have since become mandatory. The methods of analysis summarised below are intended to fully replace the methods assessed in the original review.

Report:	II A 4.5/1 Schlewitz P. 2011(d) Validation of the analytical method for the determination of Picolinafen residues in surface, ground and drinking water BASF DocID 2011/1018560
Guidelines:	SANCO/825/00 rev. 8.1 (16 November 2010); EEC 91/414; EEC 96/46; SANCO/3029/99 rev. 4 (11 July 2000)
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Report:	II A 4.5/2 Schlewitz P. 2012(c) Amendment No. 1 to report No. B0229 - Validation of the analytical method for the determination of Picolinafen residues in surface, ground and drinking water BASF DocID 2012/1216405
Guidelines:	SANCO/825/00 rev. 8.1 (16 November 2010); EEC 91/414; EEC 96/46; SANCO/3029/99 rev. 4 (11 July 2000)
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Principle of the method (DFG S19 multi-residue method)
Surface Water - samples (100 mL) are mixed with acetone (200 mL) in a separating funnel. Dichloromethane is added (150 mL), the flask is shaken for 5 minutes and the phases are allowed to separate for approximately 10 minutes. The aqueous phase is re-extracted with dichloromethane (75 mL) and the aqueous phase is discarded.

Groundwater and Drinking Water - samples (25 mL) are mixed with acetone (50 mL) in a separating funnel. Dichloromethane is added (40 mL), the flask is shaken for 5 minutes and the phases are allowed to separate for approximately 10 minutes. The aqueous phase is re-extracted with dichloromethane (20 mL) and the aqueous phase is discarded.

All samples - the solution is filtered through a paper filter (15 cm) and anhydrous sodium sulphate (20 g). The filtrate is collected and the filter paper is rinsed with dichloromethane (2 x 20 mL). The combined filtrates are concentrated to a volume of 2 mL on a rotary evaporator and remaining solvent is removed under a stream of nitrogen. The residue is reconstituted in hexane (2 mL) and transferred onto a SPE silica gel cartridge for clean up. The flask is rinsed with 65/35, v/v, hexane/toluene (6 mL) and this is added to the cartridge. The flask is further rinsed with toluene (6 mL) and this is added to the cartridge. The cartridge is eluted with 95/5, v/v, toluene/acetone (10 mL). The eluate is evaporated to dryness under a stream of nitrogen, reconstituted in ethanol (1 mL for surface water, 10 mL for drinking and ground water) and analysed by ultra high performance liquid chromatography with tandem mass specific detection (UPLC-MS/MS) in positive electrospray mode, using a Waters BEH C18 column (50 mm x 2.1 mm, 1.7 µm) with gradient elution and mobile phases of 0.1% formic acid in water and 0.1% formic acid in acetonitrile. Quantification was performed using external standards. The ion transition m/z 377.1 → 238.0 ion is used for quantification and the ion transition m/z 377.1 → 145.0 is used for confirmation.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention time of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using seven concentrations of picolinafen external standard across the range of 0.087 to 3.156 ng/mL. The results are presented in Table 4.5/1 below.

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.5/2 below.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.5/2.

Limit of Quantification (LOQ)

The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 0.1 µg/L in drinking water and groundwater and 0.0025 µg/L in surface water.

Conclusion

The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.

Table 4.5/1 Linearity Data

Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
377 → 238	0.087 – 3.156	0.9999	9.26×10^{-4}	-
377 → 145	0.087 – 3.156	0.9979	2.86×10^{-3}	0.02

Table 4.5/2 Precision and Accuracy Data

Matrix	Ion Transition (m/z)	Fortification Level (µg/L)	Number of Samples	Mean Recovery (%)	RSD (%)
Surface Water	377.1 → 238	0.0025	5	94.9	13.4
		0.025	5	83.5	9.9
		All levels	10	89.2	13.2
Ground Water	377.1 → 238	0.1	5	86.4	13.7
		1.0	5	74.2	3.9
		All levels	10	80.3	12.9
Drinking Water	377.1 → 238	0.1	5	80.6	8.4
		1.0	5	78.4	8.7
		All levels	10	79.5	8.2
Surface Water	377.1 → 145	0.0025	5	92.1	17.6
Ground Water	377.1 → 145	0.1	5	87.7	18.4
Drinking Water	377.1 → 145	0.1	5	76.3	14.4

4.6 Method for determining pesticides in sediment

This is not a requirement under Directive 91/414/EEC / Reg. (EC) No. 1107/2009.

4.7 Methods for analysis of air (parent and metabolites)

New methods of analysis are provided for the determination of residues in air (Point 4.7). The provision of new data is justified on the grounds that the methods assessed in the original review for picolinafen were not validated to the standards given in the most recent guidance documents (SANCO/825/00 rev.8.1, 16th November 2010 and SANCO/3029/99 rev.4 11th July 2000 for pre- and post-registration methods). Validation of previously assessed methods would now be inadequate in a number of important respects and new requirements have since become mandatory. The methods of analysis summarised below are intended to fully replace the methods assessed in the original review.

Report:	II A 4.7/1 Schlewitz P. 2011(e) Validation of the analytical method for the determination of Picolinafen residues in air BASF DocID 2011/1018561
Guidelines:	SANCO/825/00 rev. 8.1 (16 November 2010); EEC 91/414; EEC 96/46; SANCO/3029/99 rev. 4 (11 July 2000); SANCO/2009/10684
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Report:	II A 4.7/2 Schlewitz P. 2012(d) Amendment No. 1 to report No. R B0231 - Validation of the analytical method for the determination of Picolinafen residues in air BASF DocID 2012/1216406
Guidelines:	SANCO/825/00 rev. 8.1 (16 November 2010); EEC 91/414; EEC 96/46; SANCO/3029/99 rev. 4 (11 July 2000); SANCO/2009/10684
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Principle of the method

Adsorption tubes are placed onto a suction system linked to an AirLite pump, in a drying oven at 35°C with a relative humidity of 80%. Air is passed through the tubes with a flow of 1L/min for 6 hours. The system is removed from the oven and picolinafen residues are eluted with acetonitrile (20 mL added dropwise). The sample is made to a volume of 25 mL with acetonitrile and finally diluted 1 by 4 (nominal final volume 100 mL). An aliquot is syringe filtered (0.2 µm PTFE) and analysed by ultra high performance liquid chromatography with tandem mass specific detection (UPLC-MS/MS) in positive electrospray mode, using a Waters BEH C18 column (50 mm x 2.1 mm, 1.7 µm) with gradient elution and mobile phases of 0.1% formic acid in water and 0.1% formic acid in acetonitrile. Quantification was performed using external standards. The ion transition m/z 377.1 → 238.0 ion is used for quantification and the ion transition m/z 377.1 → 145.0 is used for confirmation.

Specificity
LC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.
No interferences at >30% of the LOQ were present at the retention time of interest in control matrix samples.

Linearity
Linearity of detector response was demonstrated using seven concentrations of picolinafen external standard across the range of 0.01 to 0.39 ng/mL. The results are presented in Table 4.7/1 below.

Precision (Repeatability)
Repeatability data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ. The relative standard deviations (RSD) obtained for each fortification level were within the guideline requirements of less than 20% and are presented in Table 4.7/2 below.

Accuracy (Recovery)
Recovery data was generated from five samples fortified at the LOQ and five samples fortified at 10 x LOQ. The mean percentage recoveries at each fortification level were within the guideline requirements of 70 - 110% and are presented in Table 4.7/2 below.

Limit of Quantification (LOQ)
The limit of quantitation (LOQ), defined as the lowest fortification level where acceptable precision and accuracy data were obtained, was determined to be 9.25 µg/m^3 in air.

Breakthrough
No breakthrough was observed for picolinafen at a level of 92.58 µg/m^3 and a sampling period of 6 hours.

Conclusion
The analytical procedure has been successfully validated in terms of specificity, linearity, precision, accuracy and LOQ, in accordance with all of the requirements of SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.

Table 4.7/1 Linearity Data

Ion Transition (m/z)	Concentration Range (ng/mL)	Correlation Coefficient (r)	Slope	Intercept
377.1 → 238	0.01 – 0.39	0.9977	1.59×10^{-4}	- 0.01
377.1 → 145	0.01 – 0.39	0.9941	4.34×10^{-4}	-

Table 4.7/2 Precision and Accuracy Data

Matrix	Ion Transition (m/z)	Fortification Level (µg/m^3)	Number of Samples	Mean Recovery (%)	RSD (%)
Air (35°C / 80% RH)	377.1 → 238	9.25	5	95.0	6.7
		92.58	5	103.6	6.8
		All levels	10	99.3	7.8
	377.1 → 145	9.25	5	94.6	12.0

4.8 Methods for analysis of body fluid/tissues (parent and metabolites)

Not required as Picolinafen is not classified as toxic or highly toxic.

4.9 Other/special studies

Report:	II A 4.9/1 Harper H. 2012(b) Picolinafen (BAS 700 H) - Validation of methodology for the determination of Picolinafen (BAS 700 H) in microcosm water and sediment, and in dose solutions BASF DocID 2011/1122556
Guidelines:	None
GLP:	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)

Principle of the method
Microcosm water - Samples (40 mL) are extracted with dichloromethane (5 mL) with vigorous shaking. The layers are allowed to separate and the lower organic layer is removed to a polypropylene tube via a drying cartridge containing sodium sulfate. The extraction step is repeated and the organic layers are combined. The combined extracts are evaporated to dryness under a stream of nitrogen in a water bath at 40°C and reconstituted in acetonitrile/water, 1/1, v/v (2 mL). The samples are further diluted with acetonitrile/water, 1/1, v/v (if required).

Sediment - Samples (5 g) are extracted with acetonitrile (10 mL) with shaking for 20 minutes. The samples are centrifuged at 3500 rpm for 3 minutes and the supernatant is decanted into a round-bottomed flask. The extraction step is repeated and the organic layers are combined. The combined extracts are evaporated to a volume of less than 5 mL under a stream of nitrogen in a water bath at 40°C and made to a volume of 10 mL with acetonitrile/water, 1/1, v/v. The samples are further diluted with control final extract (if required).

Dose solutions – Samples (5 mL) are made to a volume of 50 mL with acetonitrile (10 mL). An aliquot (1 mL) is transferred to a vial and made to a volume of 10 mL with acetonitrile/water, 1/1, v/v. The samples are further diluted with acetonitrile/water, 1/1, v/v (if required).

All samples are analysed for picolinafen content by high performance liquid chromatography with tandem mass specific detection (HPLC-MS/MS), using a Phenomenex Luna C8 column (150 mm x 2.0 mm, 5 µm particle size), with mobile phases of 90/10/0/1, v/v/v, water/methanol/formic acid containing 0.01M ammonium formate and methanol containing 0.1% formic acid. The ion transition m/z 377 → 238 is used for quantification and the ion transition m/z 377 → 359 is used for confirmation. Calibration is performed using external standards.

Specificity
HPLC-MS/MS monitoring two ion transitions is considered to be a highly specific technique.

Analysis of blank control samples demonstrated that no interferences at > 30% of LOQ were present at the retention time of interest. Analyte identity was confirmed by retention time match with analytical standards.

Linearity
Linearity of detector response was demonstrated using nine concentrations of analytical standard across the range of 0.2 to 5 ng/mL. The results are presented in Table IIA 4.9/1 below.

Repeatability (Precision)
Repeatability data was generated from five samples of microcosm water fortified at 0.02 µg/L and 10 µg/L, from five samples of sediment fortified at 1 ng/g and 100 ng/g and from five samples of dose solution fortified at 100 µg/L and 10000 µg/L. The relative standard deviations (RSD) obtained for each fortification level and matrix were within the guideline requirements of less than 20% and are presented in Table IIA 4.9/2 below.

Recovery (Accuracy)
Recovery data was generated from five samples of microcosm water fortified at 0.02 µg/L and 10 µg/L, from five samples of sediment fortified at 1 ng/g and 100 ng/g and from five samples of dose solution fortified at 100 µg/L and 10000 µg/L. The mean percentage recoveries at each fortification level and matrix were within the guideline requirements of 70 - 110% and are presented in Table IIA 4.9/2 below.

Limit of Quantification
The limit of quantitation (LOQ), defined as the lowest fortification level at which acceptable precision and accuracy data were obtained, was determined to be 0.02 µg/L for microcosm water, 1 ng/g for sediment and 100 µg/L for dose solutions.

Conclusion
This validation study fulfils all of the requirements of the guidance document on residue analytical methods, SANCO/3029/00 rev. 4, and is therefore considered applicable for the determination of picolinafen in microcosm water, sediment and dose solutions.

Table IIA 4.9/1: Linearity Data

Ion Transition	Concentration Range (ng/mL)	Coefficient of Determination (R^2)	Slope	Intercept
377 → 238	0.2 – 5	0.9977	1021.26	-12.2217
377 → 359	0.2 – 5	0.9983	357.606	8.83593

Table IIA 4.9/2: Precision and Accuracy Data

Matrix	Ion Transition (m/z)	Fortification Level	Number of Samples	Mean Recovery (%)	RSD (%)
Microcosm water	377 → 238	0.02 µg/L	5	89	15.2
		10 µg/L	5	90	7.9
		All levels	10	90	11.4
	377 → 359	0.02 µg/L	5	93	13.7
		10 µg/L	5	91	5.3
		All levels	10	92	9.9
Sediment	377 → 238	1 ng/g	5	103	5.0
		100 ng/g	5	103	4.2
		All levels	10	103	4.4
	377 → 359	1 ng/g	5	104	4.3
		100 ng/g	5	96	5.2
		All levels	10	100	6.4
Dose Solutions	377 → 238	100 µg/L	5	94	4.3
		10000 µg/L	5	93	10.0
		All levels	10	93	7.3
	377 → 359	100 µg/L	5	91	4.5
		10000 µg/L	5	92	6.8
		All levels	10	92	5.5

The Chemical Company

DOSSIER FOR THE EVALUATION OF THE ACTIVE SUBSTANCE

Picolinafen (BAS 700 H)

Data requirement according to Regulation (EU) No. 544/2011 and (EU) No. 545/2011 of 10 June 2011 (formerly Annex II and III of Directive 91/414/EEC)
using OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substance
(Dossier Guidance)
and Commission Regulation (EC) No 1141/2010 of 7 December 2010 (AIR procedure)

Document M-II

Summary and evaluation (Tier II)

Section 3

Toxicological and metabolism studies on the active substance

BASF DocID 2012/1208877

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Date: 30 August 2012

5 Toxicological and Toxicokinetic Studies on the Active Substance

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5 Toxicological and Toxicokinetic Studies on the Active Substance

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A comprehensive data package was submitted in order to secure the inclusion of picolinafen on Annex I to Directive 91/414/EEC. The previous evaluation concluded that no further data were required. Please refer to the DAR from Germany (dated September 2000) for further details.

The source of picolinafen has changed since Annex I inclusion (see Document JM II). The manufacturing process is essentially the same and this is described in Document JM II. The new source of technical material is equivalent to the material originally assessed for Annex I inclusion. The minimum purity of the new source does not result in a decrease in the level of purity, the maximum level of any impurity has not increased and no new impurities are present.

5.1 Absorption, distribution, excretion and metabolism in mammals

Such a study was submitted for the original Annex I inclusion (BASF DocID AR-440-001/MET 98-012). The study included a pilot experiment, a definitive experiment with 10 groups of male and female Sprague-Dawley rats (Crl: CD BR for single and multiple dose groups; Crl: CVF for biliary excretion groups) fed *ad libitum* and treated with either of picolinafen radiolabelled at two different positions (i.e. [^{14}C]pyridine label or [^{14}C]aniline label) and a supplemental experiment with male rats only. Nominal dosages were 10 mg/kg bw as the low dose and 1000 mg/kg bw as the high dose.

The study showed that picolinafen orally administered to rats was readily absorbed. The absorption for the low dose-bile groups within 48 hours was approximately 51% (male) and 67% (female) for the [^{14}C]pyridine label, and 60% (male) and 84% (female) for the [^{14}C]aniline label. For the high dose-bile groups, the percent absorption decreased to 17% and 25% for the aniline and pyridine label, respectively - presumably due to saturation of absorption, as 31-65% of the administered dose was still present in the gastrointestinal contents.

Picolinafen was almost completely excreted within 48 hours (86-89% of the single low dose). Males excreted significantly more pyridine-related residue in faeces (~68%) than urine (~20%) and comparable amounts of aniline-related radioactivity in faeces (~40%) and in urine (~48%), whereas females eliminated a greater amount of aniline-derived radioactivity in urine (~62%) than faeces (~25%) and comparable amounts of pyridine-derived radioactivity in faeces (~47%) and in urine (~39%).

Within 48 hours, 25-34% and 8-12% of the administered low dose was excreted in bile of rats treated with pyridine and aniline labelled picolinafen, respectively. In the same period, animals from the high dose group eliminated 12-17% (male) and 2% of the administered dose in bile of rats treated with pyridine and aniline labelled picolinafen, respectively. Overall recovery of radioactivity from the biliary study ranged from 93-99%. Animals in the multiple low dose experiments excreted 90-96% of the administered dose in urine and faeces within 24 hours after 7 consecutive days of dosing.

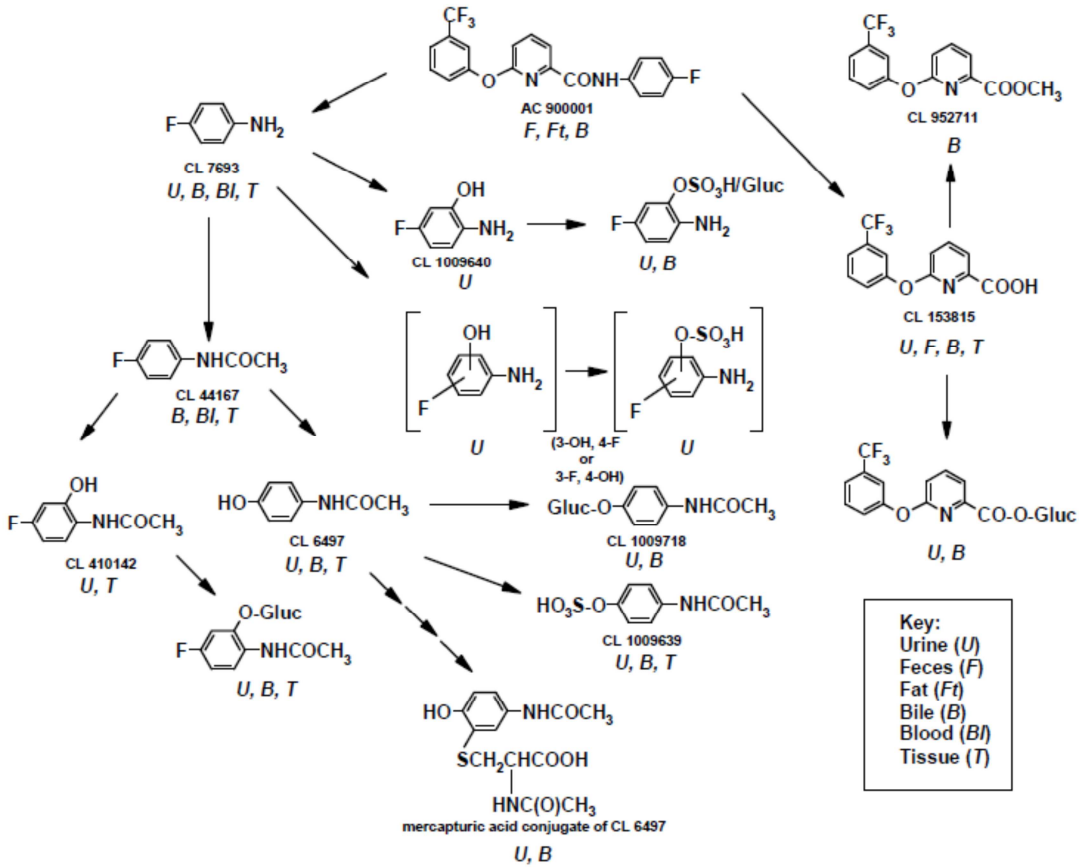
There was no evidence of a potential for bioaccumulation. Less than 0.5% of the administered dose was detected in the tissues and carcass by 7-days post-dosing. Tissue residue values ranged from 0.004-2.513 ppm in the low dose group and from 0.268-23.005 ppm in the high dose group. The tissues with the highest concentrations were fat, liver and kidneys in rats treated with pyridine labelled picolinafen and blood, spleen and liver in rats treated with aniline labelled picolinafen.

Based on the major metabolites that were identified in rat urine, faeces, bile, and specific tissues, a metabolic pathway was proposed which shows that hydrolysis, oxidation, acetylation, and subsequent glucuronide and sulfate conjugations constitute the major biotransformation processes for picolinafen in the rat.

Irrespective of the label, picolinafen was the predominant radiocomponent in faeces, accounting for 97-99% of the extractable radioactivity. In urine and bile, the substituted picolinic acid CL 153815 and its glucuronide ester were the major metabolites (58.2-84.1% and 7.2-29.2%, respectively) when the [pyridine-^{14}C]-labelled picolinafen was administered, whereas a more complex metabolic profile was obtained with the [aniline-^{14}C]-labelled picolinafen. This included the sulphate conjugates of 2-amino-5-fluorophenol and acetaminophen (52.9 and 26.1%, respectively), the mercapturic acid conjugate of acetaminophen (9.1%), acetaminophen (3.4%), the glucuronide conjugate of acetaminophen (2.7%) and the sulphate conjugate of 5-amino-2-fluorophenol (2.6%), plus several minor metabolites accounting to less than 5% of the total urinary radioactivity (including *p*-fluoroaniline CL 7693, 2-amino-5-fluorophenol, 4'-fluoro-2'hydroxyacetanilide CL410142, and several minor unknown). A trace amount of parent picolinafen (0.4%) was also detected in the bile from aniline-label treated rats.

The metabolic pathway proposed in the DAR (Germany, 2000) is presented here below.

PROPOSED METABOLIC PATHWAY OF PICOLINAFEN IN THE RAT



5.1.1 Toxicokinetic studies - Single dose, oral route, in rats

Please refer to the DAR from Germany (September 2000), Point B.6.1 (Annex IIA 5.1). No additional data are considered necessary.

5.1.2 Toxicokinetic studies - Second single dose, oral route, in rats

Please refer to the DAR from Germany (September 2000), Point B.6.1 (Annex IIA 5.1). No additional data are considered necessary.

5.1.3 Toxicokinetic studies - Repeated dose, oral route, in rats

Please refer to the DAR from Germany (September 2000), Point B.6.1 (Annex IIA 5.1). No additional data are considered necessary.

5.2 Acute toxicity

Picolinafen is of a low order of acute toxicity to Sprague-Dawley rats by the oral, dermal and respiratory routes of exposure, supporting LD_{50} values of greater than 5000 mg/kg bw (oral) and greater than 4000 mg/kg bw (dermal), and an LC_{50} value of > 5.9 mg/L (analytical) (inhalation). Picolinafen technical is non-irritating to the skin and eye of the New Zealand White rabbit and is a non-sensitizer in the Magnusson and Kligman dermal maximization study conducted in Dunkin-Hartley guinea pigs.

For further details regarding the studies assessed during the first EU review, please refer to the DAR (Germany, 2000), Point B.6.2 (Annex IIA 5.2). An overall summary of all of the acute toxicity studies which were assessed during the previous review appears in Table 5.2-1. All these values are presented in the list of endpoints appended to the Review Report for picolinafen (SANCO/1418/2001-final 18 September 2002).

Table 5.2-1: Acute oral toxicity studies assessed during the previous review (taken from the DAR, September 2000)

Study Type	Strain	Results	Reference
Rat Oral LD_{50}	Sprague-Dawley	>5,000 mg/kg bw (males and females)[a]	[redacted] (1997a)
Rat Dermal LD_{50}	Sprague-Dawley	>4,000 mg/kg bw (males and females)[b]	[redacted] (1997b)
Rat Inhalation LC_{50}	Sprague-Dawley	>5.9 mg/L (4h, dust, nose only) (males and females)[b]	[redacted] (1997)
Rabbit Dermal Irritation	New Zealand White	Non-irritating	[redacted] (1997a)
Rabbit Eye Irritation	New Zealand White	Non-irritating	[redacted] (1997b)
Guinea Pig Dermal Sensitization	Crl:(HA)BR strain	Non-sensitizer (Magnusson and Kligman assay)	[redacted] (1997)

[a]No treatment-related mortality or clinical signs of toxicity at the dose indicated.
[b]No mortality at the dose/exposure concentration indicated.

5.2.1 Acute oral toxicity

Adequate data to assess the acute oral toxicity of picolinafen were evaluated in rats during the first EU review and no further data are considered necessary. For information, the results of the study are summarised in Table 5.2-1. For further details, please refer to the DAR (September 2000), Point B.6.2.1.

5.2.2 Acute percutaneous toxicity

Adequate data to assess the acute dermal toxicity of picolinafen were evaluated in rats during the first EU review and no further data are considered necessary. For information, the results of the study are summarised in Table 5.2-1. For further details, please refer to the DAR (September 2000), Point B.6.2.2.

5.2.3 Acute inhalation toxicity

Adequate data to assess the acute inhalation toxicity of picolinafen were evaluated in rats during the first EU review and no further data are considered necessary. For information, the results of the study are summarised in Table 5.2-1. For further details, please refer to the DAR (September 2000), Point B.6.2.3.

5.2.4 Skin irritation

Adequate data to assess skin irritation by picolinafen were evaluated in rabbits during the first EU review and no further data are considered necessary. For information, the study results are summarised in Table 5.2-1. For further details, please refer to the DAR (September 2000), Point B.6.2.4.

5.2.5 Eye Irritation

Adequate data to assess skin irritation by picolinafen were evaluated in rabbits during the first EU review and no further data are considered necessary. For information, the study results are summarised in Table 5.2-1. For further details, please refer to the DAR (September 2000), Point B.6.2.5.

5.2.6 Skin sensitization

Adequate data to assess skin sensitization by picolinafen were evaluated in Guinea pigs during the first EU review and no further data are considered necessary. For information, the study results are summarised in Table 5.2-1. For further details, please refer to the DAR (September 2000), Point B.6.2.6.

5.2.7 Potentiation/interactions of multiple active substances or products

This is not a requirement under Directive 91/414/EEC / Reg. (EC) No. 1107/2009.

5.3 Short-term toxicity

For the first EU review under Directive 91/414/EEC, short-term toxicity of picolinafen was adequately investigated by the oral route in rats, mice and dogs; and by the dermal route in rats. No further studies are therefore considered necessary.

Slight anaemia was noted in both the 28-day and 13-week rat studies, as evidenced by changes in haematological parameters, increased absolute and relative spleen and liver weights, and microscopic changes in the bone marrow, kidney, and/or spleen and liver. Additionally, decreased food consumption, mean body weights and weight gains were noted in the 13-week rat study beginning at weeks 4 to 6. Based on evidence of anaemia at 1000 ppm and 400 ppm in the 28-day and 13-week rat studies, respectively, the NOAELs for these same respective studies are 100 ppm (10.5 mg/kg bw/d) and 80 ppm (6.4 mg/kg bw/d).

Slight anaemia was also noted in both the 28-day and 13-week mouse studies, as evidenced by changes in haematological parameters, increased absolute and relative spleen and liver weights, and microscopic changes in the spleen and liver. Additionally, hepatocellular hypertrophy was noted in both studies. In the 13-week study, decreased food consumption and mean body weights and weight gains were observed. Based on evidence of anaemia and liver hypertrophy at 1000 ppm and 500 ppm in the 28-day and 13-week mouse studies, respectively, the NOAELs for these same respective studies are 100 ppm (23.4 mg/kg bw/d) and 50 ppm (10.2 mg/kg bw/d).

In the 28-day dog study slight anaemia was noted, as evidenced by changes in haematological parameters. Increased absolute and relative thyroid/parathyroid weights and thyroid follicular cell hypertrophy and hyperplasia were also noted. Additionally, increased serum cholesterol was noted, and decreased mean body weights and/or weight gains observed. The NOAEL from the 28-day dietary toxicity study in dogs was 100 ppm (3.9 mg/kg bw/d), based on increased serum cholesterol and changes in the thyroid gland at 1,000 ppm, the next highest concentration tested.

In the 2 dog studies at 90 days (i.e. 90-day dietary study and at the 90-day time point in the one-year dog study), slight anaemia was noted, as evidenced by changes in haematological parameters. Increased absolute and relative thyroid/parathyroid weights and thyroid follicular cell hypertrophy and hyperplasia were also noted in the 90-day and the one-year studies. Decreased mean body weights and/or weight gain was also observed in the 90-dat study. The overall NOAEL after 90 days of treatment including the results from the one-year study was 150 ppm (5.2 mg/kg bw/d), based on reduced body weights and weight gains, reduced red blood cell parameters and thyroid hypertrophy at 500 ppm and above. The NOAEL after one year of treatment was 50 ppm (1.4 mg/kg bw/d), based on reduced body weights and body weight gains in males at 150 ppm and above in the later part of the study.

Results from a 28-day dermal toxicity study conducted in Sprague-Dawley rats with picolinafen technical revealed a slight anaemia, as evidenced by changes in haematological parameters, beginning on Study Day 5. Additionally, increases in absolute and/or relative spleen weights and microscopic changes in the spleen were noted. This study supported a dermal NOAEL of 50 mg/kg bw/d, based on haematological changes indicative of a slight anaemia at 75 mg/kg bw/d.

Table 5.3-1 summarises the agreed endpoints from the short term toxicity studies that were assessed during the first EU review.

Table 5.3-1: Summary of short term toxicity data (taken from the DAR, September 2000)

Study, Species, Reference	NOAEL	LOAEL	Principal effects at LOAEL
28-day dermal Sprague-Dawley rats 0, 25, 50, 75, 100, 200, 1000 mg/kg bw/d *Compton (1999)*	50 mg/kg bw/d	75 mg/kg bw/d	Anemia (reductions in red blood cell parameters)
28-day dietary Sprague-Dawley rats 0, 25, 50, 100, 1000 ppm *Taupin (1993)*	100 ppm (10.5 mg/kg bw/d)	1000 ppm (107 mg/kg bw/d)	Hemolytic anemia (increased liver and spleen weights, histopathological findings in the spleen, bone marrow, kidney and liver)
28-day dietary CD-1 mice 0, 100, 1000, 2000, 3500 and 7000 ppm *Ponnock (1998)*	100 ppm (23.4 mg/kg bw/d)	1000 ppm (227.2 mg/kg bw/d)	Extramedullary hematopoiesis in the spleen
28-day dietary Beagle dogs 0, 100, 1000, 2000, 10,000 ppm *Kelly (1998)*	100 ppm (3.9 mg/kg bw/d)	1000 ppm (43.9 mg/kg bw/d)	Thyroid/parathyroids (increased weights, enlarged, hyperplasia and hypertrophy of follicular epithel cells); elevated serum cholesterol levels
13-week dietary Sprague-Dawley rats 0, 80, 400, 800 ppm *Fisher (1998a)*	80 ppm (6.4 mg/kg bw/d)	400 ppm (32.2 mg/kg bw/d)	Hemolytic anemia (increased liver and spleen weights, histopathological findings in the spleen and liver)
13-week dietary CD-1 mice 0, 50, 500, 1000, 2000 ppm *Fisher (1998b)*	50 ppm (10.2 mg/kg bw/d)	500 ppm (103.5 mg/kg bw/d)	Extramedullary hematopoiesis in the spleen; increased spleen and liver weights, histopathological findings in the spleen and liver
90-day dietary Beagle dogs 0, 50, 500, 2500 ppm *Kelly (1999a)*	50 ppm (1.7 mg/kg bw/d)	500 ppm (17.3 mg/kg bw/d)	Anemia (reductions in red blood cell parameters); thyroid (increased weights, enlarged, hyperplasia and hypertrophy of follicular epithel cells)
One-year study Beagle dogs 0, 50, 150, 1500 ppm *Kelly (1999b)*	150[a] ppm (5.2[a] mg/kg bw/d)	1500[a] ppm (49.9 mg/kg bw/d)	Reduced body weights and weight gains; anemia (reductions in red blood cell parameters)
	50 ppm (1.4 mg/kg bw/d)	150 ppm (4.4 mg/kg bw/d)	Reduced body weights and weight gains [1500 ppm: thyroid (enlarged, hypertrophy of follicular epithel cells)]

[a]NOAEL/LOAEL is based on results from the 90-day timepoint in the one-year dog study with picolinafen technical.

5.3.1 Oral 28-day toxicity

Adequate data to assess the 28-day toxicity of picolinafen were evaluated in rats, mice and dogs during the first EU review and no further data are considered necessary. For information, the results of the studies are summarised in Table 5.3-1. For further details, please refer to the DAR (September 2000), Points B.6.3.1 to B.6.3.3.

5.3.2 Oral 90-day toxicity (rodents)

Adequate data to assess the 90-day toxicity of picolinafen were evaluated in rats and mice during the first EU review and no further data are considered necessary. For information, the results of the studies are summarised in Table 5.3-1. For further details, please refer to the DAR (September 2000), Points B.6.3.4 and B.6.3.5.

5.3.3 Oral 90-day toxicity (dog)

Adequate data to assess the 90-day toxicity of picolinafen were evaluated in dogs during the first EU review and no further data are considered necessary. For information, the results of the study are summarised in Table 5.3-1. For further details, please refer to the DAR (September 2000), Point B.6.3.6.

5.3.4 Oral 1 year toxicity (dog)

Adequate data to assess the one-year toxicity of picolinafen were evaluated in dogs during the first EU review and no further data are considered necessary. For information, the results of the study are summarised in Table 5.3-1. For further details, please refer to the DAR (September 2000), Point B.6.3.7.

5.3.5 28-day inhalation toxicity (rodents)

Picolinafen is not a volatile substance as its vapour pressure is 1.7×10^{-7} Pa a 20 °C. In addition, it is not acutely toxic by inhalation, as the analytically determined LC_{50} was higher than 5.9 mg/L air. A study is therefore not required.

5.3.6 90-day inhalation toxicity (rodents)

Not required.

5.3.7 Percutaneous 28-day toxicity (rodents)

Adequate data to assess the 28-day dermal toxicity of picolinafen were evaluated in rats during the first EU review and no further data are considered necessary. For information, the results of the studies are summarised in Table 5.3-1. For further details, please refer to the DAR (September 2000), Points B.6.3.8.

5.3.8 Percutaneous 90-day toxicity (rodents)

Adequate data to assess the 28-day dermal toxicity of picolinafen were evaluated in rats during the first EU review and no further data are considered necessary.

5.4 Genotoxicity

For the first EU review under Directive 91/414/EEC, Picolinafen was tested in a battery of *in vitro* mutagenicity assays measuring several different end points of potential mutagenicity, e.g. gene mutation in bacteria, gene mutation in mammalian cells and chromosomal aberration in somatic cells. The results from these studies indicate that picolinafen does not induce base-pair or frame-shift mutation in any of the bacterial tester strains or gene mutation in mammalian cells. No potential for clastogenicity was observed in the *in vitro* chromosomal aberration assay in CHO cells or in the *in vivo* mouse micronucleus assay. Therefore, it was concluded that picolinafen is not mutagenic or genotoxic.

Based on the negative results obtained in these three *in vitro* and one *in vivo* studies, an *in vivo* Unscheduled DNA Synthesis (UDS) assay and an *in vivo* study in germ cells were not required.

The studies submitted were sufficient to predict potential genotoxicity and no further testing is proposed. Table 5.4-1 summarises the agreed endpoints from the short term toxicity studies that were assessed during the first EU review.

Table 5.4-1: Summary of genotoxicity data (taken from the DAR, September 2000)

Study Type	Test System	Concentrations	Results	Reference
Bacterial/ Microsome Mutagenicity Assay	*S. typhimurium* TA98, TA100, TA1535, TA1537 and TA1538; *E. coli* WP2 *uvr A*-	100, 250, 500, 1000, 2500 µg/plate	+S9[a]:Negative -S9[b]:Negative	Mulligan (1997)
Mammalian Cell CHO/HGPRT Mutagenicity Assay	Chinese hamster ovary cells	10, 25, 50, 100, 200, 300 µg/ml	+S9[a]:Negative -S9[b]:Negative	Johnson (1997)
In Vitro Chromosome Aberration Assay	Chinese hamster ovary cells	+S9[a] : 10, 25, 50, 100, 200, 300, 400, 600 µg/ml and -S9[b] : 10, 25, 50, 100, 200, 400, 600, 800, 1000 µg/ml	+S9[a]:Negative -S9[b]:Negative	Gudi and Schadly (1997)
In Vivo Micronucleus Assay	Polychromatic erythrocytes obtained from CD-1 mice	1250, 2500, 5000 mg/kg bw	Negative	Curry (1999)

[a]with metabolic activation; [b]without metabolic activation

5.4.1 In vitro genotoxicity - Bacterial assay for gene mutation

Adequate *in vitro* testing for genotoxicity was assessed during the first EU review of picolinafen. For information, the results of these studies are summarised in Table 5.4-1. For further details, please refer to the DAR (September 2000), Point B.6.4.1.1.

5.4.2 In vitro genotoxicity - Test for clastogenicity in mammalian cells

Adequate *in vitro* testing for genotoxicity was assessed during the first EU review of picolinafen. For information, the results of these studies are summarised in Table 5.4-1. For further details, please refer to the DAR (September 2000), Point B.6.4.1.3.

5.4.3 In vitro genotoxicity - Test for gene mutation in mammalian cells

Adequate *in vitro* testing for genotoxicity was assessed during the first EU review of picolinafen. For information, the results of these studies are summarised in Table 5.4-1. For further details, please refer to the DAR (September 2000), Point B.6.4.1.2.

5.4.4 In vivo genotoxicity (somatic cells) - Bone marrow or micronucleus

Adequate *in vivo* testing for genotoxicity was assessed during the first EU review of picolinafen. For information, the results of the study are summarised in Table 5.4-1. For further details, please refer to the DAR (September 2000), Point B.6.4.2.1.

5.4.5 In vivo genotoxicity (somatic cells) - DNA repair or mouse spot tests

A study was not required and not considered necessary.

5.4.6 In vivo studies in germ cells

A study was not required and not considered necessary.

5.5 Long-term toxicity and carcinogenicity

For the first review of picolinafen under Directive 91/414/EEC, long-term toxicity and carcinogenic potential were adequately investigated by the oral route in rats and mice. Therefore, no further data are required for the Annex I renewal of picolinafen. An overview of the long-term toxicity and carcinogenicity studies considered in the DAR (September 2000) is presented in Table 5.5-1.

Table 5.5-1 Summary of the long-term toxicity and carcinogenicity studies in rodents (taken from the DAR, September 2000)

Study, Species, Doses *Reference*	NOAEL	LOAEL	Principal effects at LOAEL
24-month study Sprague-Dawley rats 0, 50,250, 500 ppm *Kelly (1999c)*	50 ppm (2.4 mg/kg bw/d)	250 ppm (12.1 mg/kg bw/d)	Anemia (decreased red blood cell parameters); spleen (increased weights, hemosiderin)
18-month study CD-1 mice 0, 40, 400, 800 ppm *Fisher (1999)*	40 ppm (6.9 mg/kg bw/d)	400 ppm (68.6 mg/kg bw/d)	Hematology (increased reticulocyte counts and MCHC); liver (increased weights, hypertrophy); spleen pigment)

Findings similar to those noted following short-term administration of picolinafen technical were also observed following long-term treatment in the Sprague-Dawley rat and CD-1 mouse.

In the 2-year rat study, a slight anaemia was observed, as evidenced by changes in haematological parameters, increased absolute and relative spleen weights and microscopic findings in the spleen at 250 and 500 ppm. In the 18-month mouse study, findings indicative of anaemia were also observed, including increased reticulocyte counts and microscopic changes in the spleen at 400 and 800 ppm. Additional findings observed in the 18-month mouse study included increased absolute and relative liver weights which generally correlated with microscopic findings of hepatocellular hypertrophy at 400 ppm (males) and 800 ppm (both sexes). Based on evidence of anaemia at 250 ppm in the 2-year rat study, the NOAEL for chronic toxicity is 50 ppm (2.4 mg/kg bw/d for males). The NOAEL for systemic toxicity from the 18-month mouse oncogenicity study was 40 ppm (6.9 mg/kg bw/d for males) based on evidence of anaemia and liver hypertrophy at 400 ppm, the next highest concentration tested.

There were some deviations to OECD guideline 453 in the 24-month rat study: (i) number of animals of the high dose satellite group (10-15 instead of the 20 required); (ii) number of animals evaluated for haematology at each time point (10 instead of 20) and (iii) survival to the end of the study. However, the study was considered acceptable, based on acceptability under US EPA guideline criteria, EEC position against needless repetition of tests on animals and historical control data from the performing laboratory evidencing the survival rate of control males in the study being within recent historical control range. Although parameters were obtained from a number of animals lower than that required, the results of the study are clear and correctly identified critical effects. In addition, the dog and not the rat was identified as the most sensitive species and subsequent ADI and AOEL values were based on the dog studies. For these reasons, it is not considered useful or necessary to repeat this study.

There was no treatment-related increase in the type or incidence of neoplastic findings in the long-term studies. The NOAEL for oncogenicity in the 24-month rat study was 500 ppm (the highest dose tested; approximately 27.8 mg/kg bw/d) and the NOAEL in the 18-month mouse study was 800 ppm (again the highest dose tested; 151.4 mg/kg bw/d). The lack of oncogenic potential of picolinafen technical was supported by the absence of genotoxicity, as determined by results from a battery of three *in vitro* and one *in vivo* genetic toxicity tests. The newly conducted Ames test with the impurity contained at a higher level in the new TGAI confirms the lack of genotoxic potential.

5.5.1 Long-term (2 years) oral toxicity in the rat

For information, the results of this study are summarised in Table 5.5-1. For further details, please refer to the DAR (September 2000), Points B.6.5.1.

5.5.2 Carcinogenicity study in the rat

For information, the results of this study are summarised in Table 5.5-1. For further details, please refer to the DAR (September 2000), Points B.6.5.1.

5.5.3 Carcinogenicity study in the mouse

For information, the results of this study are summarised in Table 5.5-1. For further details, please refer to the DAR (September 2000), Points B.6.5.2.

5.5.4 Mechanism of action and supporting data

No study is required.

5.6 Reproductive toxicity

For the first review of picolinafen under Directive 91/414/EEC, reproductive and developmental toxicity were adequately investigated by the oral route in rats and rabbits. Therefore, no further data are required for the Annex I renewal of picolinafen. An overview of the reproductive toxicity and developmental toxicity studies considered in the DAR (September 2000) is presented in Table 5.6-1.

Table 5.6-1 Summary of the reproductive toxicity and pre-natal developmental toxicity studies in mammals (taken from the DAR, September 2000)

Study, Species, References	NOAEL	LOAEL	Principal effects at LOAEL
2-generation reproduction Sprague-Dawley rats 0, 50, 250, 500 ppm *Schroeder (1999b)*	50 ppm (4.0 mg/kg bw/d) Parental and offspring	250 ppm (21 mg/kg bw/d) Parental and offspring	Hemolytic anemia
	500 ppm (43.0 mg/kg bw/d) Reproductive		
Oral teratology New Zealand White rabbits 0, 5, 20, 50 mg/kg bw/d *Hoberman (1998)*	5 mg/kg bw/d (maternal)	20 mg/kg bw/d (maternal)	Reduced food consumption and body weight gains; haemolytic anemia (maternal)
	5 mg/kg bw/d (foetal/developmental)	20 mg/kg bw/d (foetal/developmental)	Decreased mean foetal body weights (foetal/developmental)
Oral teratology, Sprague-Dawley rats 0, 5, 25, 50, 100, 500, 1000 mg/kg bw/d *Hoberman (1999)*	50 mg/kg bw/d (maternal)	100 mg/kg bw/d (maternal)	Reduced food consumption, body weights and body weight gains; haemolytic anemia (maternal)
	1000 mg/kg bw/d (foetal/developmental)		

In the 2-generation reproduction study conducted with Sprague-Dawley rats, anaemia was noted for both parental generations, as evidenced by changes in haematological parameters, increased absolute and relative spleen weights, and microscopic changes in the spleen. Anaemia was also noted for F2 pups on postnatal Day 21, as evidenced by changes in haematological parameters (haematology examinations were only conducted for F2 pups on postnatal Day 21). The results from this study support NOAELs for parental toxicity and growth and development of offspring of 50 ppm (4.0 mg/kg bw/d) based on evidence of anaemia in both parental generations and in F2 pups at 250 ppm, the next highest concentration tested. Picolinafen technical did not affect reproductive performance, supporting a NOAEL for reproductive toxicity of 500 ppm (43.0 mg/kg bw/d), highest concentration tested.

Developmental toxicity tests conducted with picolinafen technical in Sprague-Dawley rats and New Zealand White rabbits revealed no evidence of teratogenic effects in either the rat or rabbit. In the rat, maternal toxicity was evidenced by reductions in food consumption, mean body weights and body weight gains, as well as haematological changes, increased absolute and relative spleen weights and microscopic splenic changes indicative of anaemia. The NOAEL for maternal toxicity in this study is 50 mg/kg bw/d, based on evidence of anaemia at 100 mg/kg bw/d (next highest dose tested). Based on the absence of any treatment-related findings in uterine or foetal parameters, the NOAEL for developmental toxicity is 1000 mg/kg bw/d, the highest dose tested. Picolinafen technical is not a developmental toxicant in the Sprague-Dawley rat. In the rabbit, maternal toxicity was evidenced by reductions in food consumption and body weight gains, as well as haematological changes and microscopic splenic changes indicative of anaemia. An increase in resorption rate and decreased mean foetal body weights were also noted in this study. The NOAEL for maternal toxicity in this study was 5 mg/kg bw/d, based on evidence of anaemia and reductions in food consumption and body weight gain at 20 mg/kg bw/d (next highest dose tested), and the NOAEL for developmental toxicity is 5 mg/kg bw/d, based on decreased mean foetal body weights at 20 mg/kg bw/d. Picolinafen technical is not a developmental toxicant in the New Zealand White rabbit.

5.6.1 Two generation reproductive toxicity in the rat

For information, the results of this study are summarised in Table 5.6-1. For further details, please refer to the DAR (September 2000), Points B.6.6.2.

5.6.2 Separate male and female studies

Not triggered/not required.

5.6.3 Three segment designs

Not triggered/not required.

5.6.4 Dominant lethal assay for the male fertility

Not triggered/not required.

5.6.5 Cross-matings of treated males with untreated females and vice versa

Not triggered/not required.

5.6.6 Effects on spermatogenesis

Not triggered/not required.

5.6.7 Effects on oogenesis

A quantitative assessment of primordial follicles in the ovaries for 10 randomly selected F1 females from the control and high-dose groups was included in the 2-generation reproductive toxicity study.

5.6.8 Sperm motility, mobility and morphology

Sperm assessments (motility, count of caudal epididymal sperm and homogenization resistant sperm heads in the testes, and morphology) for all P and F1 males were included in the 2-generation reproductive toxicity study.

5.6.9 Investigation of hormonal activity

Not triggered/not required.

5.6.10 Teratogenicity test by the oral route in the rat

For information, the results of this study are summarised in Table 5.6-1. For further details, please refer to the DAR (September 2000), Points B.6.6.4.

5.6.11 Teratogenicity test by the oral route in the rabbit

For information, the results of this study are summarised in Table 5.6-1. For further details, please refer to the DAR (September 2000), Points B.6.6.3.

5.7 Neurotoxicity

There were no clinical signs of neurotoxicity in the toxicological studies conducted for the first EU review under Directive 91/414/EEC. The DAR concluded that since there was no evidence for a neurotoxic potential of picolinafen and picolinafen is not structurally related to an organophosphate, no further studies were required. Please refer to the DAR (September 2000), Point B.6.7 Delayed neurotoxicity (Annex IIA 5.7) for details.

5.7.1 Acute neurotoxicity - rat

Picolinafen is not acutely toxic by oral administration and there was no evidence for a neurotoxic potential of picolinafen in the toxicological studies conducted. Please refer to the DAR (September 2000), Point B.6.7 Delayed neurotoxicity (Annex IIA 5.7) for details.

5.7.2 Delayed neurotoxicity following acute exposure

Picolinafen is not structurally related to an organophosphate. Please refer to the DAR (September 2000), Point B.6.7 Delayed neurotoxicity (Annex IIA 5.7) for details.

5.7.3 28-day delayed neurotoxicity

Picolinafen is not structurally related to an organophosphate. Please refer to the DAR (September 2000), Point B.6.7 Delayed neurotoxicity (Annex IIA 5.7) for details.

5.7.4 Subchronic neurotoxicity - rat - 90-day

There was no evidence for a neurotoxic potential of picolinafen in the toxicological studies conducted. Please refer to the DAR (September 2000), Point B.6.7 Delayed neurotoxicity (Annex IIA 5.7) for details.

5.7.5 Postnatal developmental neurotoxicity

There was no evidence for a neurotoxic potential of picolinafen in the toxicological studies conducted, and there was no evidence in the reproductive and developmental toxicity studies that the offspring are more sensitive than the adult animals. Please refer to the DAR (September 2000), Point B.6.7 Delayed neurotoxicity (Annex IIA 5.7) for details.

5.8 Toxicity studies on metabolites

The metabolic pathway of picolinafen appears very similar in plants and rats, and all the metabolites identified in plants were also identified in the rat metabolism study. As such, the toxicity of these metabolites was effectively assessed in the short- and long-term toxicity studies conducted in rats with picolinafen. For further details, please refer to the DAR (September 2000), Point B.6.8.1 Toxicity studies of metabolites.

5.9 Medical and clinical data

Report: II A 5.9/1
Bormann U. 2012(a)
Picolinafen - Medical and clinical investigations
BASF DocID 2012/1219568
Date of report: 10-Jul-2012
Testing facility: [redacted]; [redacted] Germany Fed.Rep.
Guidelines: none
GLP: No, not subject to GLP regulations

5.9.1 Report on medical surveillance on manufacturing plant personnel

Based on information received from the production site ([redacted], Germany) the plant manufactures approximately 63 tons of picolinafen (BAS 700 H) per year, using maximum 15 employees; in addition to these, the intermediate 'picolinafen 1' (first step of the synthesis) has employed maximum 30 employees for producing 55 tons of 40% solution per year, in production intervals of 2 years.

There have been no reports of illness or adverse health effects for any of the workers either in the plant or in the medical department.

All workers are subjected to obligatory medical investigations according to the ArbMedVV following the guidelines of the "Berufsgenossenschaft der Chemischen Industrie".

For the workers involved in the production of 'picolinafen 1', these include the following:

- Medical examination (once a year)
- Haematology, clinical chemistry and urinalysis ('methanol package' - once a year)
- Evaluation of the respiratory system (including spirography/spirometry) (once a year)
- Dermatological examination (every 3 years)

and, starting in 2012,

- Additional blood and functional investigations (i.e. ECG at rest) for a selected subgroup
- Additional blood and other investigations ('benzene-homologues' package, including RX of the thorax).

For the workers involved in the production of picolinafen, these include the following:

- Medical examination (once a year)
- Haematology, clinical chemistry and urinalysis ('methanol package' - once a year)
- Dermatological examination (every 3 years)
- Additional blood and functional investigations (i.e. ECG at rest) for a selected subgroup
- Additional blood and other investigations ('benzene-homologues' package, including RX of the thorax).

The medical department could decide if any additional investigation is required in order to biomonitoring exposure (e.g. detection of picolinafen metabolites in blood).

5.9.2 Report on clinical cases and poisoning incidents

The medical department of [redacted] (Germany) has not received any reports of clinical cases or poisoning.

5.9.3 Observations on general population exposure & epidemiological studies

Neither data on exposure of the general public nor epidemiologic studies specifically addressing exposure to picolinafen are available.

5.9.4 Clinical signs and symptoms of poisoning and details of clinical tests

Methods for determination of the active substance picolinafen or its metabolites in biological fluids are not established. Specific signs of poisoning or clinical tests are not known.

5.9.5 First aid measures

See safety data sheet (BASF DocID 2012/1219501)/precautions; symptomatic and supportive treatment, no specific antidote known.

5.9.6 Therapeutic regimes

See safety data sheet (BASF DocID 2012/1219501)/precautions; symptomatic and supportive treatment, no specific antidote known.

5.9.7 Expected effects & duration of poisoning as a function of exposure

See safety data sheet (BASF DocID 2012/1219501)/precautions; symptomatic and supportive treatment, no specific antidote known.

5.9.8 Effects & duration of poisoning as a function of time

See safety data sheet (BASF DocID 2012/1219501)/precautions; symptomatic and supportive treatment, no specific antidote known.

5.9.9 Dermal penetration

The study is summarised under the Annex III dossier update (August 2012), Section 3, point 7.6.2.

5.10 Other/special studies

According to the DAR (September 2000), Point B.6.8.2 Supplemental studies on the active ingredient, no supplementary studies to clarify observed effects were required.

5.11 Summary of mammalian toxicity and overall evaluation

The technical specification being supported for the renewal approval of picolinafen is equivalent to the material originally assessed for the Annex I inclusion under Directive 91/414/EEC. The minimum purity of the new source does not result in a decrease in the level of purity, the maximum level of any impurity has not increased and no new impurities are present. It is concluded that all of the mammalian toxicity data previously considered by the Rapporteur Member State (Germany) and the EU agreed endpoints remain representative to the current technical material. The only exception is dermal absorption, for which a study is now available.

An *in vitro* dermal absorption study using human skin has been carried out with the representative formulation BAS 700 03 H (75 WG). Results were as follows:

Table 5.11-1: Endpoints for dermal absorption for BAS 700 03 H (75 WG)

Test	% of applied dose			Reference
	Concentrate	1:1500 spray dilution	1:6000 spray dilution	
BAS 700 H				
In vitro (human)	0.3	3	12	Bernard F., 2012 BASF DocID 2011/1016543

The overall summary and evaluation of mammalian toxicity remains unchanged from Section B.6.10 (Annex IIA 5.10) of the Draft Assessment Report prepared by Germany (September 2000).

The reference doses for picolinafen are currently set as follows (Review report, SANCO/1418/2001-final, dated 18 September 2002) and should remain unchanged, with the exception of dermal absorption for which a study is now available:

Acute RfD

0.05 mg/kg bw/day: on the basis of reduced food consumption and body weight gains and haemolytic anaemia seen in the oral teratogenicity study in rabbits, using a standard safety factor of 100.

ADI

0.014 mg/kg bw/day on the basis of body weight changes seen in the 1 year dietary dog study, using a standard safety factor of 100 (picolinafen is neither mutagenic, carcinogenic or a reproductive toxin).

AOEL

0.03 mg/kg bw/day on the basis of the NOAEL of 5.2 mg/kg bw/day obtained as collective results from the 90-day and 1 year dog studies, an oral absorption of 60% and the usual safety factor of 100.

Dermal absorption

Based on results of the newly available *in vitro* dermal absorption study, a value of 0.3% for the commercial WG formulation, and values of 3% or 12% for the spray dilutions should be used for risk assessment purposes.

Drinking water limit

The determination of a maximum allowable concentration (MAC) value in drinking water was not necessary, because according to Directive 91/414/EEC only the ADI and AOEL values have to be determined.
Furthermore according to Directive 80/778/EEC the maximum admissible concentration of an active ingredient for drinking water is set to 0.1 µg/L.

The Chemical Company

DOSSIER FOR THE EVALUATION OF THE ACTIVE SUBSTANCE

Picolinafen (BAS 700 H)

Data requirement according to Regulation (EU) No. 544/2011 and (EU) No. 545/2011
of 10 June 2011 (formerly Annex II and III of Directive 91/414/EEC)
using OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substance (Dossier Guidance)
and Commission Regulation (EC) No 1141/2010 of 7 December 2010 (AIR procedure)

Document M-II

Summary and evaluation (Tier II)

Section 4

Residues and plant metabolism

BASF DocID 2012/1208878

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Date: 30 August 2012

6 Metabolism and Residues Data

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This document supports the application for renewal of the registration of picolinafen under Commission Regulation (EU) No 1141/2010 of 7 December 2010. This document reviews the metabolism and residues data, including additional data and risk assessments, for picolinafen.

Picolinafen is approved as an active substance under Regulation (EC) 1107/2009; Reference: Commission Implementing Regulation (EU) No. 540/2011 of 25 May 2011 (repealing Commission Directive 91/414/EEC; & Inclusion Directive 2000/80/EC of 4 December 2000).

The European Commission review report for picolinafen (SANCO/1418/2001-final dated 18 September 2002), and in particular background documents A, B and C to the review report are considered to provide the relevant review information.

Where appropriate this document still refers to the Annex I Inclusion Directive for picolinafen (2002/64/EC of 15 July 2002).

This document covers data and risk assessments which were not part of the original dossier and which are necessary to complete residue trial data according to representative use of picolinafen on winter cereals.

Each section of this document refers to the agreed EU endpoints and if relevant provides proposals for amended endpoints.

Where the conclusions of the EU review required additional data and/or new data on picolinafen, a justification has been included. A justification is also given if new data are required but none are provided.

Where new risk assessment guidance has been introduced since the EU review of picolinafen an updated evaluation of picolinafen has been included.

To adequately assess picolinafen according to the new risk assessment guidance, it may have been necessary to provide new data, if so these are also included.

The LII document contains the list of references included in this document for support of the evaluation and a list of published data.

6.1 Stability of residues

6.1.1 Stability of residues during storage of samples

The DAR section B.7.6.4 (September 2000) for picolinafen concluded that residues of picolinafen in cereal grain, straw and whole green plant were stable in deep frozen storage (≤ -18°C) for at least one year. No further data are required or submitted.

6.1.2 Stability of residues in samples extracts

Residues in sample extracts were considered to be stable within the time frame of the analytical procedure as verified by procedural recovery experiments with untreated matrices fortified with picolinafen (refer to DAR (September 2000), B.7.6.5).

6.2 Metabolism, distribution and expression of residues

6.2.1 In plants, at least three crops from three different crop categories

According to DAR section B.7.1 (September 2000), the metabolism of picolinafen has been studied in spring wheat. No other crops have been studied as picolinafen will only be recommended for use in cereals, all of which are covered by this study on wheat. The main metabolic route of picolinafen in wheat is through cleavage of the amide bond to form the picolinic acid *6-(3-trifluoromethyl-phenoxy)-pyridine-2-carboxylic acid and 4-fluoroaniline* in the first step. The aniline and its possible further reaction products are never identified in any matrix because of very low concentrations. The predominant component of the residue was unchanged parent picolinafen.

No further studies on the metabolism in plants are required or submitted for the proposed use of picolinafen on cereals.

6.2.2 Poultry

Residues of picolinafen in grain are <0.05 mg/kg (or 0.01 mg/kg, respectively), and therefore intakes by poultry will be below 0.1 mg/kg diet. Hen metabolism studies are therefore not required or submitted.

6.2.3 Lactating ruminants (goat or cow)

According to DAR section B.7.2 (September 2000), based on the major metabolites that were identified in goat urine, faeces, milk, and specific tissues, a metabolic pathway is proposed which shows that hydrolysis, oxidation, acetylation, and subsequent glucuronide and sulfate conjugations constitute the major biotransformation processes for picolinafen in the goat. The results of this study show that picolinafen is metabolised readily in lactating goats by hydrolytic cleavage of the amide bond to yield the substituted picolinic acid (CL 153815) and 4-fluoroaniline (CL 7693) as a transient metabolite which was acetylated to form 4-fluoroacetanilide (CL 44167). This acetylated metabolite underwent further metabolic transformation through two mechanisms. Both proceeded by initial oxidation of the aromatic ring to either directly produce a hydroxylated component, which was conjugated with glucuronic acid, or to eliminate the fluorine substituent first and then form the glucuronide ester of the defluorinated precursor. The metabolism of orally administered picolinafen in goat was shown to be similar to the metabolism in the rat.

No further studies on the metabolism in livestock are required or submitted for the proposed use of picolinafen on cereals.

6.2.4 Pigs

The metabolism of picolinafen in ruminants is similar to that in rats and a metabolism study in pigs is therefore not required. A metabolism study in pigs has not been conducted.

6.2.5 Nature of residue in fish

This is not required under Directive 91/414/EEC / Reg. (EC) No. 1107/2009.

6.2.6 Chemical identity

This is not required under Directive 91/414/EEC / Reg. (EC.) No. 1107/2009.

6.3 Residue trials (supervised field trials)

Refer to the DAR section B.7.6 for residue trials data for use on winter wheat and barley.

For winter wheat a total of twenty-four residue trials (10 x decline, 14 x harvest) were conducted in northern Europe, and twenty residue trials (9 x decline, 11 x harvest) were conducted in southern Europe. For northern Europe, nine residue trials (3 x decline, 6 x harvest) were applied according to GAP. For southern Europe, three residue trials (1 x decline, 2 x harvest) were applied according to GAP. GAP compliant trial data for winter wheat evaluated in DAR section B.7.6 is given in Table 6.3-1.

Table 6.3-1 GLP compliant trial data on winter wheat evaluated for the previous submission (winter wheat)

Country/ Year	Formulation (g as/kg)	Application			Portion analysed	Residues (mg/kg)	DAT (d)	References
		Rate per treatment (kg as/ha)	Growth stage	No.				
Northern Europe								
N-FR / 1997-1998	WG 750	0.1	BBCH 30	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	82 119 119	RIP1999-970
N-FR / 1995/1996	SC 250	0.1	BBCH 25	1	Whole plant Grain Straw	4.6 <0.05 <0.05 <0.05 <0.05	0 79 95 134 134	RIP1999-987
N-FR / 1995/1996	SC 250	0.1	BBCH 25	1	Whole plant Grain Straw	4.8 <0.05 <0.05 <0.05 <0.05	0 79 95 134 134	RIP1999-987
N-FR / 1995/1996	SC 250	0.1	BBCH 29-30	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	97 134 134	RIP1999-988
N-FR / 1995/1996	WG 750	0.1	BBCH 29-30	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	97 134 134	RIP1999-988
DE / 1995/1996	SC 250	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	76 113 113	RIP1999-989
DE / 1995/1996	WG 750	0.101	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	76 113 113	RIP1999-989
DE / 1995/1996	SC 250	0.102	BBCH 29	1	Whole plant Grain Straw	6.1 <0.05 <0.05 <0.05 <0.05	0 46 76 113 113	RIP1999-990

Country/ Year	Formulation (g as/kg)	Application			Portion analysed	Residues (mg/kg)	DAT (d)	References
		Rate per treatment (kg as/ha)	Growth stage	No.				
DE / 1995/1996	WG 750	0.102	BBCH 29	1	Whole plant Grain Straw	6.2 <0.05 <0.05 <u>≤0.05</u> <0.05	0 46 76 113 113	RIP1999-990
DE / 1997/1998	WG 750	0.099	BBCH 30	1	Whole plant Grain Straw	<0.05 <u>≤0.05</u> 0.08	74 106 106	RIP1999-992
GB / 1996/1997	WG 750	0.097	BBCH 30	1	Whole plant Grain Straw	4.74 <0.05 <0.05 <u>≤0.05</u> <0.05	0 64 95 141 141	RIP1999-995
Southern Europe								
S-FR / 1997/1998	WG 750	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <u>≤0.05</u> <0.05	84 112 112	RIP1999-985
IT / 1996/1997	WG 750	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <u>≤0.05</u> <0.05	70 91 91	RIP1999-991
S-FR / 1996/1997	WG 750	0.1	BBCH 29-30	1	Whole plant Grain Straw	2.83 0.12 <0.05 <u>≤0.05</u> <0.05	0 55 77 118 118	RIP1999-993

This is sufficient data to support the use of picolinafen in the North. For southern Europe, five new residue trials according to GAP were conducted in 2010/2011 to complete the data set on winter wheat.

For winter barley a total of twenty-four residue trials (3 x decline, 21 x harvest) were conducted in northern Europe, and nine residue trials (6 x decline, 3 x harvest) were conducted in southern Europe. For northern Europe, seven residue trials (1 x decline, 6 x harvest) were applied according to GAP. For southern Europe, two residue trials (2 x harvest) were applied according to GAP. GAP compliant trial data for winter barley evaluated in DAR section B.7.6 is given in Table 6.3-2.

Table 6.3-2 GLP compliant trial data on winter barley evaluated for the previous submission (winter barley)

Country/ Year	Formul-ation (g as/kg)	Application			Portion analysed	Residues (mg/kg)	DAT (d)	References
		Rate per treatment (kg as/ha)	Growth stage	No.				
Northern Europe								
DE / 1996/1997	WG 750	0.097	BBCH 29	1	Whole plant Grain Straw	3.2 <0.05 <0.05 <0.05 <0.05	0 44 73 100 100	RIP1999-998
GB / 1997/1998	WG 750	0.096	BBCH 30	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	70 116 116	RIP1999-999
GB / 1997/1998	WG 750	0.099	BBCH 30	1	Whole plant Grain Straw	0.05 <0.05 0.06	66 110 110	RIP1999-999
GB / 1995/1996	SC 250	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	100 136 136	RIP1999-1002
GB / 1995/1996	WG 750	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	100 136 136	RIP1999-1002
GB / 1995/1996	SC 250	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	100 136 136	RIP1999-1002
GB / 1995/1996	WG 750	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	100 136 136	RIP1999-1002
Southern Europe								
ES / 1996/1997	WG 750	0.115	BBCH 23-30	1	Whole plant Grain Straw	4.14 0.06 <0.05 0.17	0 62 92 92	RIP1999-1000
S-FR / 1996/1997	WG 750	0.1	BBCH 29	1	Whole plant Grain Straw	<0.05 <0.05 <0.05	77 104 104	RIP1999-1001

For northern Europe, one new residue trial and for southern Europe, six new residue trials according to GAP were conducted in 2010/2011 to complete the data set on winter barley.

For this submission, Good Agricultural Practice (GAP) relevant to the highest residue levels likely to occur is presented in Table 6.3-3.

Table 6.3-3 Good Agricultural Practices (GAPs) proposed for active substance

SUMMARY OF GOOD AGRICULTURAL PRACTICES FOR PESTICIDE USES
(Application on agricultural and horticultural crops)

Applicant : BASF SE
Pesticide(s) (common name(s)) : Picolinafen
EEC, CIPAC and CCPR No(s). : CIPAC No. 639
Trade name(s) : BAS 700 03H
Main uses e.g. insecticide, fungicide : Herbicide
Use Pattern

Crop and/or situation (a)	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days)	Remarks: (m)
				Type (d-f)	Conc. of as (i)	method kind (f-h)	GS & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Winter cereals (wheat, barley, rye, triticale)	BAS 700 03H	F	Broad leaved weeds	WG	75% (w/w) Picolinafen	Foliar Spray	BBCH 11 - 29	1	n.a.	0.0125 to 0.05	200 to 400	0.05 to 0.1	—	

(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)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/l
(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
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

6.3.1 Winter wheat

Report:	II A 6.3.1/1 Perny A. 2011(a) Determination of Picolinafen residues after a single application of BAS 700 03 H on winter wheat under field conditions in Southern Europe in 2010-2011 BASF DocID 2011/1016544
Guidelines:	EEC 91/414; EC 1107/2009 (14 June 2011)
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Executive Summary

Five at harvest trials were conducted on winter wheat under open field conditions in Southern France, Spain and Italy in 2010/2011. Each trial consisted of one control plot and one treated plot. The treated plots were applied once with BAS 700 03 H at a nominal rate of 100 g as/ha at BBCH 26 - 29.

Samples (wheat grain and straw) were sampled at BBCH 89 and analysed for residues of picolinafen. The study provided procedural recoveries at levels of 0.01 mg/kg, 0.1 mg/kg for wheat grain and 0.01 mg/kg, 0.1 mg/kg, 1.0 mg/kg for wheat straw. Following this, the limit of quantification (LOQ) for grain and straw is 0.01 mg/kg.

In all wheat grain samples, residues of picolinafen were found to be below LOQ (<0.01 mg/kg). In wheat straw, residues of picolinafen were in the range of <LOQ to 0.69 mg/kg.

I. MATERIAL AND METHODS

A. MATERIALS

1. Test Material: BAS 700 03 H
Description: Picolinafen formulated as water dispersible granules (WG)
Lot/Batch #: 1030
Purity: 75% (nominal)
77.2% (certified)
CAS#: 137641-05-5 (active substance)
Development code: —
Spiking levels: 0.01 mg/kg, 0.1 mg/kg (grain)
0.01 mg/kg, 0.1 mg/kg, 1.0 mg/kg (straw)

2. Test Commodity
Crop: Winter wheat
Type: cereals
Variety: Provençal, Paledor, Taylor, Aubusson, Concadoro
Botanical name: *Triticum* L.
Crop parts(s) or processed commodity: Grain, straw
Sample size: Grain: 1.01 - 1.30 kg
Straw: 0.50 - 0.76 kg

B. STUDY DESIGN

1. Test procedure

Five residue at harvest trials were conducted on winter wheat under open field conditions in Southern France, Spain and Italy in 2010/2011. Each trial consisted of one control (untreated) plot and one treated plot. In these trials, picolinafen (BAS 700 03 H) was formulated as water dispersible granules (WG) formulation containing 75% active substance (nominal), applied once at a rate of 100 g as/ha. Applications were made in water volumes ranging from 147 to 160 L/ha. Application timing was at BBCH 26 - 29.

Wheat was sampled at normal commercial harvest (BBCH 89) at PHI's in the range of 63 - 127 days after treatment. For analysis whole wheat samples were separated into grain and straw. Samples of grain and straw were stored frozen for up to 81 days until analysis. All these trials are considered appropriate to support the proposed EU critical GAP for winter wheat.

2. Description of analytical procedures

Samples were analysed for residues of picolinafen according to Anadiag method B0232 "Independent Laboratory Validation of an Analytical Method for the Analysis of Picolinafen Residues in Crops (barley grain, tomatoes, oilseed rape, orange)" based on the PTRL Europe method ID P 2064 G.

Residues of picolinafen are extracted from wheat grain and straw material with acetonitrile. After addition of $MgSO_4$, NaCl, and buffering citrate salts (pH 5 - 5.5), the mixture is shaken intensively and centrifuged for phase separation. An aliquot of the organic phase is cleaned-up by dispersive SPE on primary secondary amine (PSA) sorbent and $MgSO_4$. Extracts are diluted with a mixture of water/acetonitrile (1/1, v/v) containing 0.1% formic acid and residues of picolinafen are determined by HPLC-MS/MS.

Procedural recoveries of picolinafen were in the range of 86% - 102% (n = 2), mean = 94%, for wheat grain, and in the range of 80% - 96% (n = 7), mean = 89%, RSD = 7% for wheat straw.

II. RESULTS AND DISCUSSION

Table 6.3-4 Summary of residue data supporting EU critical GAPs for picolinafen on winter wheat

GAP is generally for all countries: 1 x 0.1 kg as/ha with application at GS 11 - 29 (BBCH)								
GLP and Trial details	Crop / Variety	Country	Application rate kg as/ha	Crop growth stage (BBCH)	PHI (days)	Portion analysed	Residues found (mg/kg)	Recovery data
Study B0224 Report no. R B0224 - Study to GLP - Study carried out in 2010/2011	Winter wheat (Provençal)	Southern France	0.100	26	102	Grain Straw	<0.01 0.18	Method: Anadiag B0232 Grain = 94%, RSD = n/a (n = 2 in 0.01 - 0.10 mg/kg spiking range) Straw = 89%, RSD = 7% (n = 7 in 0.01 - 1.0 mg/kg spiking range) Maximum storage period ≤ 3 months
	Winter wheat (Paledor)	Spain	0.107	26 - 29	105	Grain Straw	<0.01 0.06	
	Winter wheat (Taylor)	Italy	0.100	29	95	Grain Straw	<0.01 0.05	
	Winter wheat (Aubusson)	Southern France	0.105	27	127	Grain Straw	<0.01 <0.01	
	Winter wheat (Concadoro)	Greece	0.098	26 - 28	63	Grain Straw	<0.01 0.69	

III. CONCLUSION

The residue data clearly indicates that residues of picolinafen should not be determinable in winter wheat grain at harvest when BAS 700 03 H is applied early post-emergence (BBCH 26 - 29) in a single application at a rate of 0.1 kg as/ha. In winter wheat straw residues were found in the range of below the limit of quantification to 0.69 mg/kg under the same conditions.

6.3.2 Winter barley

Report:	II A 6.3.2/1 Perny A. 2011(b) Determination of Picolinafen residues after a single application of BAS 700 03 H on winter barley under field conditions in Northern and Southern Europe in 2010-2011 BASF DocID 2011/1016545
Guidelines:	EEC 91/414; EC 1107/2009 (14 June 2011)
GLP:	Yes (laboratory certified by Groupe Interministeriel des Produits Chimiques, France)

Executive Summary

Seven at harvest trials were conducted on winter barley under open field conditions in 2010/2011, six in southern Europe (Southern France, Spain, Italy and Greece) and one in northern Europe (Northern France). Each trial consisted of one control plot and one treated plot. The treated plots were applied once with BAS 700 03 H at a nominal rate of 100 g as/ha at BBCH 26 - 29.

Samples (barley grain and straw) were sampled at BBCH 89 and analysed for residues of picolinafen. The study provided procedural recoveries at levels of 0.01 mg/kg, 0.1 mg/kg for barley grain and 0.01 mg/kg, 0.1 mg/kg, 1.1 mg/kg for barley straw. Following this, the limit of quantification (LOQ) for grain and straw is 0.01 mg/kg.

In all barley grain samples, residues of picolinafen were found to be below LOQ (<0.01 mg/kg). In barley straw, residues of picolinafen were in the range of <LOQ to 1.04 mg/kg.

I. MATERIAL AND METHODS

A. MATERIALS

1. **Test Material:** BAS 700 03 H
   Description: Picolinafen formulated as water dispersible granules (WG)
   Lot/Batch #: 1030
   Purity: 75% (nominal)
   77.2% (certified)
   CAS#: 137641-05-5 (active substance)
   Development code: —
   Spiking levels: 0.01 mg/kg, 0.1 mg/kg (grain)
   0.01 mg/kg, 0.1 mg/kg, 1.1 mg/kg (straw)

2. **Test Commodity**
   Crop: Winter barley
   Type: cereals
   Variety: Caravan, Campanil, Kotos, Seduction, Pewter, Ketos, Nure
   Botanical name: *Hordeum vulgare* L.
   Crop parts(s) or processed commodity: Grain, straw
   Sample size: Grain: 1.01 - 1.48 kg
   Straw: 0.50 - 0.79 kg

B. STUDY DESIGN

1. Test procedure

Seven at harvest trials were conducted on winter barley under open field conditions in 2010/2011, six in southern Europe (Southern France, Spain, Italy and Greece) and one in northern Europe (Northern France). Each trial consisted of one control (untreated) plot and one treated plot. In these trials, picolinafen (BAS 700 03 H) was formulated as water dispersible granules (WG) formulation containing 75% active substance (nominal), applied once at a rate of 100 g as/ha. Applications were made in water volumes ranging from 148 to 158 L/ha. Application timing was at BBCH 26 - 29.

Barley was sampled at normal commercial harvest (BBCH 89) at PHI's in the range of 71 - 96 days after treatment. For analysis whole barley samples were separated into grain and straw. Samples of grain and straw were stored frozen for up to 75 days until analysis. All these trials are considered appropriate to support the proposed EU critical GAP for winter barley.

2. Description of analytical procedures

Samples were analysed for residues of picolinafen according to Anadiag method B0232 "Independent Laboratory Validation of an Analytical Method for the Analysis of Picolinafen Residues in Crops (barley grain, tomatoes, oilseed rape, orange)" based on the PTRL Europe method ID P 2064 G.

Residues of picolinafen are extracted from barley grain and straw material with acetonitrile. After addition of $MgSO_4$, NaCl, and buffering citrate salts (pH 5 - 5.5), the mixture is shaken intensively and centrifuged for phase separation. An aliquot of the organic phase is cleaned-up by dispersive SPE on primary secondary amine (PSA) sorbent and $MgSO_4$. Extracts are diluted with a mixture of water/acetonitrile (1/1, v/v) containing 0.1% formic acid and residues of picolinafen are determined by HPLC-MS/MS.

Procedural recoveries of picolinafen were in the range of 90% - 93% (n = 2), mean = 92%, for barley grain, and in the range of 89% - 98% (n = 4), mean = 95%, RSD = 4% for barley straw.

II. RESULTS AND DISCUSSION

Table 6.3-5 Summary of residue data supporting EU critical GAPs for picolinafen on winter barley

GAP is generally for all countries: 1 x 0.1 kg as/ha with application at GS 11 - 29 (BBCH)								
GLP and Trial details	Crop / Variety	Country	Application rate kg as/ha	Crop growth stage (BBCH)	PHI (days)	Portion analysed	Residues found (mg/kg)	Recovery data
Study B0225 Report no. R B0225 - Study to GLP - Study carried out in 2010/2011	Winter barley (Caravan)	Northern France	0.105	27	91	Grain Straw	<0.01 <0.01	Method: Anadiag B0232 Grain = 92%, RSD = n/a (n = 2 in 0.01 - 0.10 mg/kg spiking range) Straw = 95%, RSD = 4% (n = 4 in 0.01 - 1.0 mg/kg spiking range) Maximum storage period ≤ 2.5 months
	Winter barley (Campanil)	Southern France	0.105	28	96	Grain Straw	<0.01 0.04	
	Winter barley (Kotos)	Southern France	0.105	27	82	Grain Straw	<0.01 0.60	
	Winter barley (Seduction)	Southern France	0.100	29	91	Grain Straw	<0.01 0.03	
	Winter barley (Pewter)	Spain	0.102	28 - 29	79	Grain Straw	<0.01 0.03	
	Winter barley (Ketos)	Italy	0.099	26	89	Grain Straw	<0.01 <0.01	
	Winter barley (Nure)	Greece	0.102	26 - 28	71	Grain Straw	<0.01 1.04	

III. CONCLUSION

The residue data clearly indicates that residues of picolinafen should not be determinable in winter barley grain at harvest when BAS 700 03 H is applied early post-emergence (BBCH 26 - 29) in a single application at a rate of 0.1 kg as/ha. In winter barley straw residues were found in the range of below the limit of quantification to 1.04 mg/kg under the same conditions.

6.4 Livestock feeding studies

6.4.1 Poultry

Residues of picolinafen in grain are <0.05 mg/kg (or 0.01 mg/kg, respectively), and therefore intakes by poultry will be below 0.1 mg/kg diet. Poultry feeding studies are therefore not required or submitted.

6.4.2 Lactating ruminants (goat or cow)

Refer to DAR section B.7.8 (September 2000) no feeding studies on domestic animals have been conducted. As observed in the lactating goat metabolism study residues of unchanged picolinafen and its metabolites are extensively (> 90%) and rapidly excreted. At low and high dosing levels highest residues of mainly substituted aniline metabolites in tissues are found in the excreting organs liver and kidney and at much lower level in fat including some unchanged picolinafen. Even lower residues of metabolites are detected in milk.

At normal harvest no residues above the LOQ (<0.05 mg/kg or <0.01 mg/kg for studies since 2010) are found in treated cereal grain. Straw in most cases was found to be also free of detectable residues. However, out of a total of 23 results obtained from trials according to the critical GAP, twelve straw samples from wheat and barley were found as high as 0.03 - 1.04 mg picolinafen/kg as summarised in Table 6.4-1 (table taken from DAR section B.7.8 and updated for new trial results, see section 6.3, omitting data obtained from trials not according to cGAP):

Table 6.4-1 Straw samples containing detectable residues of picolinafen

Crop	Application rate (kg a.s./ha)	Residue (mg picolinafen/kg)	DAT
Wheat Straw	0.099	0.08	106
	0.100	0.18	102
	0.107	0.06	105
	0.100	0.05	95
	0.098	0.69	63
Barley Straw	0.099	0.06	110
	0.115	0.17	92
	0.105	0.04	96
	0.105	0.60	82
	0.100	0.03	91
	0.102	0.03	79
	0.102	1.04	71

Referring to the metabolism study on lactating goat (see DAR section B.7.2) residues at significant levels were found in the edible tissues liver and kidney only. Picolinic acid was identified as the main metabolite in liver and kidney whereas no picolinafen was found. In milk picolinic acid did not reach a plateau level during the seven consecutive days of dosing, therefore it can be assumed that uptake of residues by animal will be rather slow. In consequence it can be justified to use the STMR value of the straw residues for calculation of the dietary burden for animal. The dietary inputs into the calculation are summarised in Table 6.4-2.

Table 6.4-2 Picolinafen residue values used for calculation of livestock dietary burdens

Commodity	Crop Group [1)]	STMR (mg/kg)	HR (mg/kg)	Origin
Wheat Grain	Grains	**0.05**	0.05	DAR and this dossier section 6.3
Barley Grain		**0.05**	0.05	
Wheat Straw	Straws cereals	**0.05**	0.69	
Barley Straw		**0.05**	1.04	

1) As defined in *Doc. 7031/VI/95 rev.4; 22/7/96*

Tables 6.4-3 to 6.4-8 contain details of the exposure calculations for picolinafen in dairy ruminants, meat ruminants, pigs, poultry and turkey using the OECD dietary burden calculator version 2.02.

Table 6.4-3 Dietary burden of dairy ruminants

Body weight (kg): 650
Daily feed consumption (kg DM): 25

Median dietary burden (mg/kg bw/day):	0.0015
Median dietary burden (mg/kg feed DM):	0.0396
Highest contributing commodity:	Barley grain

DM – dry matter; bw – body weight

Table 6.4-4 Dietary burden of meat ruminants

Body weight (kg): 500
Daily feed consumption (kg DM): 12

Median dietary burden (mg/kg bw/day):	0.0014
Median dietary burden (mg/kg feed DM):	0.0566
Highest contributing commodity:	Barley grain

DM – dry matter; bw – body weight

Table 6.4-5 Dietary burden of pigs (finishing swine)

Body weight (kg): 100
Daily feed consumption (kg DM): 3

Median dietary burden (mg/kg bw/day):	0.0014
Median dietary burden (mg/kg feed DM):	0.0455
Highest contributing commodity:	Barley grain

DM – dry matter; bw – body weight

Table 6.4-6 Dietary burden of poultry (laying hen)

Body weight (kg): 1.9
Daily feed consumption (kg DM): 0.13

Median dietary burden (mg/kg bw/day):	0.0039
Median dietary burden (mg/kg feed DM):	0.0568
Highest contributing commodity:	Barley grain

DM – dry matter; bw – body weight

Table 6.4-7 Dietary burden of poultry (broiler hen)

Body weight (kg): 1.7
Daily feed consumption (kg DM): 0.12

Median dietary burden (mg/kg bw/day):	0.0028
Median dietary burden (mg/kg feed DM):	0.0398
Highest contributing commodity:	Barley grain

DM – dry matter; bw – body weight

Table 6.4-8 Dietary burden of turkey

Body weight (kg): 7
Daily feed consumption (kg DM): 0.5

Median dietary burden (mg/kg bw/day):	0.0020
Median dietary burden (mg/kg feed DM):	0.0284
Highest contributing commodity:	Barley grain

DM – dry matter; bw – body weight

As it can be concluded from the calculated data, the median dietary burden for livestock, intended for use as food stuff, will not exceed the trigger of 0.1 mg/kg (DM), therefore animal feeding studies are not required.

Also the conclusion of the EU evaluation was not to request a feeding study on ruminants (see the Review Report (SANCO/1418/2001-final, 18 September 2002)).

6.4.3 Pigs

Residue transfer studies in pigs are not required for picolinafen because the metabolism in the rat is not different from that in ruminants.

6.4.4 Fish

This is not required under Directive 91/414/EEC / Reg. (EC) No. 1107/2009.

6.5 Effects of industrial processing and/or household preparation

The metabolism study on wheat and supervised residue trials on wheat and barley reveal that under practical conditions no residues of picolinafen or any relevant metabolite are expected to be present in grain exceeding the LOQ (0.05 mg/kg for studies before 2010, 0.01 mg/kg for studies since 2010). Therefore, no studies on the level and nature of residues in food of processed grain have been conducted and they are not required.

6.5.1 The nature of residue

Not required since residues of individual hydrolysis products will not exceed the trigger value of 0.05 mg/kg, equal to the LOQ for picolinafen for studies conducted before 2010 (see 6.5).

6.5.2 Distribution of the residue in peel/pulp

Not relevant for use on cereals.

6.5.3 Residue levels - balance studies on set of representative processes

No significant residues of picolinafen or its metabolites are expected to be found in grain exceeding the LOQ of 0.05 mg/kg of the analysis method. Therefore, no studies on the level of residues in food of processed grain are required and have been conducted (see 6.5).

No further studies have been performed.

6.5.4 Residue levels - follow-up studies: concentration or dilution factors

No significant residues of picolinafen or its metabolites are expected to be found in grain exceeding the LOQ of 0.05 mg/kg of the analysis method. Therefore, no studies on the level of residues in food of processed grain are required and have been conducted (see 6.5).

No further studies have been performed.

6.6 Residues in succeeding crops

The EU review of picolinafen (DAR, September 2000) concluded that soil decline studies conducted with picolinafen gave DT90 values ranging from 56 to 212 days. Thus it is possible that significant residue levels could remain in the soil at the time of planting following crops.

6.6.1 Theoretical consideration of the nature and level of the residue

Theoretical consideration of the nature and level of residues of picolinafen in succeeding or rotated crops has not been undertaken.

6.6.2 Metabolism and distribution studies on representative crops

According to DAR section B.7.9 (September 2000), the results from a rotational crop study conducted using picolinafen radiolabelled at two positions (aniline-ring and pyridine-ring) at a rate of 100 g as/ha show no accumulation of residues in follow-up crops at plant back intervals of 30 days (lettuce, carrot, soy bean, sugar beet, pea, sunflower) and 11 months (lettuce, carrot, soy bean) after application. The residue levels detected were consistently below 0.01 mg/kg ranging from <0.002 mg/kg to 0.006 mg/kg TRR.

6.6.3 Field trials on representative crops

As concluded in DAR section B.7.9 (September 2000), no significant residues more than 0.01 mg/kg can be expected in rotational crops after post-emergence application of picolinafen to winter wheat or barley at the intended GAP rate of 100 g as/ha. In consequence no field trials on representative crops are required.

6.7 Proposed residue definition and maximum residue levels

6.7.1 Proposed residue definition

Plant:
According to DAR section B.7.16.3 (September 2000), metabolism studies on wheat reveal very low total radioactive residues in grain. Forage and straw contain residues consisting mainly of unchanged picolinafen. Other components are the substituted picolinic acid, 6-(3-trifluoromethyl-phenoxy)-pyridine-2-carboxylic acid, accounting for a maximum of 9% in straw and other not identified metabolites amounting up to 21% (extractable) or 33% (non-extractable). The extractable TRR levels contain up to 16 different metabolites of less than 9% TRR each. The identified metabolites and derivatives of 4-fluoroaniline were included in the rat metabolism studies resulting in no toxicological significance.

The definition of the residue in commodities of plant origin for MRL-setting and monitoring purposes should be parent picolinafen only.

The definition of the residue in commodities of plant origin for risk assessment purposes should be parent picolinafen only.

Livestock:
According to DAR section B.7.16.3 (September 2000), picolinafen is extensively excreted unchanged via faeces and via urine as the substituted picolinic acid (>90% of administered dose). Lower amounts of several metabolites are also excreted in the urine. There is only a very low tendency of bioaccumulation of unchanged picolinafen and substituted picolinic acid in tissues, fat and in milk. These two major components and other metabolites are included in the rat metabolism study.

The definition of the residue in commodities of animal origin for MRL-setting and monitoring purposes should be parent picolinafen only.

The definition of the residue in commodities of animal origin for risk assessment purposes should be parent picolinafen only.

6.7.2 Proposed maximum residue levels (MRLs) and justification

Based on the intended use pattern, picolinafen will be applied to cereals as winter wheat and winter barley only. For winter wheat a total of 19 supervised residue trials (11 x northern EU, 8 x southern EU) were conducted according to GAP. For winter barley a total of 16 supervised residue trials (8 x northern EU, 8 x southern EU) were conducted according to GAP. Residues of picolinafen in cereal grain (wheat and barley) of supervised trials already presented in the previous submission (see DAR section B.7.6.3 and section 6.3 of this submission) were found to be below the previously submitted LOQ of 0.05 mg/kg. Since new trial data provided in this submission to complete the data set, also show a zero residue situation of below the new LOQ of 0.01 mg/kg, it can be assumed that residues of picolinafen in cereals are well below the default MRL already set for cereal. Therefore, the current EU MRL of 0.05 mg/kg for picolinafen in cereal grain does not need to be changed.

6.8 Proposed pre-harvest intervals, re-entry or withholding periods

6.8.1 Pre-harvest interval (in days) for each relevant crop

The intended use of picolinafen in cereals is post-emergence of the crop at up to developing stage BBCH 29 in autumn or spring. Residues found in green plant samples collected on the day of application usually decline to levels below the LOQ within a period of about two months. In twelve trials residues in straw were detected between 0.03 and 1.04 mg/kg. Residues in grain are never quantified in any of the wheat and barley trials. Therefore, due to the sufficient time between application and harvest it is not necessary to set pre-harvest intervals (PHI) in days.

6.8.2 Re-entry period (in days) for livestock, to areas to be grazed

Not relevant since picolinafen is not intended to be applied to areas that are grazed by livestock animals.

6.8.3 Re-entry period for man to crops, buildings or spaces treated

It is not necessary to determine a particular re-entry time for workers following use of picolinafen.

6.8.4 Withholding period (in days) for animals feedingstuffs

It is not necessary to determine a withholding period for animal feeding stuffs.

6.8.5 Waiting period between last application and sowing or planting crop to be protected

Not applicable since picolinafen is use post-emergence only.

6.8.6 Waiting periods between application and handling treated products

No waiting period is considered necessary.

6.8.7 Waiting period before sowing/planting succeeding crops

No waiting period is considered necessary (see also section 6.6.3 of this submission).

6.9 Estimation of exposure through diet and other means

Referring to the European Commission Review Report (SANCO/1418/2001-final, 18 September 2002) the ADI and ARfD for picolinafen are summarised below.

End-Point	Value	Study	Safety factor
Acceptable Daily Intake (ADI)	0.014 mg/kg bw/d	1-year dog study	100
Acute Reference Dose (ARfD)	0.05 mg/kg bw/d	Developmental rabbit study	100

6.9.1 TMDI calculations

The calculation of the TMDI was performed taking into account all crops to which picolinafen may be applied. The current EU MRLs have been used (0.05* mg/kg for fruit, vegetables, pulses, olives, cereals and sugar plants, and 0.1* mg/kg for oilseeds, oilfruits (except olives), tea, coffee, herbal infusions, hops, and spices). The summary of the calculation using the EFSA PRIMo model rev 2.0 is presented in Table 6.9-1. A summary of the input values for picolinafen is given in Table 6.9-3.

Using the EFSA model, the chronic risk assessment ranges from 2.7 to 16.6% of ADI. The diet with the highest TMDI is “UK Toddler” with 16.6% of the ADI.

Table 6.9-1 TMDI calculation for picolinafen using the EFSA PRIMo model Rev. 2.0

Picolinafen

Status of the active substance:	**included**	Code no.	
LOQ (mg/kg bw):	0.01	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.014**	ARfD (mg/kg bw):	**0.05**
Source of ADI:	**02/64/EC**	Source of ARfD:	**02/64/EC**
Year of evaluation:	**2002**	Year of evaluation:	**2002**

Prepare workbook for refined calculations

Undo refined calculations

Explain choice of toxicological reference values.

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment

TMDI (range) in % of ADI
minimum - maximum
3 17

No of diets exceeding ADI: ---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
16.6	UK Toddler	8.2	SUGAR PLANTS	2.3	FRUIT (FRESH OR FROZEN)	2.1	VEGETABLES	
14.6	WHO Cluster diet B	5.2	VEGETABLES	4.2	CEREALS	2.6	FRUIT (FRESH OR FROZEN)	
13.4	FR infant	7.5	VEGETABLES	5.4	FRUIT (FRESH OR FROZEN)	0.3	CEREALS	
13.2	DE child	8.2	FRUIT (FRESH OR FROZEN)	2.6	VEGETABLES	2.0	CEREALS	
11.9	NL child	5.3	FRUIT (FRESH OR FROZEN)	4.1	VEGETABLES	2.0	CEREALS	
11.7	FR toddler	6.2	VEGETABLES	4.2	FRUIT (FRESH OR FROZEN)	1.1	CEREALS	
10.7	UK Infant	3.6	SUGAR PLANTS	2.3	VEGETABLES	2.0	FRUIT (FRESH OR FROZEN)	
10.1	IE adult	3.8	FRUIT (FRESH OR FROZEN)	3.2	VEGETABLES	2.4	CEREALS	
9.1	WHO cluster diet E	3.2	VEGETABLES	2.2	CEREALS	2.1	FRUIT (FRESH OR FROZEN)	
8.2	DK child	3.7	CEREALS	2.6	VEGETABLES	1.8	FRUIT (FRESH OR FROZEN)	
8.1	WHO cluster diet D	3.3	VEGETABLES	3.0	CEREALS	1.0	FRUIT (FRESH OR FROZEN)	
7.5	SE general population 90th percentile	3.6	VEGETABLES	2.1	FRUIT (FRESH OR FROZEN)	1.8	CEREALS	
7.1	WHO Cluster diet F	2.5	VEGETABLES	1.9	CEREALS	1.4	FRUIT (FRESH OR FROZEN)	
6.8	PT General population	2.3	FRUIT (FRESH OR FROZEN)	2.0	VEGETABLES	1.9	CEREALS	
6.6	ES child	2.0	FRUIT (FRESH OR FROZEN)	1.9	CEREALS	1.7	VEGETABLES	
6.5	WHO regional European diet	3.3	VEGETABLES	1.3	CEREALS	1.2	FRUIT (FRESH OR FROZEN)	
5.9	IT kids/toddler	3.0	CEREALS	1.5	VEGETABLES	1.3	FRUIT (FRESH OR FROZEN)	
5.3	UK Adult	1.4	SUGAR PLANTS	1.1	VEGETABLES	1.0	FRUIT (FRESH OR FROZEN)	
5.2	FR all population	2.2	FRUIT (FRESH OR FROZEN)	1.3	VEGETABLES	1.2	CEREALS	
5.0	UK vegetarian	1.3	SUGAR PLANTS	1.3	VEGETABLES	1.2	FRUIT (FRESH OR FROZEN)	
5.0	NL general	2.1	VEGETABLES	1.7	FRUIT (FRESH OR FROZEN)	1.0	CEREALS	
4.4	ES adult	1.5	FRUIT (FRESH OR FROZEN)	1.4	VEGETABLES	1.1	CEREALS	
4.3	IT adult	1.8	CEREALS	1.4	VEGETABLES	1.0	FRUIT (FRESH OR FROZEN)	
3.7	LT adult	1.8	VEGETABLES	1.0	CEREALS	0.8	FRUIT (FRESH OR FROZEN)	
3.5	DK adult	1.3	VEGETABLES	1.2	FRUIT (FRESH OR FROZEN)	1.0	CEREALS	
3.4	PL general population	2.2	VEGETABLES	1.2	FRUIT (FRESH OR FROZEN)	0.0	PULSES, DRY	
2.7	FI adult	1.0	VEGETABLES	0.9	FRUIT (FRESH OR FROZEN)	0.7	CEREALS	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Picolinafen is unlikely to present a public health concern.

6.9.2 NEDI calculations

The TMDI calculations showed that the ADI was not exceeded by any population subgroup, and therefore NEDI calculations are not required.

6.9.3 NESTI calculations

NESTI calculations were performed for the crops/commodities relevant to this application. The existing EU MRLs have been used for these crops/commodities (0.05* mg/kg for wheat, barley and ray). The summary of the calculations using the EFSA PRIMo model rev 2.0 is presented in Table 6.9-2. A summary of the input values for picolinafen is given in Table 6.9-3.

Using the current EFSA model, the ARfD is not exceeded for any of these crops/commodities by either children or adults/general population. The highest NESTI is from wheat at 1.4 % ARfD for children and 0.8% ARfD for adults/general population.

Table 6.9-2 NESTI calculation for picolinafen using the EFSA PRIMo model Rev. 2.0

Acute risk assessment /children						Acute risk assessment / adults / general population					
The acute risk assessment is based on the ARfD. For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation. In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3. **Threshold MRL** is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
	IESTI 1	*)	**)	**IESTI 2**	*)	**)	**IESTI 1**	*)	**)	**IESTI 2**	*)	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	1.4	Wheat	0.05 / -	1.4	Wheat	0.05 / -	0.8	Wheat	0.05 / -	0.8	Wheat	0.05 / -
	0.6	Rye	0.05 / -	0.6	Rye	0.05 / -	0.7	Barley	0.05 / -	0.7	Barley	0.05 / -
	0.2	Barley	0.05 / -	0.2	Barley	0.05 / -	0.5	Rye	0.05 / -	0.5	Rye	0.05 / -
	No of critical MRLs (IESTI 1)		---				**No of critical MRLs (IESTI 2)**		---			
Processed commodities	**No of commodities for which ARfD/ADI is exceeded:**		---				**No of commodities for which ARfD/ADI is exceeded:**		---			
			***)						***)			
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)				Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)			
	1.2	Wheat flour	0.05 / -				0.4	Bread/pizza	0.05 / -			
*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported. **) pTMRL: provisional temporary MRL ***) pTMRL: provisional temporary MRL for unprocessed commodity												
Conclusion: For Picolinafen IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available. No exceedance of the ARfD/ADI was identified for any unprocessed commodity. For processed commodities, no exceedance of the ARfD/ADI was identified.												

Table 6.9-3 Existing EU MRLs

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
100000	1. FRUIT FRESH OR FROZEN; NUTS	0.05*
110000	(i) Citrus fruit	0.05*
110010	Grapefruit (Shaddocks, pomelos, sweeties, tangelo (except mineola), ugli and other hybrids)	0.05*
110020	Oranges (Bergamot, bitter orange, chinotto and other hybrids)	0.05*
110030	Lemons (Citron, lemon)	0.05*
110040	Limes	0.05*
110050	Mandarins (Clementine, tangerine, mineola and other hybrids)	0.05*
110990	Others	0.05*
120000	(ii) Tree nuts (shelled or unshelled)	0.05*
120010	Almonds	0.05*
120020	Brazil nuts	0.05*
120030	Cashew nuts	0.05*
120040	Chestnuts	0.05*
120050	Coconuts	0.05*
120060	Hazelnuts (Filbert)	0.05*
120070	Macadamia	0.05*
120080	Pecans	0.05*
120090	Pine nuts	0.05*
120100	Pistachios	0.05*
120110	Walnuts	0.05*
120990	Others	0.05*
130000	(iii) Pome fruit	0.05*
130010	Apples (Crab apple)	0.05*
130020	Pears (Oriental pear)	0.05*
130030	Quinces	0.05*
130040	Medlar	0.05*
130050	Loquat	0.05*
130990	Others	0.05*
140000	(iv) Stone fruit	0.05*
140010	Apricots	0.05*
140020	Cherries (sweet cherries, sour cherries)	0.05*
140030	Peaches (Nectarines and similar hybrids)	0.05*
140040	Plums (Damson, greengage, mirabelle, sloe)	0.05*
140990	Others	0.05*
150000	(v) Berries & small fruit	0.05*
151000	(a) Table and wine grapes	0.05*
151010	Table grapes	0.05*
151020	Wine grapes	0.05*
152000	(b) Strawberries	0.05*
153000	(c) Cane fruit	0.05*
153010	Blackberries	0.05*
153020	Dewberries (Loganberries, boysenberries, and cloudberries)	0.05*
153030	Raspberries (Wineberries, arctic bramble/raspberry, (Rubus arcticus), nectar raspberries (Rubus arcticus x idaeus))	0.05*
153990	Others	0.05*
154000	(d) Other small fruit & berries	0.05*
154010	Blueberries (Bilberries)	0.05*
154020	Cranberries (Cowberries (red bilberries))	0.05*
154030	Currants (red, black and white)	0.05*
154040	Gooseberries (Including hybrids with other ribes species)	0.05*
154050	Rose hips	0.05*
154060	Mulberries (arbutus berry)	0.05*
154070	Azarole (mediteranean medlar) (Kiwiberry (Actinidia arguta))	0.05*
154080	Elderberries (Black chokeberry (appleberry), mountain ash, buckthorn (sea sallowthorn), hawthorn, service berries, and other treeberries)	0.05*
154990	Others	0.05*
160000	(vi) Miscellaneous fruit	0.05*
161000	(a) Edible peel	0.05*
161010	Dates	0.05*
161020	Figs	0.05*
161030	Table olives	0.05*
161040	Kumquats (Marumi kumquats, nagami kumquats, limequats (Citrus aurantifolia x Fortunella spp.))	0.05*
161050	Carambola (Bilimbi)	0.05*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
161060	Persimmon	0.05*
161070	Jambolan (java plum) (Java apple (water apple), pomerac, rose apple, Brazilean cherry Surinam cherry (grumichama Eugenia uniflora),)	0.05*
161990	Others	0.05*
162000	(b) Inedible peel, small	0.05*
162010	Kiwi	0.05*
162020	Lychee (Litchi) (Pulasan, rambutan (hairy litchi), mangosteen)	0.05*
162030	Passion fruit	0.05*
162040	Prickly pear (cactus fruit)	0.05*
162050	Star apple	0.05*
162060	American persimmon (Virginia kaki) (Black sapote, white sapote, green sapote, canistel (yellow sapote), and mammey sapote)	0.05*
162990	Others	0.05*
163000	(c) Inedible peel, large	0.05*
163010	Avocados	0.05*
163020	Bananas (Dwarf banana, plantain, apple banana)	0.05*
163030	Mangoes	0.05*
163040	Papaya	0.05*
163050	Pomegranate	0.05*
163060	Cherimoya (Custard apple, sugar apple (sweetsop), llama and other medium sized Annonaceae)	0.05*
163070	Guava (Red pitaya or dragon fruit (Hylocereus undatus))	0.05*
163080	Pineapples	0.05*
163090	Bread fruit (Jackfruit)	0.05*
163100	Durian	0.05*
163110	Soursop (guanabana)	0.05*
163990	Others	0.05*
200000	2. VEGETABLES FRESH OR FROZEN	0.05*
210000	(i) Root and tuber vegetables	0.05*
211000	(a) Potatoes	0.05*
212000	(b) Tropical root and tuber vegetables	0.05*
212010	Cassava (Dasheen, eddoe (Japanese taro), tannia)	0.05*
212020	Sweet potatoes	0.05*
212030	Yams (Potato bean (yam bean), Mexican yam bean)	0.05*
212040	Arrowroot	0.05*
212990	Others	0.05*
213000	(c) Other root and tuber vegetables except sugar beet	0.05*
213010	Beetroot	0.05*
213020	Carrots	0.05*
213030	Celeriac	0.05*
213040	Horseradish (Angelica roots, lovage roots, gentiana roots,)	0.05*
213050	Jerusalem artichokes	0.05*
213060	Parsnips	0.05*
213070	Parsley root	0.05*
213080	Radishes (Black radish, Japanese radish, small radish and similar varieties, tiger nut (Cyperus esculentus))	0.05*
213090	Salsify (Scorzonera, Spanish salsify (Spanish oysterplant))	0.05*
213100	Swedes	0.05*
213110	Turnips	0.05*
213990	Others	0.05*
220000	(ii) Bulb vegetables	0.05*
220010	Garlic	0.05*
220020	Onions (Silverskin onions)	0.05*
220030	Shallots	0.05*
220040	Spring onions (Welsh onion and similar varieties)	0.05*
220990	Others	0.05*
230000	(iii) Fruiting vegetables	0.05*
231000	(a) Solanacea	0.05*
231010	Tomatoes (Cherry tomatoes, tree tomato, Physalis, gojiberry, wolfberry (Lycium barbarum and L. chinense))	0.05*
231020	Peppers (Chilli peppers)	0.05*
231030	Aubergines (egg plants) (Pepino)	0.05*
231040	Okra, lady's fingers	0.05*
231990	Others	0.05*
232000	(b) Cucurbits - edible peel	0.05*
232010	Cucumbers	0.05*
232020	Gherkins	0.05*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
232030	Courgettes (Summer squash, marrow (patisson))	0.05*
232990	Others	0.05*
233000	(c) Cucurbits-inedible peel	0.05*
233010	Melons (Kiwano)	0.05*
233020	Pumpkins (Winter squash)	0.05*
233030	Watermelons	0.05*
233990	Others	0.05*
234000	(d) Sweet corn	0.05*
239000	(e) Other fruiting vegetables	0.05*
240000	(iv) Brassica vegetables	0.05*
241000	(a) Flowering brassica	0.05*
241010	Broccoli (Calabrese, Chinese broccoli, broccoli raab)	0.05*
241020	Cauliflower	0.05*
241990	Others	0.05*
242000	(b) Head brassica	0.05*
242010	Brussels sprouts	0.05*
242020	Head cabbage (Pointed head cabbage, red cabbage, savoy cabbage, white cabbage)	0.05*
242990	Others	0.05*
243000	(c) Leafy brassica	0.05*
243010	Chinese cabbage (Indian (Chinese) mustard, pak choi, Chinese flat cabbage (tai goo choi), choi sum, peking cabbage (pe-tsai),)	0.05*
243020	Kale (Borecole (curly kale), collards, Portuguese Kale, Portuguese cabbage, cow cabbage)	0.05*
243990	Others	0.05*
244000	(d) Kohlrabi	0.05*
250000	(v) Leaf vegetables & fresh herbs	0.05*
251000	(a) Lettuce and other salad plants including Brassicacea	0.05*
251010	Lamb´s lettuce (Italian cornsalad)	0.05*
251020	Lettuce (Head lettuce, lollo rosso (cutting lettuce), iceberg lettuce, romaine (cos) lettuce)	0.05*
251030	Scarole (broad-leaf endive) (Wild chicory, red-leaved chicory, radicchio, curld leave endive, sugar loaf)	0.05*
251040	Cress	0.05*
251050	Land cress	0.05*
251060	Rocket, Rucola (Wild rocket)	0.05*
251070	Red mustard	0.05*
251080	Leaves and sprouts of Brassica spp (Mizuna, leaves of peas and radish and other babyleaf brassica crops (crops harvested up to 8 true leaf stage))	0.05*
251990	Others	0.05*
252000	(b) Spinach & similar (leaves)	0.05*
252010	Spinach (New Zealand spinach, amaranthus spinach)	0.05*
252020	Purslane (Winter purslane (miner's lettuce), garden purslane, common purslane, sorrel, glassworth, Agretti (Salsola soda))	0.05*
252030	Beet leaves (chard) (Leaves of beetroot)	0.05*
252990	Others	0.05*
253000	(c) Vine leaves (grape leaves)	0.05*
254000	(d) Water cress	0.05*
255000	(e) Witloof	0.05*
256000	(f) Herbs	0.05*
256010	Chervil	0.05*
256020	Chives	0.05*
256030	Celery leaves (Fennel leaves, Coriander leaves, dill leaves, Caraway leaves, lovage, angelica, sweet cisely and other Apiacea leaves)	0.05*
256040	Parsley	0.05*
256050	Sage (Winter savory, summer savory,)	0.05*
256060	Rosemary	0.05*
256070	Thyme (Marjoram, oregano)	0.05*
256080	Basil (Balm leaves, mint, peppermint)	0.05*
256090	Bay leaves (laurel)	0.05*
256100	Tarragon (Hyssop)	0.05*
256990	Others (Edible flowers)	0.05*
260000	(vi) Legume vegetables (fresh)	0.05*
260010	Beans (with pods) (Green bean (french beans, snap beans), scarlet runner bean, slicing bean, yardlong beans)	0.05*
260020	Beans (without pods) (Broad beans, Flageolets, jack bean, lima bean, cowpea)	0.05*
260030	Peas (with pods) (Mangetout (sugar peas, snow peas))	0.05*
260040	Peas (without pods) (Garden pea, green pea, chickpea)	0.05*
260050	Lentils	0.05*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
260990	Others	0.05*
270000	(vii) Stem vegetables (fresh)	0.05*
270010	Asparagus	0.05*
270020	Cardoons	0.05*
270030	Celery	0.05*
270040	Fennel	0.05*
270050	Globe artichokes	0.05*
270060	Leek	0.05*
270070	Rhubarb	0.05*
270080	Bamboo shoots	0.05*
270090	Palm hearts	0.05*
270990	Others	0.05*
280000	(viii) Fungi	0.05*
280010	Cultivated (Common mushroom, Oyster mushroom, Shi-take)	0.05*
280020	Wild (Chanterelle, Truffle, Morel, Cep)	0.05*
280990	Others	0.05*
290000	(ix) Sea weeds	0.05*
300000	3. PULSES, DRY	0.05*
300010	Beans (Broad beans, navy beans, flageolets, jack beans, lima beans, field beans, cowpeas)	0.05*
300020	Lentils	0.05*
300030	Peas (Chickpeas, field peas, chickling vetch)	0.05*
300040	Lupins	0.05*
300990	Others	0.05*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
400000	4. OILSEEDS AND OILFRUITS	
401000	(i) Oilseeds	0.1*
401010	Linseed	0.1*
401020	Peanuts	0.1*
401030	Poppy seed	0.1*
401040	Sesame seed	0.1*
401050	Sunflower seed	0.1*
401060	Rape seed (Bird rapeseed, turnip rape)	0.1*
401070	Soya bean	0.1*
401080	Mustard seed	0.1*
401090	Cotton seed	0.1*
401100	Pumpkin seeds (Other seeds of cucurbitacea)	0.1*
401110	Safflower	0.1*
401120	Borage	0.1*
401130	Gold of pleasure	0.1*
401140	Hempseed	0.1*
401150	Castor bean	0.1*
401990	Others	0.1*
402000	(ii) Oilfruits	
402010	Olives for oil production	0.05*
402020	Palm nuts (palmoil kernels)	0.1*
402030	Palmfruit	0.1*
402040	Kapok	0.1*
402990	Others	0.1*
500000	5. CEREALS	0.05*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
500010	Barley	0.05*
500020	Buckwheat (Amaranthus, quinoa)	0.05*
500030	Maize	0.05*
500040	Millet (Foxtail millet, teff)	0.05*
500050	Oats	0.05*
500060	Rice	0.05*
500070	Rye	0.05*
500080	Sorghum	0.05*
500090	Wheat (Spelt, triticale)	0.05*
500990	Others	0.05*
600000	6. TEA, COFFEE, HERBAL INFUSIONS AND COCOA	0.1*
610000	(i) Tea (dried leaves and stalks, fermented or otherwise of Camellia sinensis)	0.1*
620000	(ii) Coffee beans	0.1*
630000	(iii) Herbal infusions (dried)	0.1*
631000	(a) Flowers	0.1*
631010	Camomille flowers	0.1*
631020	Hybiscus flowers	0.1*
631030	Rose petals	0.1*
631040	Jasmine flowers (Elderflowers (Sambucus nigra))	0.1*
631050	Lime (linden)	0.1*
631990	Others	0.1*
632000	(b) Leaves	0.1*
632010	Strawberry leaves	0.1*

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
632020	Rooibos leaves (Ginkgo leaves)	0.1*
632030	Maté	0.1*
632990	Others	0.1*
633000	(c) Roots	0.1*
633010	Valerian root	0.1*
633020	Ginseng root	0.1*
633990	Others	0.1*
639000	(d) Other herbal infusions	0.1*
640000	(iv) Cocoa (fermented beans)	0.1*
650000	(v) Carob (st johns bread)	0.1*
700000	7. HOPS (dried) , including hop pellets and unconcentrated powder	0.1*
800000	8. SPICES	0.1*
810000	(i) Seeds	0.1*
810010	Anise	0.1*
810020	Black caraway	0.1*
810030	Celery seed (Lovage seed)	0.1*
810040	Coriander seed	0.1*
810050	Cumin seed	0.1*
810060	Dill seed	0.1*
810070	Fennel seed	0.1*
810080	Fenugreek	0.1*
810090	Nutmeg	0.1*
810990	Others	0.1*
820000	(ii) Fruits and berries	0.1*
820010	Allspice	0.1*
820020	Anise pepper (Japan pepper)	0.1*
820030	Caraway	0.1*
820040	Cardamom	0.1*
820050	Juniper berries	0.1*
820060	Pepper, black and white (Long pepper, pink pepper)	0.1*
820070	Vanilla pods	0.1*
820080	Tamarind	0.1*
820990	Others	0.1*
830000	(iii) Bark	0.1*
830010	Cinnamon (Cassia)	0.1*
830990	Others	0.1*
840000	(iv) Roots or rhizome	0.1*
840010	Liquorice	0.1*
840020	Ginger	0.1*
840030	Turmeric (Curcuma)	0.1*
840040	Horseradish	0.1*
840990	Others	0.1*
850000	(v) Buds	0.1*
850010	Cloves	0.1*
850020	Capers	0.1*
850990	Others	0.1*
860000	(vi) Flower stigma	0.1*
860010	Saffron	0.1*
860990	Others	0.1*
870000	(vii) Aril	0.1*
870010	Mace	0.1*
870990	Others	0.1*
900000	9. SUGAR PLANTS	0.05*
900010	Sugar beet (root)	0.05*
900020	Sugar cane	0.05*
900030	Chicory roots	0.05*
900990	Others	0.05*
1000000	10. PRODUCTS OF ANIMAL ORIGIN-TERRESTRIAL ANIMALS	
1010000	(i) Meat, preparations of meat, offals, blood, animal fats fresh chilled or frozen, salted, in brine, dried or smoked or processed as flours or meals other processed products such as sausages and food preparations based on these	
1011000	(a) Swine	
1011010	Meat	
1011020	Fat free of lean meat	
1011030	Liver	
1011040	Kidney	
1011050	Edible offal	
1011990	Others	
1012000	(b) Bovine	
1012010	Meat	
1012020	Fat	

Code number	Groups and examples of individual products to which the MRLs apply (a)	Picolinafen
1012030	Liver	
1012040	Kidney	
1012050	Edible offal	
1012990	Others	
1013000	(c) Sheep	
1013010	Meat	
1013020	Fat	
1013030	Liver	
1013040	Kidney	
1013050	Edible offal	
1013990	Others	
1014000	(d) Goat	
1014010	Meat	
1014020	Fat	
1014030	Liver	
1014040	Kidney	
1014050	Edible offal	
1014990	Others	
1015000	(e) Horses, asses, mules or hinnies	
1015010	Meat	
1015020	Fat	
1015030	Liver	
1015040	Kidney	
1015050	Edible offal	
1015990	Others	
1016000	(f) Poultry -chicken, geese, duck, turkey and Guinea fowl-, ostrich, pigeon	
1016010	Meat	
1016020	Fat	
1016030	Liver	
1016040	Kidney	
1016050	Edible offal	
1016990	Others	
1017000	(g) Other farm animals (Rabbit, Kangaroo)	
1017010	Meat	
1017020	Fat	
1017030	Liver	
1017040	Kidney	
1017050	Edible offal	
1017990	Others	
1020000	(ii) Milk and cream, not concentrated, nor containing added sugar or sweetening matter, butter and other fats derived from milk, cheese and curd	
1020010	Cattle	
1020020	Sheep	
1020030	Goat	
1020040	Horse	
1020990	Others	
1030000	(iii) Birds' eggs, fresh preserved or cooked Shelled eggs and egg yolks fresh, dried, cooked by steaming or boiling in water, moulded, frozen or otherwise preserved whether or not containing added sugar or sweetening matter	
1030010	Chicken	
1030020	Duck	
1030030	Goose	
1030040	Quail	
1030990	Others	
1040000	(iv) Honey (Royal jelly, pollen)	
1050000	(v) Amphibians and reptiles (Frog legs, crocodiles)	
1060000	(vi) Snails	
1070000	(vii) Other terrestrial animal products	

6.10 Other/special studies

None other/special studies submitted or required.

6.11 Summary and evaluation of residue behaviour and reasonable grounds

6.11.1 Summary and evaluation of residue behaviour

This dossier is presented to support picolinafen for use on winter cereals (wheat, barley, rye, triticale). For picolinafen, the main information and data are available in the DAR (September 2000) and Review Report (SANCO/1418/2001-final, 18 September 2002).

Data on metabolism in crops and livestock, storage stability and residues in crops and rotational crops have been reviewed for picolinafen during the Annex I inclusion process and considered to be acceptable. The proposed GAP for picolinafen on cereals is within the critical GAPs supported for Annex I inclusion for picolinafen. Also by the first Annex I inclusion it was noted that no further data were required many of the reviewed residue trials do not match the critical GAP. Therefore, to complete the data package new harvest residue trials were conducted according to GAP in 2010/2011 on winter wheat (5 x S-EU) and winter barley (1 x N-EU, 6 x S-EU) and presented in this dossier.

Straw, in most trials, has been shown to be free of detectable residues. Residue levels found in straw in 12 trials ranged between 0.03 and 1.04 mg/kg. The higher values of 0.69 - 1.04 mg/kg are all trials performed in Greece having the shortest sampling periods of 63 - 71 days after treatment.

Residues of picolinafen in wheat and barley grain are <0.05 mg/kg or <0.01 mg/kg for the new residue trial data, respectively, and therefore do not exceed the EU MRL of 0.05* mg/kg.

New dietary risk assessments have been carried out and the results are presented in point 6.9. Calculations were performed taking into account all the crops in/on which the active substances may be applied.

The results of the TMDI calculations with the EFSA PRIMo model are summarized in Point 6.9.1 and show that there is no chronic risk to the consumer from picolinafen. The TMDI estimation according to the EU calculations ranges from 2.7 to 16.6% of ADI.

The results of the NESTI calculations demonstrate that in no case is the NESTI is above the acute reference dose (ARfD) of 0.05 mg/kg bw/day. The highest NESTI is from wheat at 1.4% ARfD for children and 0.8% ARfD for adults/general population.

Based on the calculations made to estimate the risk to the consumer though diet, it can be concluded that the use of picolinafen on winter cereals (wheat, barley, rye and triticale) does not lead to unacceptable risk for consumers when applied according to the recommendations.

6.11.2 Reasonable grounds in support of the petition

Not required.

The Chemical Company

DOSSIER FOR THE EVALUATION OF THE ACTIVE SUBSTANCE

Picolinafen (BAS 700 H)

Data requirement according to Regulation (EU) No. 544/2011 and (EU) No. 545/2011
of 10 June 2011 (formerly Annex II and III of Directive 91/414/EEC)
using OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substance (Dossier Guidance)
and Commission Regulation (EC) No 1141/2010 of 7 December 2010 (AIR procedure)

Document M-II

Summary and evaluation (Tier II)

Section 5

Fate and behaviour in the environment

BASF DocID 2012/1208879

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Date: 30 August 2012

7 Fate and Behaviour in the Environment

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7.1 Route of degradation in soil - laboratory studies

7.1.1 Aerobic degradation

Adequate data to assess the aerobic route of degradation of picolinafen in soil were evaluated during the first EU review (Steinführer 1997 and 1998) and no further data were considered necessary. For further details, please refer to the DAR dated September 2000.
However, in the route and rate soil studies, only picolinafen labelled in the pyridine and aniline rings was tested but not in the third fluoro-phenoxy-ring. To further address this apparent gap, an additional aerobic soil route and rate degradation study in 3 soils with the third label was performed and is summarised below.

Additionally, in the soil degradation and metabolism study (Steinführer, (1998); IIA-7.1.1.1.1/01), non-identified radioactivity exceeded 5% of the applied radioactivity (% AR) on at least two consecutive occasions, which is a trigger for further identification according to the guidance document for relevant metabolites (Sanco/221/2000 – rev.10- final 25 February 2003). This fraction consisted only of radioactivity bound to the extracted organic matter and remained as start activity on the TLC plates as well as background unresolved integrated activity, due to the very high adsorption of picolinafen and its metabolites in soil. It was not an issue highlighted in the DAR, but given that these unidentified degradation products exceed the Sanco/221/2000 thresholds, a detailed summary of the results is provided to properly account for the non resolved activity.

Unidentified radioactivity

- *T. Steinführer (1998): ^{14}C-AC 900001 (CL 900001): Route of Degradation in Soil Under Aerobic Conditions. American Cyanamid Report No. CFS 1997-013; BOD 2000-4*

For details, please refer to the DAR dated September 2000.

The figures in the report show that the unidentified radioactivity corresponds to the sum of TLC origin radioactivity and the unresolved radioactivity originating from the integrated background. These residues exceeded 5% AR, reaching the maximum of 5.6% in the samples treated with the pyridine label. The major part of the unidentified radioactivity corresponded to the TLC origin radioactivity. This radioactivity increased with increasing polarity of the extraction solvent. It showed the highest relative amounts in the harsh extracts such as using EDTA and reflux. However, by considering all integrated fractions none exceeded 5% AR.

- *T. Steinführer (1997): ^{14}C-AC 900001 (CL 900001): Rate of Degradation in Three Different Soils Under Aerobic Conditions. American Cyanamid Report No. CFS 1997-027; BOD 2000-7*

For details, please refer to the DAR dated September 2000. The rapporteur MS (Germany) commented the following:

The study is acceptable. On some days, the amounts of unidentified radioactivity exceeded 10 %. The highest amounts of unidentified* radioactivity was detected on day 3 after application: 16, 11 and 17.9 %TAR in the Engelstadt/Benz, Ingelheim/Moers and Kloppenheim/Untere Gewann soil, respectively.*

** calculated from the difference between extractable radioactivity (% TAR) and the sum of picolinafen and CL 153815 (% TAR).*

In this study, the soil samples were treated with the pyridine labelled picolinafen. No TLC origin radioactivity was observed, as a much polar TLC solvent system was used. The unidentified radioactivity was only due to the integrated unresolved background activity.

Soil route and rate of fluoro-phenoxy-labelled picolinafen

Report:	II A 7.1.1/1 Turk R.S. 2012(a) (14C)Picolinafen - Aerobic route and rate of degradation in soil BASF DocID 2011/1018565
Guidelines:	OECD 307; EPA 835.4100
Testing Laboratory and dates:	Smithers Viscient LLC; Wareham MA; United States of America 17-Feb-2012 - 16-May-2012
GLP:	Yes (laboratory certified by United States Environmental Protection Agency)

Executive Summary

The degradation rate and metabolism of the test item, ^{14}C-picolinafen, was investigated in three soils incubated under aerobic conditions for a period of up to 89 days. The following soils were used: Fislis (silt loam; France), Horn (loam; Switzerland) and Sevelen (sandy loam; Switzerland). The study was performed with picolinafen labelled at the fluoro-phenoxy ring.

For the study, 100 g (dry weight) soil samples were treated with ^{14}C-labelled-picolinafen at a concentration of 0.1 mg/kg, corresponding to a field rate of 100 g a.s. /ha, based on the assumption that the test item is homogeneously distributed in the upper 10 cm of the soil layer with a soil density of 1 g/cm^3. All samples were incubated under aerobic conditions at 20 ± 2°C in the dark at soil water content of pF 2.5. Mass balance was reported as relative to the total applied radioactivity.

Duplicate samples were taken for each interval. Mean recoveries of radioactivity for the samples ranged from 91.8% to 101.5% AR.

High mineralization to carbon dioxide of the radioactive residues was observed in all soils and ranged from 40.7% to 50.2% AR. The level of other volatile organic compounds trapped in the ethylene glycol traps were less than 0.1% AR throughout the study for all soils used.

The rate of degradation of picolinafen was rapid in all soils. The calculated DT_{50} and DT_{90} values of degradation of picolinafen in the soils, according to FOCUS guidance and based on first order reaction kinetics, ranged from 2.2 to 2.6 days and from 7.3 to 8.5 days, respectively. The extractable radioactivity declined from 90.1%-94.8% AR to 5.3%-9.5% over 89 days. The non-extractable ranged from 37.3%to 42.0% AR after 89 days of incubation.
One major transformation product, identified as CL 153815, 6-[3-(trifluoromethyl)phenoxy]-2-pyridienecarboxylic acid, was detected in all three soils and reached the maximum of 66.4%. Other minor fractions were observed but never exceeded 5% AR.

I. MATERIAL AND METHODS

A. MATERIALS

Test Materials:	^{14}C-picolinafen; specific activity 10.2 MBq/mg Batch No. 1037-0101
Purity:	Radiochemical Purity 99.3%
CAS#:	137641-05-05
Stability of compound:	The test item was stable in the application solution during the treatment of the soil samples.
Soil:	The soils were collected from the top 20 cm layer at specific locations with restricted access managed to ensure that no pesticides or organic fertilizer treatments took place for at least three years prior to collection. A summary of the physical and chemical properties of the soils is provided in Table 7.1.1-1.

Table 7.1.1-1: Characteristics of the Soils Used

Soil ID **USDA Textural Class**	**Fislis** **Silt Loam**	**Horn** **Loam**	**Sevelen** **Sandy Loam**
Agvise No.	**12-97**	**12-96**	**12-95**
% Sand	19	47	59
% Silt	55	33	37
% Clay	26	20	4
Bulk Density disturbed (gm/cc)	0.92	1.14	1.03
Calcium (ppm)	3030	2740	1140
Magnesium (ppm)	51	97	38
Sodium (ppm)	16	16	18
Potassium (ppm)	87	63	19
Hydrogen (ppm)	22	22	6
Olsen Phosphorus (ppm)	46	47	8
Total Nitrogen (%)	0.24	0.26	0.15
Soluble Salts (mmhos/cm)	0.40	0.35	0.26
% Organic Matter	4.4	4.1	2.5
% Organic Carbon[a]	2.6	2.4	1.5
pH (1:1 soil/water ratio)	7.3	7.4	7.6
Cation Exchange Capacity (meq/100 g)	18.0	17.0	6.8
Field Moisture:			
Capacity at 1/3 bar [pF2.5] (%)[c]	31.0	28.5	21.5
Capacity at 1/10 bar [pF2.0](%)	39.7	33.5	31.5

a % organic matter/1.724

B. STUDY DESIGN AND METHODS

1. Experimental Conditions

The aerobic soil metabolism of picolinafen was studied using fluoro-phenoxy ^{14}C labelled picolinafen applied at a rate of 0.1 mg/kg soil (equivalent to 100 g a.s. /ha).

The soils were acclimated to room temperature for at least one week prior to the test substance application. Portions of the sieved soil, equivalent to 100 g dry soil, adjusted to soil water content at pF2.5 in glass metabolism flasks were used. An application solution of radiolabelled picolinafen dissolved in acetone was prepared and applied to the soil in metabolism flasks. The organic solvent was allowed to evaporate after which the soil was mixed to ensure homogeneity. Duplicate samples were incubated in darkness in an environmentally controlled room at a temperature of 20 ± 2ºC for an incubation period of 89 days.

2. Sampling

Duplicate soil samples were taken for extraction and analysis immediately after treatment (day 0) and after 2, 7, 14, 28, 55 and 89 days of incubation.
Microbial biomass was determined at pre-initiation, at zero time, during and at the end of the incubation using the fumigation/extraction method. Volatile traps were taken for analysis weekly.

3. Description of analytical procedures

Samples were extracted with 200 mL of acetone and sonicated for approximately 30 minutes. The samples were then centrifuged at 1000 rpm for ten minutes and the extract was transferred into a graduated cylinder. The volume was recorded and the sample was analyzed by liquid scintillation counting (2 × 1.0 mL). The extraction procedure was repeated up to four additional times with methanol/ water, (60:40, v/v, 100 or 150 mL) with the procedure as described above. If necessary samples were centrifuged at 10,000 rpm for five minutes and analyzed (1 × 0.05 mL) by LSC to verify loss of radioactivity. Extractions were performed until less than 5% AR was extracted.

The resulting post-extracted soil was further submitted for Soxhlet extraction. The samples were extracted with approximately acetonitrile/water, 80:20 (v/v) by boiling for six hours. Following Soxhlet extraction, the extracts were pooled and concentrated to a volume of 2.0 to 4.0 mL using rotary evaporator. The concentrate was then transferred using acetonitrile to a graduated cylinder, sonicated for approximately 2 minutes and the total volume recorded. The recovered radioactivity after concentration ranged from 83 – 112% of the initial radioactivity. The extracts were analysed by means of High Performance Liquid Chromatography (HPLC) and Thin Layer Chromatography (TLC) for the test item and degradation products.
The KOH and ethylene glycol solutions for trapping volatiles were analyzed for radioactivity at the respective sampling intervals by Liquid Scintillation Counting (LSC). Residual radioactivity in the soil after extraction was determined by combustion followed by LSC.

The limit of quantification (LOQ) was calculated to be 0.06% AR by HPLC.

II. RESULTS AND DISCUSSION

A. DATA

Table 7.1.1-2: ^{14}C Distribution in Fislis soil treated with ^{14}C-picolinafen under aerobic Conditions (as percentage of applied radioactivity, mean of duplicates)

Day	Extractables	Soxhlet	Unextractables	$^{14}CO_2$	VOC	Recovery	PPM
0	91.0	NA	3.4	NA	NA	94.4	0.091
2	80.1	6.1	10.0	0.5	<0.1	96.6	0.093
7	64.5	7.0	20.2	2.1	<0.1	93.8	0.091
14	54.1	8.0	26.4	8.8	<0.1	97.3	0.094
28	33.6	6.5	34.0	20.4	<0.1	94.6	0.091
55	14.0	5.1	45.3	36.4	<0.1	100.7	0.097
89	5.3	2.7	41.1	50.2	<0.1	99.4	0.096

NA: Not applicable
VOC = volatile organic compounds

Table 7.1.1-3: ^{14}C Distribution in Horn soil treated with ^{14}C-picolinafen under aerobic conditions (as percentage of applied radioactivity, mean of duplicates)

Day	Extractables	Soxhlet	Unextractables	$^{14}CO_2$	VOC	Recovery	PPM
0	90.1	NA	3.4	NA	NA	93.5	0.090
2	80.6	11.3	9.4	0.3	<0.1	101.5	0.098
7	61.3	7.3	21.4	4.3	<0.1	94.3	0.091
14	47.9	8.9	27.9	7.0	<0.1	91.8	0.089
28	32.9	7.2	32.0	20.3	<0.1	92.4	0.089
55	20.3	3.1	39.1	31.0	<0.1	93.5	0.090
89	5.6	5.1	37.3	49.5	<0.1	97.5	0.094

NA: Not applicable
VOC = volatile organic compounds

Table 7.1.1-4: ^{14}C Distribution in Sevelen soil treated with ^{14}C-picolinafen under aerobic conditions (as percentage of applied radioactivity, mean of duplicates)

Day	Extractables	Soxhlet	Unextractables	$^{14}CO_2$	VOC	Recovery	PPM
0	94.8	NA	2.3	NA	NA	97.1	0.094
2	88.4	4.2	5.1	0.2	<0.1	98.0	0.095
7	71.2	7.0	14.0	3.1	<0.1	95.4	0.092
14	58.7	13.0	17.9	6.2	<0.1	95.7	0.092
28	46.0	13.6	21.3	13.0	<0.1	93.9	0.091
55	29.7	9.5	31.9	26.2	<0.1	97.3	0.094
89	9.5	8.4	42.0	40.7	<0.1	100.6	0.097

NA: Not applicable
VOC = volatile organic compounds

Table 7.1.1-5: Picolinafen and its metabolites in soil Filsis (as percentage of applied radioactivity, mean of duplicates)

Day	Picolinafen	Polars*	CL 153815	Others
Day 0	90.2	ND	ND	0.8
Day 2	50.2	ND	36.0	ND
Day 7	15.1	ND	56.3	ND
Day 14	5.0	ND	56.7	0.4
Day 28	3.2	ND	35.7	1.2
Day 55	2.8	1.8	12.3	2.1
Day 89	3.1	1.5	2.8	0.7

ND: Not detected
* unretained radioactivity

Table 7.1.1-6: Picolinafen and its metabolites in soil Horn (as percentage of applied radioactivity, mean of duplicates)

Day	Picolinafen	Polars*	CL 153815	Others
Day 0	90.1	ND	ND	ND
Day 2	49.4	ND	42.5	ND
Day 7	13.9	ND	54.7	ND
Day 14	7.2	ND	49.2	0.5
Day 28	4.1	ND	33.2	2.8
Day 55	3.2	1.6	16.4	2.3
Day 89	2.9	2.2	3.1	2.5

ND: Not detected
* unretained radioactivity

Table 7.1.1-7: Picolinafen and its metabolites in soil Sevelen (as percentage of applied radioactivity, mean of duplicates)

Day	Picolinafen	Polars*	CL 153815	Others
0	94.8	ND	ND	ND
2	57.8	ND	34.8	ND
7	11.8	ND	66.4	ND
14	7.6	ND	63.5	0.5
28	5.9	ND	53.1	0.6
55	3.9	0.7	33.7	0.8
89	2.7	2.0	11.2	2.0

ND: Not detected
* unretained radioactivity

B. MASS BALANCE

Material balance for the transformation of ^{14}C-picolinafen in the aerobic soil system ranged from 91.1% to 104.9% AR (individual values) over the 89-day study. The overall average material balance from all sampling intervals was 96.7 ± 3.0, 94.9 ± 3.6 and 96.9% ± 2.4 AR for the Fislis, Horn and Sevelen soils, respectively.

C. BOUND RESIDUES

The amount of non-extractable radioactivity after soxhlet and acetonitrile: water extractions increased from 3.4% AR at day 0 to 45.3% and 39.1% AR at day 55 and remained practically constant till the end of incubation for soils Fislis and Horn, respectively. For soil Sevelen it increased from an average of 2.3% AR at day 0 to 42.0% AR at day 89.

D. FORMATION OF VOLATILES / MINERALISATION

The radioactivity in the 1 M KOH traps, corresponding to $^{14}CO_2$, reached an accumulative average maximum of 50.2%, 49.5% and 40.7% AR at day 89 for soils Fislis, Horn and Sevelen, respectively. Negligible radioactivity was detected (< 0.1% AR) in the ethylene glycol volatile organic traps for all soils after 89 days of incubation.

E. METABOLITES

Picolinafen was rapidly degraded with a calculated DT_{50} of about 2 days and a DT_{90} of about 7-9 days. One major radioactive fraction exceeding 5% AR was detected in the total extractable fraction of the soils and was characterised as CL 153815. The amount of CL 153815 in the extracts increased continuously and reached a maximum between day 7 and 14 at levels between 54.7% and 66.4% for all soils. CL 153815 decreased thereafter representing between 2.8% and 11.2% AR at the end of the incubation (day 89). Other minor fractions were detected but none exceeded 3% AR.

III. CONCLUSION

The rate of degradation of picolinafen was similar in all soils. The calculated DT_{50} and DT_{90} values of degradation of picolinafen in soil, based on first order reaction kinetics, ranged from 2.2 to 2.6 days and from 7.3 to 8.5 days, respectively. Picolinafen was degraded to one major radioactive metabolite CL 153815 reaching the maximum of 66.4% AR. CL 153815 was further degraded with DT_{50} values ranging from 19.3 to 34.6 days. Other minor fractions were detected but none exceeded 3% AR.

Overall, picolinafen degrades by microbial degradation primarily to CL 153815. CL 153815 is further degraded to mainly bound residues and carbon dioxide.

7.1.2 Anaerobic degradation

Adequate data to assess the anaerobic route of degradation of picolinafen in soil were evaluated during the first EU review (Bissinger 1998) and no further data are considered necessary.

For further details, please refer to the DAR dated September 2000.

Under anaerobic incubation conditions, the rate of degradation of picolinafen (pyridine and aniline label) was not affected and the pattern of degradates remained identical to that under aerobic conditions. The amount of CL 153815 (including its methyl ester CL 197393) increased continuously to a maximum of 87.5% AR after 2 months and remained at that level until the end of the test period after 4 months. CL 7693 (4-fluoroaniline) was found at 7% AR after one week and 7.6% AR was still detected on day 120. Mineralisation was low and amounted to a maximum of 0.4% (pyridine label) and 5.1% (aniline label) within 120 days. The amount of non-extractable residues was lower, when compared to the aerobic degradation, i.e. maximum of 2.6% for the pyridine label and 46.1% for the aniline label.

The major soil metabolite CL 153815 was shown to be stable under anaerobic conditions.

Low recovery was observed for the aniline label. Due to the low amount of $^{14}CO_2$ formed, this can only be due to the losses of the metabolite CL 7693. The vapour pressure of CL 7693 is about 133 Pa, based on HSDB (hazardous substances data bank). The fact that this metabolite was not detected under aerobic conditions, even when using very harsh extraction, and based on the literature data, demonstrates that CL 7693 will be rapidly degraded by mineralisation and strongly bound to the soil organic matter.

7.1.3 Soil photolysis

Adequate data to assess the soil photolysis of picolinafen in soil were evaluated during the first EU review (Schlüter 1998) and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

The photolysis study with pyridine labelled picolinafen on soil revealed several polar degradates none of which exceeded 5% AR at any time during 15 days of continuous irradiation. CL 153815 was not detected at levels >0.7% AR. The degradation half-life was calculated to be 30.2 days of continuous irradiation. The rate of degradation was recalculated following FOCUS kinetics guidance and a DT_{50} of 29.2 days of continuous irradiation was obtained (Mamouni A. & Jarvis T. 2012(a)) – BASF DocID 2012/1206414).

Summary of Route of Degradation in Soil

The previous assessment concluded that the degradation of picolinafen in soil under aerobic conditions occurs by cleavage of the amide bond to form the degradates CL 153815, 6-(3-trifluoromethylphenoxy)-2-pyridine carboxylic acid (max 44%) and CL 7693, 4- fluoroaniline (detected only in the NaOH harsh extractions). These compounds are incorporated into the soil matrix where they are further metabolized under aerobic conditions. Mineralisation was significant from the aniline and pyridine label, with 16-50 % AR identified as CO_2 after 122 to 152 days of incubation in the aerobic degradation studies. Between 20 and 61 % AR was found as bound residues after 122 – 152 days. In the soil degradation and metabolism study (Steinführer, 1998a); AIIA-7.1.1.1.1/01), non-identified radioactivity reached a maximum of 5.6% at two consecutive timepoints. However, this was due to TLC origin radioactivity bound to the extractable organic matter as well as integrated background non resolved radioactivity. The background non resolved radioactivity was due to the high binding of picolinafen and its metabolites to the extractable soil organic matter. However, no single fraction exceeded 5% AR. In the soil degradation study (Steinführer, 1997) the non identified unknown radioactivity amounted to a maximum of 17% AR. However, this was only due to the integrated background non resolved radioactivity.

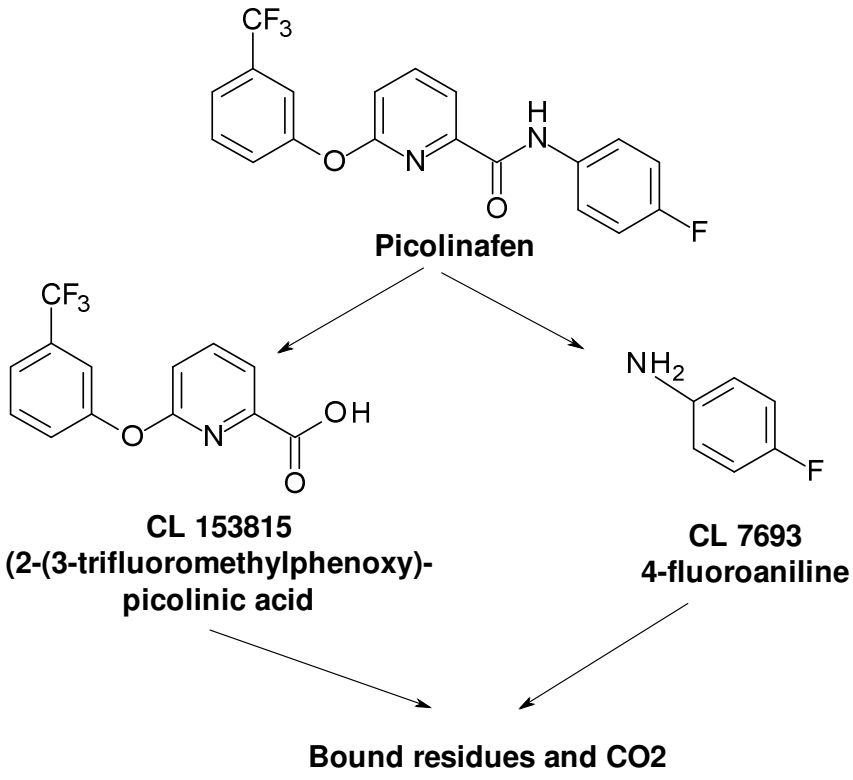
In the soil degradation (Steinführer (1998b)) performed at low temperature (8 ºC) Picolinafen was degraded to only CL 153815 as a metabolite. The differences between the amounts of extractable radioactivity (% AR) and the sum of picolinafen and CL 153815 (% TAR) was 8 % AR on day 0 and increased to amounts of 19 % AR on day 100. Similarly to the studies performed at 20 ºC, the unknown radioactivity was only due to the non resolved background radioactivity. The amounts of $^{14}CO_2$ increase to 9.6 % on day 100 and to 12.7 % AR on day 160. The non-extractable residues increased to 32.8 % AR after 160 days of incubation.

The new aerobic route and rate of degradation study in three soils using the fluoro-phenoxy-ring labelled picolinafen confirms the results of the previously evaluated studies, with picolinafen rapidly degrading to CL 153815 (maximum 66.4%). No other fraction exceeded 5% AR. The non-extractable radioactivity and $^{14}CO_2$ reached the maximum of 42.0-45.3% and 40.7-50%, respectively, within the 89 days of incubation. The proposed route of degradation is summarised in Figure 7.1/1.

Soil photolysis of picolinafen will not be a significant route of degradation in the environment. The extractable minor photodegradates were composed of several products; none exceeded 5 % AR.

Under anaerobic incubation conditions in soil, the rate of degradation of picolinafen (pyridine and aniline label) was not affected and the pattern of degradates remained identical to that under aerobic conditions. The amount of CL 153815 (including its methyl ester CL 197393) increased continuously to a maximum of 87.5% AR after 2 months and remained at that level until the end of the test period after 4 months. The methyl ester CL 197393 is expected to degrade rapidly to the acid CL 153815 under aerobic conditions. CL 7693 (4-fluoroaniline) was formed at maximum of 7.6% AR. However, due to its volatility and the low observed recovery, CL 7693 might have been formed at up to 29% AR based on the lowest recovery of 71% AR. CL 7693 will however be rapidly degraded under aerobic conditions. Mineralisation was low and amounted to maximum 0.4% (pyridine label) and 5.1% (aniline label) within 120 days. The amount of non-extractable residues was lower, when compared to the aerobic degradation, i.e. maximum of 2.6% for the pyridine label and 46.1% for the aniline label.

Figure 7.1/1: Proposed degradation pathway of picolinafen in soil



Note: Under anaerobic conditions, the carboxylic acid group of CL 153815 will be methylated to give CL 197393

7.2 Rate of degradation in soil(s) - laboratory studies

Adequate data to assess the aerobic rate of degradation of picolinafen in soil were evaluated during the first EU review and no further data were considered necessary. For further details, please refer to the DAR dated September 2000.

However, in the route and rate soil studies, only picolinafen labelled in the pyridine and aniline rings was tested but not in the third fluoro-phenoxy-ring. To further address this apparent gap, an additional aerobic soil route and rate degradation study in 3 soils with the third label was performed and the results are summarised in section 7.1.

The rates of degradation of picolinafen and CL 153815 in the aerobic soil degradation studies of Steinführer (1997, 1998a and 1998b) have been re-evaluated according to the recommendations of the FOCUS Kinetics Group (FOCUS 2006). Details of the calculations are given below.

7.2.1 Aerobic degradation of the active substance in soils at 20°C

Report:	II A 7.2.1/1 Turk R.S. 2012(b) (14C)Picolinafen - Aerobic route and rate of degradation in soil BASF DocID 2011/1018565
Guidelines:	OECD 307; EPA 835.4100
Testing Laboratory and dates:	Smithers Viscient LLC; Wareham MA; United States of America 17-Feb-2012 - 16-May-2012
GLP:	Yes (laboratory certified by United States Environmental Protection Agency)

I. MATERIAL AND METHODS

For experimental details see IIA 7.1.1/01.

II. RESULTS AND DISCUSSION

For results and discussion see IIA 7.1.1/01.

The rate of degradation was calculated according to FOCUS guidance. Practically the same persistence and modelling endpoints were obtained by using SFO or FOMC. Therefore, SFO which showed good statistical as well as visual fits, was selected and the DT_{50} and DT_{90} values obtained are presented in Table 7.2.1-1.

Table 7.2.1-1: Persistence and modelling degradation endpoints of picolinafen and CL 153815 in soil under aerobic conditions

Compound		Picolinafen			CL 153815			
Soil	**Model**	**DT_{50} (days)**	**DT_{90} (days)**	**Chi-Squared (χ^2)**	**DT_{50} (days)**	**DT_{90} (days)**	**Chi-Squared (χ^2)**	**FF**
Fislis (silt loam)	SFO	2.6	8.5	8.2	19.3	64.0	4.8	0.92
Horn (loam)	SFO	2.2	7.3	11.6	20.4	67.6	9.8	0.84
Sevelen (sandy loam)	SFO	2.6	8.5	11.3	34.6	115	4.8	0.88

The rate of degradation of picolinafen and its metabolite CL 153815 were normalised to soil humidity at pF2. The following equation was used. No correction for temperature was needed.

$$DT_{50ref} = DT_{50act} * Q_{10}^{((T-T_{ref})/10)} * \left(\frac{MC_{act}}{MC_{ref}}\right)^{B}$$

B= 0.7

Table 7.2.1-2: pF 2 normalised degradation endpoints of picolinafen and CL 153815 in soil under aerobic conditions

Soil type	Soil Moisture during the study (g/100g)	Reference moisture content at pF2 (g/100g soil)	Moisture Correction factor	Picolinafen DT_{50} [days]		CL 153815 DT_{50} [days]	
				Study	Normalised 20°C/pF2	Study	Normalised 20°C/pF2
Silty loam	22.12	39.7	0.664	2.6	1.7	19.3	12.8
Loam	21.91	33.5	0.743	2.2	1.6	20.4	15.2
Sandy loam	16.97	31.5	0.649	2.6	1.7	34.6	22.4

III. CONCLUSION

The rate of degradation of picolinafen was similar in all soils. The calculated DT_{50} and DT_{90} values of degradation of picolinafen in soil, based on first order reaction kinetics, ranged from 2.2 to 2.6 days and from 7.3 to 8.5 days, respectively. Picolinafen was degraded to one major radioactive metabolite CL 153815 reaching the maximum of 66.4% AR. CL 153815 was further degraded with DT_{50} values ranging from 19.3 to 34.6 days.

Report: II A 7.2.1/2
Mamouni A., Jarvis T. 2012(a)
Determination of rate of decline for Picolinafen and its metaboite CL 153815 in laboratory degradation studies according to the guidance within the FOCUS Kinetics Guidance Document
BASF DocID 2012/1206414

Guidelines: None

Testing Laboratory and dates: Exponent International Ltd.; Harrogate North Yorkshire HG2 8RE; United Kingdom 01-Aug-2012 - 01-Aug-2012

GLP: No, not subject to GLP regulations

Executive Summary

The degradation of picolinafen was examined at 20°C in four soils in two studies (Steinführer, 1997 & 1998a) and at 8°C in one soil (Steinführer, 1998b). The decline was modelled according to the recommendations of the FOCUS Kinetics Guidance document. Generally, the rate of degradation followed SFO kinetics, however biphasic models (FOMC and DFOP) generally provided a better visual and statistical fit to the data. This was due to a slow phase observed from around the time when DT_{90} had been reached. Nevertheless, the biphasic degradation was considered appropriate for the determination of the endpoints. For picolinafen, the persistence DT_{50} values ranged from 3.2 to 16.0 days and the modelling DT_{50} values ranged from 4.5 to 118 days. For CL 153815, the persistence and modelling DT_{50} values ranged from 15.3 to 10.4 days.

I. MATERIAL AND METHODS

Experimental details for Steinführer (1997, 1998a and 1998b) are summarised in the DAR dated September 2000, Point B.8.1 and in the following Table 7.2.1-3.

Table 7.2.1-3: Picolinafen soil studies: Experimental design

Study report	soil type	soil properties		appl. rate	temperature	humidity
		% Corg	pH [a]	mg/kg	°C	% MWC
Steinführer T. (1998a)	loamy sand	2.32	5.6	0.162	20	40
Steinführer T. (1997)	silty loam	2.03	7.5	0.133	20	40
	sandy loam	1.09	7.6	0.133	20	40
	silty loam	1.40	7.1	0.133	20	40
Steinführer T. (1998b)	silty loam	2.03	7.5	0.133	8	40

Values used for the kinetics

In the soil degradation studies, part of the radioactivity given as unresolved was due mainly to the integrated background as well as to TLC origin radioactivity. The TLC origin residue corresponded to the radioactivity still bound to the extractable organic matter. For the pyridine labelled soils, this was only bound CL 153815 as shown by the TLC chromatograms. This was also confirmed by a new soil degradation study in three soils using a third label (phenoxy), where the samples were analysed by HPLC and TLC (Turk R, 2012). Another part of radioactivity, which was due to the harsh extraction using aqueous NaOH was not considered in the extractable radioactivity as it was not analysed.

Therefore, as practically only picolinafen and its metabolite CL 153815 were detected, the obtained values were normalised to the extractable radioactivity. This gives approximately the same results as a new integration of the chromatograms. The values used for the kinetics for the normalised soils are presented in Tables 7.2.1-4 to -6. For all soil fits, the values after DT_{90} were not used for kinetics for picolinafen since these are likely to exert undue influence on the fitting process for FOMC and DFOP kinetics.

No normalisation was done for the aniline label, as the unresolved radioactivity did not exceed 5% of the applied radioactivity.

Table 7.2.1-4: Normalised residues of picolinafen and CL 153815 in the loamy sand soil (Steinführer T. (1998a)) treated with the pyridine label at 20 °C

Days after application	Extractable radioactivity	picolinafen	CL 153815
Soil Engelstadt / Benz			
0	99.88	99.88	
0	97.89	97.89	
1	100.52	99.54	0.98
1	99.55	98.54	1.01
3	98.98	94.02	4.96
3	99.79	95.01	4.78
8	88.57	67.23	21.34
8	91.39	76.19	15.20
14	78.36	54.69	23.67
14	77.45	49.67	27.78
29	58.96	37.60	21.36
29	57.64	38.35	19.29
60	33.60	26.69	6.91
60	33.05	25.52	7.53
100	22.80	19.31	3.49
100	23.03	18.45	4.58
133	19.69	16.63	3.06
133	19.32	16.94	2.38
150	17.31	15.30	2.01
150	17.32	15.74	1.58

Table 7.2.1-5: Normalised residues of picolinafen and CL 153815 in the soils (Steinführer T. (1997)) treated with the pyridine label at 20 °C

Days after application	Extractable radioactivity	picolinafen	CL 153815
Soil Engelstadt / Benz			
0	99.07	99.07	
0	95.00	95.00	
3	72.80	60.15	12.65
3	59.28	54.21	5.07
7	63.79	27.79	36.00
7	70.40	30.29	40.11
14	43.17	14.28	28.89
14	55.17	13.63	41.54
21	52.14	9.22	42.92
21	46.91	10.13	36.78
30	43.09	8.98	34.11
30	46.63	10.69	35.94
60	25.84	7.45	18.39
60	25.33	6.84	18.49
100	11.47	8.48	2.99
122	10.18	5.98	4.20
Soil Ingelheim/Moers			
0	98.49	98.49	
0	100.48	100.48	
3	57.52	49.41	8.11
3	66.51	50.12	16.39
7	72.71	34.37	38.34
7	65.69	36.01	29.68
14	70.64	23.12	47.52
14	58.09	15.79	42.30
21	60.36	12.28	48.08
21	57.40	13.32	44.08
30	57.32	8.87	48.45
30	59.12	10.37	48.75
60	47.64	6.92	40.72
60	47.83	7.45	40.38
100	29.43	5.34	24.09
122	30.61	5.34	25.27
Soil Kloppenheim / Untere Gewann			
0	97.38	97.38	
0	98.85	98.85	
3	68.96	59.61	9.35
3	77.03	62.09	14.94
7	75.19	42.09	33.10
7	76.51	45.33	31.18
14	63.52	26.86	36.66
14	58.99	24.26	34.73
21	51.76	10.03	41.73
21	57.83	15.23	42.60
30	54.23	12.95	41.28
30	57.35	18.26	39.09
60	40.48	7.17	33.31
60	41.30	7.54	33.76

Days after application	Extractable radioactivity	picolinafen	CL 153815
100	23.95	7.88	16.07
122	22.43	6.70	15.73

Table 7.2.1-6: Normalised residues of picolinafen and CL 153815 in the loamy sand soil (Steinführer T. (1998b) treated with the pyridine label at 8 °C

Days after application	Extractable radioactivity	picolinafen	CL 153815
Soil Engelstadt / Benz			
0	96.24	96.00	
0	94.97	94.80	
3	88.63	82.15	6.48
3	87.55	79.53	8.02
7	78.00	58.25	19.75
7	72.18	46.17	26.01
14	63.68	32.98	30.70
14	67.42	40.63	26.79
21	63.51	27.14	36.37
21	63.09	22.87	40.22
28	55.86	25.61	30.25
28	60.29	24.67	35.62
62	59.68	13.37	46.31
62	57.17	10.57	46.60
100	56.54	9.28	47.26
100	55.90	11.99	43.91
118	50.81	9.43	41.38
118	48.80	8.07	40.73
160	48.03	8.73	39.30
160	48.18	6.77	41.41

Rates of degradation were calculated according to the guidance of the FOCUS Degradation Kinetics Workgroup, using CAKE 1.3 (Prepared by Tessla for Syngenta).

The approach used followed that given in Chapter 7 and 8 of the FOCUS Kinetics Guidance Document. The suitability of the fit of the models was evaluated both visually and statistically by calculating the minimum % error required to pass the χ^2 test at a probability of 0.05 (acceptability criteria χ^2 error < 15%). A t-test was also performed to evaluate whether the determined parameters were significantly different to 0 (acceptability criteria $P \leq 0.05$).

II. RESULTS AND DISCUSSION

The visual fit of the SFO model to the decline of picolinafen and its metabolite was generally adequate and the statistical fit was acceptable. The results of the persistence and modelling endpoints for both picolinafen and CL 153815 are summarised in the Table 7.2.1-7.

Table 7.2.1-7: Persistence and modelling degradation endpoints of picolinafen and CL 153815 in soil under aerobic conditions

Picolinafen	Soil type	Model	Temp. °C	DT_{50} (days)	DT_{90} (days)	X^2 error (%)
Steinführer T. (1998a)	loamy sand (pyridine and aniline)	DFOP (persistence)	20	16.0	191.7	9.52
		slow phase DFOP (modelling)		118.0	391.7	
Steinführer T. (1997)	silty loam	FOMC (persistence)	20	3.9	18.1	3.07
		SFO (modelling)		4.5	14.9	7.02
	sandy loam	DFOP (persistence)	20	3.2	25.4	3.52
		DFOP (modelling)		10.4	34.7	
	silty loam	FOMC (persistence)	20	5.7	35.9	6.50
		FOMC (modelling)		10.8		
Steinführer T. (1998b)	silty loam	DFOP (persistence)	8	9.4	99.0	6.27
		DFOP (modelling)		79.3	263.4	

CL 153815	Soil type	Model	Temp. ° C	DT_{50} (days)	DT_{90} (days)	X^2 error (%)	FF
Steinführer T. (1998a)	Loamy sand (pyridine)	SFO (persistence & modelling)	20	15.3	50.7	20.02	0.71
Steinführer T. (1997)	silty loam	SFO (persistence & modelling)	20	34.8	115.5	17.23	0.56
	sandy loam	SFO (persistence & modelling)	20	104.6	347.5	16.4	0.56
	silty loam	SFO (persistence & modelling)	20	61.9	205.6	10.58	0.60

FF: formation fraction

The rate of degradation of picolinafen and its metabolite CL 153815 are normalised to soil humidity at pF2 and to 20 ºC. The following equation is used.

$$DT_{50ref} = DT_{50act} * Q_{10}^{((T-T_{ref})/10)} * \left(\frac{MC_{act}}{MC_{ref}}\right)^{B}$$

B= 0.7
Q_{10} = 2.58

Table 7.2.1-8: Persistence and modelling degradation endpoints of picolinafen in soil under aerobic conditions

Soil type	T°C study [°C]	Temperature correction factor	Soil MWHC %	Soil Moisture during the study (g/100g	Reference moisture content at pF 2* (g/100g soil)	Moisture correction factor	DT_{50} [days]	
							Study	Normalised 20°C/pF2
loamy sand	20	1.00	44.8	17.9	14	1.000	118.0	118.0
silty loam	20	1.00	47.3	18.9	27	0.780	4.5	3.5
sandy loam	20	1.00	41	16.4	19	0.902	10.4	9.4
silty loam	20	1.00	46.9	18.8	27	0.775	10.8	8.4
silty loam	8	0.32	47.3	18.9	27	0.780	79.3	19.6

* FOCUS default values for moisture content were used

Table 7.2.1-9: Persistence and modelling degradation endpoints of CL 158315 in soil under aerobic conditions

Soil type	T°C study [°C]	Temperature correction factor	Soil MWHC %	Soil Moisture during the study (g/100g)	Reference moisture content at pF 2* (g/100g soil)	Moisture correction factor	DT_{50} [days]	
							Study	Normalised 20°C/pF2
loamy sand	20	1.00	44.8	17.9	14	1.000	15.3	15.3
silty loam	20	1.00	47.3	18.9	27	0.780	34.8	27.1
sandy loam	20	1.00	41	16.4	19	0.902	104.6	94.4
silty loam	20	1.00	46.9	18.8	27	0.775	61.9	48.0

III. CONCLUSION

Generally, the rate of degradation followed SFO kinetics, however biphasic models (FOMC and DFOP) generally provided a better visual and statistical fit to the data. This was due to a slow phase observed from around the DT_{90}. Nevertheless, the biphasic degradation was considered appropriate for the determination of the endpoints. For picolinafen, the persistence DT_{50} values ranged from 3.2 to 16.0 days and the modelling DT_{50} values ranged from 4.5 to 118 days. For CL 153815, the persistence and modelling DT_{50} values ranged from 15.3 to 104.6 days.

7.2.2 Aerobic degradation of the active substance in soils at 10°C

Adequate data to assess the aerobic rate of degradation of picolinafen in soil at 8°C were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

The degradation rate of [pyridine-^{14}C] picolinafen was investigated in a freshly collected silty loam soil. The rate of degradation in the aerobic soil degradation study of Steinführer (1998b) have been re-evaluated according to the recommendations of the FOCUS Kinetics Group (FOCUS 2006). Details of this exercise are given under section 7.2.1.

7.2.3 Aerobic degradation of relevant metabolites in soils at 20°C

Adequate data to assess the aerobic rate of degradation of the metabolites of picolinafen in soil were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

The rates of degradation of the major soil metabolite CL 153815 in the aerobic soil degradation studies of Steinführer (1997, 1998a and 1998b) have been re-evaluated according to the recommendations of the FOCUS Kinetics Group (FOCUS 2006). Details of the calculation are given under section 7.2.1.

7.2.4 Anaerobic degradation of the active substance in soil

Adequate data to assess the anaerobic rate of degradation of the metabolites of picolinafen in soil were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

Picolinafen was rapidly degraded under anaerobic conditions. Very little mineralization occurred (5.1 % for aniline label and 0.3 % for pyridine label after 120 days). In addition to the aerobic soil metabolite CL 153815, two further metabolites CL197393[1] and CL7693[2] (>5%) were detected.

The rates of degradation in the anaerobic soil degradation study of Bissinger (1998) have been re-evaluated according to the recommendations of the FOCUS Kinetics Group (FOCUS 2006).

[1] CL197393 - (2-(3-trifluoromethylphenoxy)-6-pyridine carboxylic acid methyl ester)
[2] CL7693 - 4-fluoroaniline

Report: II A 7.2.4/1
Mamouni A., Jarvis T. 2012(b)
Determination of rates of decline for Picolinafen and its metabolite CL 153815 in field dissipation studies according to the guidance within the FOCUS Kinetics Guidance Document
BASF DocID 2012/1206416
Guidelines: FOCUS Kinetics (2006)
Testing Laboratory and dates: Exponent International Ltd.; Harrogate North Yorkshire HG2 8RE; United Kingdom 01-Aug-2012 - 01-Aug-2012
GLP: No, not subject to GLP regulations

Executive Summary

The anaerobic degradation of picolinafen was examined at 20°C in one soil (Bissinger (1998)). The decline was modelled according to the recommendations of the FOCUS Kinetics Guidance document. The rate of degradation followed biphasic kinetics. For picolinafen, the persistence DT_{50} value was 7.6 days.

I. MATERIAL AND METHODS

Experimental details for the study Bissinger (1998) are summarised in the DAR dated September 2000, Point B.8.1.

The values used for the kinetics are presented in Table 7.2.4-1.

Table 7.2.4.-1: Residues of picolinafen incubated under anaerobic conditions, without harsh basic and acidic extractions (Bissinger (1998))

Intervals (day)	Label	% applied in total system
0	Pyridine	96.2
0	Aniline	93.4
7	Pyridine	48.3
7	Aniline	47.1
14	Pyridine	36.6
14	Aniline	36.3
28	Pyridine	16.5
28	Aniline	15.7
63	Pyridine	10.2
63	Aniline	8.9
120	Pyridine	5.1
120	Aniline	5.7

Other details are presented under section 7.2.1

II. RESULTS AND DISCUSSION

The visual fit of the FOMC model to the decline of picolinafen adequate and the statistical fit was very good. Both the visual and statistical fit was better than SFO and DFOP kinetics. The persistence endpoint chosen from the study is summarised in Table 7.2.4-2. As no significant degradation was observed for its major metabolites, no kinetics were calculated.

Table 7.2.4-2: Persistence and modelling degradation endpoints of picolinafen in soil under anaerobic conditions

Picolinafen aerobic soil study	Soil type	Model	Temp. °C	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)
Bissinger, (1998)	loamy sand	FOMC (persistence)	20	7.6	58.6	5.08

III. CONCLUSION

The rate of degradation of picolinafen under anaerobic conditions in soil followed biphasic kinetics, best described by the FOMC model. The persistence DT_{50} and DT_{90} values of picolinafen were 7.6 and to 58.6 days, respectively.

7.2.5 Anaerobic degradation of relevant metabolites in soil

Adequate data to assess the anaerobic rate of degradation of the metabolites of picolinafen in soil were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

The major aerobic soil metabolite CL 158315 was shown to be stable under anaerobic conditions. The metabolites formed under anaerobic conditions (CL 197393 and CL 7693), were also be stable under anaerobic conditions.

7.3 Field studies

7.3.1 Soil dissipation testing in a range of representative soils

Laboratory DT_{50}s for picolinafen summarised under Point AII 7.2 are all below the threshold of 60 days and thus field dissipation studies are not required. However, during the first review field dissipation data were submitted. No further data are considered necessary. For further details, please refer to the DAR dated September 2000.

Eight field dissipation studies (Cronin (1998, 1999a, b, c), Steinführer (1998a, b, c, d) have been performed to investigate the degradation and dissipation of picolinafen in soil and to determine the concentrations of the main metabolite CL 153815 in soil. In total 8 trials were conducted: 2 trials in Southern France, 1 trial in Northern France, 1 trial in the United Kingdom and 4 trials in Germany.

The conclusion in the DAR was that field studies showed similar results with DT_{50} values between 46 and 51 days (1st order kinetics). CL 153815 was the only metabolite determined > 10 % AR. Field studies showed metabolite concentrations between 18-55 % of applied active ingredient equivalents. The second cleavage product CL 7693 was not detected with the standard extraction procedures and was only identified in trace amounts following extreme extraction procedures that destroyed the soil organic matter (e.g., Bleidner distillation) and might be also a result of hydrolysis of picolinafen or CL 153815.

The rates of degradation in the field dissipation studies have been re-evaluated according to the recommendations of the FOCUS Kinetics Group (FOCUS 2006). Details of this calculation are given below.

Report: II A 7.3.1/1
Mamouni A., Jarvis T. 2012(b)
Determination of rates of decline for Picolinafen and its metabolite CL 153815 in field dissipation studies according to the guidance within the FOCUS Kinetics Guidance Document
BASF DocID 2012/1206416
Guidelines: FOCUS Kinetics (2006)
Testing Laboratory and dates: Exponent International Ltd.; Harrogate North Yorkshire HG2 8RE; United Kingdom 01-Aug-2012 - 01-Aug-2012
GLP: No, not subject to GLP regulations

Executive Summary

The decline of picolinafen and its soil metabolite CL 153815 in eight field dissipation studies (J. Cronin (1998, 1999) and T. Steinführer (1998)) was modelled according to the recommendations of the FOCUS Kinetics Guidance document (2006).

The visual fit of the SFO model to the decline of picolinafen and its metabolite was adequate and the statistical fit was acceptable. For all trials no sign of biphasic degradation was observed.
The dissipation DT_{50}s for picolinafen ranged from 4.5 to 64.5 days and the DT_{50}s for CL 153815 from 32.6 to 104.7 days.

I. MATERIAL AND METHODS

Experimental details for J. Cronin (1999) and T. Steinführer (1998, 1999) studies are summarised in the DAR dated September 2000, Point B.8.1 and in the following Table 7.3.1-1.

Table 7.3.1-1: Picolinafen field dissipation studies: Experimental design

Study report	Location, dates	Soil type	Soil Properties		Appl. rate	sampling depth (cm)
			% Corg	pH	(kg as/ha)	
J. Cronin (1999) 4458	Tournedos Bois Hubert, N-France 13 March 98 - 18 November 98	silt loam	1	7.4[b]	0.200 S	0-30
J. Cronin (1999) 4385	Derbyshire, UK 14 November 96 – 24 July 97	sandy clay loam	1.2	6.8[b]	0.206 A	0-60
J. Cronin (1998) 4417	St Quentin de Baron, S-France 9 December 96 – 19 August 97	loam	1.2	8.3[b]	0.200 A	0-60
J. Cronin (1999) 4459	La Sauve, S-France 17 March 98 – 23 November 98	loam	10.9	6.3[b]	0.196 S	0-30
Steinführer T. (1998) 1997-074	Euskirchen, Germany 5 November 96 – 15 July 97	silt loam	1	6.2[a]	0.190 A	0-60
Steinführer T. (1998) 1998-005	Euskirchen, Germany 14 April 97 – 11 September 97	silt loam	1	6.5[a]	0.196 S	0-60
Steinführer T. (1998) 1998-063	Lutter/ Hildesheim, Germany 28 October 97 – 2 July 1998	silt loam	1.2	7.1[a]	0.199 A	0-30
Steinführer T. (1998) 1998-125	Lutter/ Hildesheim, Germany 8 May 98 – 5 October 98	silt loam	1.2	7.1[a]	0.185 S	0-30

[a] 0.01 M CaCl2, [b] H2O, A (autumn), S (spring)

The results have not been corrected for recovery values obtained and are presented in Table 7.3.1-2. No residues were detected below the 10 cm layer.

Table 7.3.1-2: Residues of picolinafen (Picol.) and CL 153815 in the top 10 cm layer

Country	N-France		UK			South France		
Report	J. Cronin(1999) 4458		J. Cronin(1999) 4385			J. Cronin (1998) 4417		
Interval (days)	Picol.	CL 153815	Interval (days)	Picol.	CL 153815	Interval (days)	Picol.	CL 153815
0	0.061	0.008	0	0.076	0.010	0	0.109	0.011
3	0.086	0.019	4	0.088	0.012	3	0.062	0.014
7	0.087	0.021	8	0.079	0.011	7	0.073	0.026
13	0.097	0.023	15	0.073	0.020	14	0.031	0.021
27	0.038	0.043	27	0.060	0.021	28	0.034	0.028
84	0.005	0.027	84	0.043	0.037	84	<0.005	0.005
138	<0.005	0.021	139	0.020	0.036	140	<0.005	0.026
164	<0.005	0.017	166	0.015	0.033	168	<0.005	0.011
194	<0.005	0.012	193	0.008	0.026	196	<0.005	0.011
250	<0.005	0.008	252	0.006	0.020	253	<0.005	<0.005

Country	South France		Germany			Germany		
Report	J. Cronin (1999) 4459		T. Steinführer (1998) 1997-074			T. Steinführer (1998) 1998-005		
Interval (days)	Picol.	CL 153815	Interval (days)	Picol.	CL 153815	Interval (days)	Picol.	CL 153815
0	0.060	<0.005	0	0.099	<0.005	0	0.104	<0.005
3	0.070	<0.005	3	0.079	0.010	3	0.082	<0.005
6	0.086	<0.005	7	0.062	0.021	7	0.090	<0.005
13	0.025	<0.005	14	0.044	0.026	14	0.093	0.019
28	0.016	0.009	28	0.036	0.040	22	0.049	0.032
83	<0.005	0.016	84	0.029	0.054	30	0.038	0.043
139	<0.005	0.010	140	0.008	0.049	52	0.024	0.046
168	<0.005	<0.005	167	0.006	0.041	85	0.010	0.024
196	<0.005	<0.005	196	0.006	0.037	150	<0.005	<0.005
			252	<0.005	<0.005			

Country	Germany		Germany		
Report	T. Steinführer (1998) 1998-063		T. Steinführer (1998) 1998-125		
Interval (days)	Picolinafen	CL 153815	Interval (days)	Picolinafen	CL 153815
0	0.097	0.006	0	0.086	<0.005
3	0.014	<0.005	3	0.088	0.008
7	0.101	0.005	8	0.066	0.007
14	0.092	0.015	14	0.071	0.008
28	0.090	0.016	20	0.059	0.014
83	0.042	0.041	28	0.042	0.024
139	0.018	0.030	55	0.011	0.027
167	0.014	0.041	83	0.020	0.021
195	0.007	0.038	130	0.005	0.019
247	<0.005	0.016	150	<0.005	0.010

Values used for the kinetics

For the kinetics calculations, the initial amounts of the formed metabolite were set to 0. Therefore, in accordance with FOCUS (2006) guidance, the sum of the picolinafen and CL 153815 detections was used as the initial value for picolinafen, after conversion by using the molecular weights.
The values given as below LOQ were set to the ½(LOQ + LOD) value of 0.003 mg/kg.

Rates of degradation were calculated according to the guidance of the FOCUS Degradation Kinetics Workgroup, using CAKE 1.3 (Prepared by Tessla for Syngenta).

The approach used followed that given in Chapter 7 and 8 of the FOCUS Kinetics Guidance Document. The suitability of the fit of the models was evaluated both visually and statistically by calculating the minimum % error required to pass the χ^2 test at a probability of 0.05 (acceptability criteria χ^2 error < 15%). A t-test was also performed to evaluate whether the determined parameters were significantly different to 0 (acceptability criteria $P \leq 0.05$).

II. RESULTS AND DISCUSSION

Generally the visual fit of the SFO model to the decline of picolinafen and formation/ decline of its metabolite was good and there was no sign of biphasic degradation. The statistical fit to the data was generally acceptable. The persistence endpoints for both picolinafen and CL 153815 are summarised in Table 7.3.1-3.

Table 7.3.1-3: Persistence degradation endpoints of picolinafen and CL 153815 in field studies

Picolinafen	Site	Soil type	Model	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)
J. Cronin (1998, 1999)	N-France	silt loam	SFO	24.6	81.7	21.94
	UK	sandy clay loam	SFO	61.5	204.2	6.05
	S-France	loam	SFO	7.8	26.0	23.00
	S-France	loam	SFO	4.5	15.1	17.68
T. Steinführer (1998)	Germany	silt loam	SFO	24.0	79.8	21.54
	Germany	silt loam	SFO	25.9	85.9	13.95
	Germany	silt loam	SFO	**64.5**	214.1	44.6
	Germany	silt loam	SFO	28.2	93.6	11.21

CL 153815	Site	Soil type	Model	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)
J. Cronin (1998, 1999)	N-France	silt loam	SFO	42.5	141.2	22.33
	UK	sandy clay loam	SFO	79.0	262.4	13.18
	S-France	loam	SFO	**104.7**	347.8	26.04
	S-France	loam	SFO	51.6	171.3	16.95
T. Steinführer (1998, 1999)	Germany	silt loam	SFO	104.0	345.5	19.11
	Germany	silt loam	SFO	32.6	108.4	30.31
	Germany	silt loam	SFO	85.0	282.4	18.84
	Germany	silt loam	SFO	57.2	190.2	17.43

III. CONCLUSION

The DT_{50}s for picolinafen ranged from 4.5 to 64.5 days and the DT_{50}s for CL 153815 from 32.6 to 104.7 days.

7.3.2 Soil residue testing

Laboratory DT_{50}s for picolinafen summarised under Point AII 7.2 are all below the threshold of 60 days and thus soil residue testing is not required.

7.3.3 Soil accumulation testing on relevant soils

Field DT_{90}s for picolinafen summarised under IIA Point 7.3.1 are all below the threshold of 365 days and thus field dissipation studies are not required.

Summary of Rate of Degradation in soil

In the first review of picolinafen reported laboratory DT_{50}s for picolinafen were 46 - 51 days (n = 4, SFO) and laboratory DT_{50}s for CL 153815 were 30 – 77 days (n = 4).

DT_{50}s have been re-calculated for the studies presented in the DAR according to the recommendations of the FOCUS kinetics workgroup (FOCUS 2006) and ranged from 3.2 to 16 days for picolinafen and from 15.3 to 104.6 for CL 153815 metabolite. The new study performed with the fluoro-phenoxy label confirmed the rapid degradation of picolinafen with DT_{50}s ranging from 2.2 to 2.6 days. CL 153815 was degraded with DT50 values ranging from 19.3 to 34.6 days. The obtained persistence DT_{50}s as well as the modelling normalised values to pF 2 and 20 ºC are summarised in Table 7.3.3/1 to 7.3.3/3 below.

Eight field dissipation studies are available and in the first review calculated field DT_{50}s were 9 to 64 days for picolinafen and 19 to 107 days for the metabolite CL 153815. DT_{50}s from these field studies have been recalculated according the recommendations of FOCUS (2006). The visual fit of the SFO model to the decline of picolinafen and its metabolite was adequate and the statistical fit was acceptable. The DT_{50}s for picolinafen were 4.5 to 64.5 days and the DT_{50}s for CL 153815 were 32.6 to 104.7 days.

Table 7.3.3/1 Summary of the laboratory rates of degradation of Picolinafen (persistence endpoints)

Picolinafen aerobic soil study	Soil type	Model	Temp. ℃	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)
Steinführer T. (1998a)	loamy sand	DFOP	20	16.0	191.7	9.52
Steinführer T. (1997)	silty loam	FOMC	20	3.9	18.1	3.07
	sandy loam	DFOP	20	3.2	25.4	3.52
	silty loam	FOMC	20	5.7	35.9	6.50
Steinführer T. (1998b)	silty loam	DFOP	8	9.4	99.0	6.27
Turk R. (2012)	silt Loam	SFO	20	2.6	8.5	8.2
	silty loam	SFO	20	2.2	7.3	11.6
	silty loam	SFO	20	2.6	8.5	11.3

Table 7.3.3/2 Summary of the laboratory rates of degradation of CL 153815 (persistence endpoints)

Picolinafen aerobic soil study	Soil type	Model	Temp. °C	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)	FF
Steinführer T. (1998a)	loamy sand	DFOP	20	15.3	50.7	20.0	0.71
Steinführer T. (1997)	silty loam	FOMC	20	34.8	115.5	17.2	0.56
	sandy loam	DFOP	20	104.6	347.5	16.4	0.56
	silty loam	FOMC	20	61.9	205.6	10.6	0.60
Turk R. (2012)	silt Loam	DFOP	20	19.3	64.0	4.8	0.92
	silty loam	DFOP	20	20.4	67.6	9.8	0.84
	silty loam	DFOP	20	34.6	115	4.8	0.88

Table 7.3.3/3 Laboratory modelling rate of degradation for picolinafen and CL 153815 normalised to 20°C and a moisture content of pF 2.

Aerobic soil Source	Soil type	Model	DT_{50} (days)	Corr. for Temp	Corr. for moisture	Normalised DT_{50} (days)
Picolinafen						
Steinführer T. (1998a)	loamy sand	DFOP	118	1.00	1.000	118.0
Steinführer T. (1997)	silty loam	SFO	4.5	1.00	0.780	3.5
	sandy loam	DFOP	10.4	1.00	0.902	9.4
	silty loam	FOMC	10.8	1.00	0.775	8.4
Steinführer T. (1998b)	silty loam	DFOP	79.3	0.32	0.780	19.6
Turk R. (2012)	silt Loam	SFO	2.6	1.00	0.664	1.7
	silty loam	SFO	2.2	1.00	0.743	1.6
	silty loam	SFO	2.6	1.00	0.649	1.7
					Geometric mean	**6.5**
CL 153815						
Steinführer T. (1998a)	loamy sand	DFOP	15.3	1.00	1.000	15.3
Steinführer T. (1997)	silty loam	SFO	34.8	1.00	0.780	27.1
	sandy loam	DFOP	104.6	1.00	0.902	94.4
	silty loam	FOMC	61.9	1.00	0.775	48.0
Turk R. (2012)	silt Loam	SFO	19.3	1.00	0.664	12.8
	silty loam	SFO	20.4	1.00	0.743	15.2
	silty loam	SFO	34.6	1.00	0.649	22.4
					Geometric mean	**26.1**

7.4 Mobility studies

7.4.1 Adsorption and desorption of the active substance

Adequate data to assess the adsorption/desorption of picolinafen were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000 (B.8.2).

The obtained Koc values are presented in Table 7.4.1-1:

Table 7.4.1-1: Adsorption and desorption parameters of picolinafen

Soil name	Soil (USDA)	pH	OC (%)	K_d	K_F	K_{oc}	1/n	K_{des}
Ingelheim/Moers	loam	7.6	1.33	248	200	15000	0.969	182
Englestadt/Benz	Silt loam	7.4	2.27	396	389	17100	0.999	236
Speyer 2.2	Sandy loam	5.6	2.32	764	603	26000	0.972	510
Schwabenheim/ Schlag IIIb	silty loam	5.9	1.09	292	347	31800	1.03	335
Arithmetic mean				**425**	**385**	**22475**	**0.993**	**316**
pH dependence	Not clear							

In the DAR (September 2000) it is concluded that adsorption was pH dependent with stronger binding in acidic soils. However, this is a very small dataset, the correlation is not particularly good and the relative difference between the Kocs is not great (up to 2X across the whole range of values).

It was also concluded that due to the high soil/water ratio and the low concentration range in the study that there was a high level of uncertainty of the estimated Freundlich parameters and that linear adsorption coefficients should be used for further calculations. It should be mentioned that due to the low water solubility a high range of concentration will not give better data. The study was performed with radioactive substance and the measurements at this concentration levels was accurate as LSC counting was used and no degradation of picolinafen was observed. The study used a soil/aqueous ratio of 1:40 which is within the guideline and needed for such high adsorbing compound. A high soil/aqueous of 1:40 can be considered as worst case, as a lower ratio will give much higher Koc values. Furthermore, the mean of the liner adsorption coefficients will give a higher mean Koc value when compared to the Kfoc mean value.

7.4.2 Adsorption & desorption of rel. metabolites, degr. & react. products

Adequate data to assess the adsorption/desorption of the metabolites of picolinafen were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000 (B.8.2).

The obtained Koc values are presented Table 7.4.1-2:

Table 7.4.1-2: Adsorption and desorption parameters of CL 153815

Soil name	Soil (USDA)	pH	OC (%)	K_d	K_F	K_{oc}	1/n	K_{des}
Ingelheim/Moers	loam	7.6	1.33	7.60	5.16	388	0.959	5.45
Englestadt/Benz	Silt loam	7.4	2.27	6.30	3.64	160	0.902	15.2
Speyer 2.2	Sandy loam	5.6	2.32	16.2	9.98	430	0.920	27.1
Schwabenheim/ Schlag IIIb	silty loam	5.9	1.09	7.13	8.53	783	1.04	14.4
Arithmetic mean				**9.3**	**6.8**	**440**	**0.955**	**16**
pH dependence	No							

It was also concluded that due to the high soil/water ratio and the low concentration range in the study that there was a high level of uncertainty of the estimated Freundlich parameters and that linear adsorption coefficients should be used for further calculations.

It should be mentioned that the study for the metabolite was performed with radioactive substance. The measurements at this concentration levels was accurate as LSC counting was used and no degradation of CL 153815 was observed. The study used a soil/aqueous ratio of 1:40 which can be considered as worst case, as a lower ratio will give much higher Koc values. Furthermore, the mean of the liner adsorption coefficients will give a higher mean Koc value when compared to the Kfoc mean value.

Therefore, the Freundlich values are used in the risk assessment as these represent a worst case.

7.4.3 Column leaching studies with the active substance

Adequate data to assess the column leaching of picolinafen were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000 (B.8.2.1).

In a standard column leaching study with four soils treated at a rate equivalent to 0.1 kg a.s./ha using pyridine label, no significant amount of radioactivity was detected in the leachates.

7.4.4 Column leaching studies rel. metabolites, degr. & and react. products

Adequate data to assess the column leaching of picolinafen were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000 (B.8.2.1).

7.4.5 Aged residue column leaching

Adequate data to assess the aged residue column leaching of picolinafen were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000 (B.2.1.2).

In an aged column leaching study with two soils treated at a rate equivalent to 0.1 kg a.s./ha using both pyridine and aniline labels, no significant amount of radioactivity was detected in the leachates.

7.4.6 Leaching (TLC)

Not currently required according to Directive 91/414/EEC

7.4.7 Lysimeter studies

Not required based on available data.

7.4.8 Field leaching studies

Not required based on available data.

7.4.9 Volatility - laboratory study

Adequate data to assess the volatility of picolinafen were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000 (B.8.7).

The results from a study on volatilisation from soil and leaf surfaces have shown that picolinafen exhibits no significant volatilisation (i.e., 5.2% and 9.8%, respectively) over the 24-hour period of the laboratory experiment.
These findings are in good agreement with its vapour pressure of 1.66 x 10^{-7} Pa at 20°C and its Henry's law constant of 1.6 x 10^{-3} Pa m^3 mol^{-1}. Volatility from soil and plants is therefore not expected to be a major entry route into air after post-emergence application of the herbicide to winter cereals. The vapour pressure of picolinafen is well below the threshold for consideration under FOCUS air and therefore no further data are necessary.

Summary of mobility in soil

Picolinafen is immobile in soil based on its very high Koc value (15000 – 31800 mL/g) as well as the column and aged leaching studies in various soils.

Picolinafen major soil metabolite, CL 153815 is classified as having medium to low mobility according to the McCall scale with a Koc value of 160 – 783 mL/g and was not detected in the leachates of the column and aged leaching studies. CL 7693 was not detected in any soil metabolism study under aerobic conditions (field or laboratory studies). Its detections at very low levels following very harsh extractions showed that it will be immobile in soil.

7.5 Hydrolysis rate of active substance and relevant metabolites at pH values 4, 7 and 9

Adequate data to assess the hydrolysis of picolinafen and its metabolites were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

There was no degradation of picolinafen in pH 4, pH 7, and pH 9 buffers over 5 days at 50°C. There are no functional groups on CL 153815 which can be readily hydrolysed. Its stability under the harsh acidic and basic extraction conditions from the soil and water sediment studies confirm its stability to hydrolysis.

7.6 Direct phototransformation of active substance and relevant metabolites in water

Adequate data to assess the aqueous photolysis of picolinafen and its metabolites were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the first EU review (DAR dated September 2000).

Picolinafen (pyridine and aniline labels) undergoes slow photodegradation in aqueous solution with extrapolated 1st order half-lives of 24.8, 31.4 and 22.6 days of continuous irradiation at pH 5, pH 7 and pH 9, respectively. None of the multiple more polar degradation products exceeded 5 % of the applied dose. The quantum yield of picolinafen was determined to be 2.14 x 10^{-6}. Direct photolysis by sunlight cannot be considered to be a relevant pathway for the degradation of picolinafen in the environment.

The photodegradation of CL 153815 (acid metabolite of picolinafen) in sterile pH 5, 7 and 9 buffer solutions was investigated using [^{14}C]-CL 153815 labelled at the 2 and 6 position of the pyridine ring. CL 153815 is very slowly photodegraded under neutral, basic and acidic conditions.

On further examination of the studies summarised in the DAR it was concluded that the apparent photodegradation of picolinafen in the DAR studies was mainly due to the integration of the background radioactivity on TLC plate. The whole TLC run area was considered as non-resolved radioactivity which apparently reduced the TLC percentages of picolinafen. For confirmation, another study was performed and is summarised below.

Report:	II A 7.6/1 McLaughlin S.P., Lian P. 2012(a) Photodegradation of Picolinafen in water, based on the OECD 316 - Direct photolysis Guideline, Tier I and Tier II BASF DocID 2011/1018566
Guidelines:	OECD 316 (Photodegradation in Water)
Testing Laboratory and dates:	Smithers Viscient LLC; Wareham MA; United States of America 24-Oct-2011 - 15-Nov-2011
GLP:	Yes (laboratory certified by United States Environmental Protection Agency)

Executive Summary

The tier I calculation showed DT50 values <<30 days. Therefore, the photolytic fate of picolinafen in aqueous systems was investigated in sterilized buffer solution at pH 7 using ^{14}C-pyridine and ^{14}C-fluoroaniline labelled picolinafen. Samples treated with picolinafen at a concentration of 18 µg/L were continuously irradiated at 25 ± 2°C in quartz tubes with a Suntest CPS+ apparatus equipped with a Xenon lamp with filters blocking irradiation below 290 nm. Treated samples were exposed to continuous irradiation for 15 days (equivalent to about 43 natural solar days).
Picolinafen was stable in the dark control sterile pH 7.0 buffer solution but only a very slow degradation was observed under the irradiated conditions. The calculated half-life for the light-exposed samples, based on continuous irradiation, was calculated to be 76.4 days. This corresponds to about 217 day midsummer sunlight at latitude 30 to 50 °N. No radioactive fraction was observed at greater than 5% of the applied radioactivity in the irradiated aqueous samples. However, the HPLC detected fractions might be only due to background integration, as these could not be confirmed by TLC, which is much more sensitive.

Total mean recovery of radioactivity for the irradiated and dark control samples throughout the study ranged from 93.4% to 99.4% of the applied radioactivity. The accumulated quantities of pyridine-^{14}C and Fluoroaniline-^{14}C detected in the NaOH volatiles traps were 3.9% and 3.1%, respectively. Negligible quantities of volatile organic compounds were detected in the ethylene glycol volatiles traps.

I. MATERIAL AND METHODS

A. MATERIALS

Test Materials:	Pyridine ^{14}C-picolinafen; specific activity 4.72 MBq/mg (lot No. 804-1101) Fluoroaniline ^{14}C-picolinafen; specific activity 5.68 MBq/mg (Lot No. 805-1201)
Purity:	≥ 99.7%
CAS#:	137640-84-7 / AC12214-129
Stability of compound:	Stable in the application solutions
System:	0.01M phosphate buffer solution, at pH 7 was prepared using 0.02 M sodium phosphate dibasic dihydrate and monobasic dehydrate and 1 M HCl solutions.

B. STUDY DESIGN AND METHODS

4. Experimental Conditions

Two radiolabelled forms of the test substance were initially prepared as solutions in acetonitrile. 5 mL samples of sterile aqueous buffer (pH 7.0, 0.01 M sodium phosphate) were treated separately with 50 µL of stock solution of each label at a concentration of 18 µg/L.

Quartz sample tubes (100 mm length by 12 mm diameter), equipped with Teflon®-lined caps were used. For the dark control samples, pyrex sample tubes with Teflon®-lined silicon septum screw caps were used. All glassware was autoclaved at 121°C and 15 psi for 30 minutes prior to use. Light-exposed sample tubes were placed on their side in a water bath (at a depth of approximately 1 to 3 mm) which was set to maintain the temperature at 25 ± 2 ºC. Test samples were continuously irradiated with artificial light from a Xenon arc lamp. A comparison of the emission spectrum of midday sun with Xenon arc lamp emission spectrum over the wavelengths 250 nm - 800 nm showed excellent overlap. The photolysis cells and dark control cells were fitted with traps for CO_2 and volatile compounds. The trapping solutions used were NaOH for CO_2 and ethylene glycol for volatile organic compounds.

5. Sampling

Duplicate irradiated and dark control samples were analyzed immediately after the test substance was placed into the test vessels (day 0) and after 2, 4, 7, 10 and 15 days of irradiation. Dark control samples were analyzed after 7 and 15 days of incubation.
The sterility of the prepared buffer and dosed samples was confirmed at the start and end of the study. Sterility was evaluated using 3M Petrifilm Aerobic Count Plates.

6. Description of analytical procedures

At each sampling interval the volume in each test tube was measured using a 2.50-mL accurate grading syringe which was further washed with 1.0 mL of acetonitrile. The solution was pooled, vortex-mixed for LSC (2 x 1 mL) and HPLC analysis. The residual in test tube was collected by vortex-mixing with 0.5 mL of 0.1% formic acid in acetonitrile for 30 seconds, 1.5 mL 0.0375% ammonium acetate for 30 seconds and then further sonicating for 2 minutes. Duplicate samples were measured by LSC (2 x 0.15 mL) and separately analysed by HPLC.
The samples were analysed by HPLC using reverse phase (0.0375% ammonium acetate in water and 0.1% formic acid in acetonitrile). The limit of quantification was calculated to be at least 1% of the applied radioactivity. Selected samples were analysed by TLC.

II. RESULTS AND DISCUSSION

A. DATA

Table 7.6-1: Distribution of radioactivity in the irradiated buffer treated with Picolinafen (pyridine-label)

Pyridine-label pH7 Interval (days) [a]	Picolinafen 21.6-min		Others		Total (% AR)	Total mean (% AR)[c]	Conc. (µg/L)
	% AR	AQ Conc. (µg/L)	(%AR) [b]	Conc (µg/L)			
0_T	72.91	12.87	0.00	0.00	72.91		12.87
0_R	25.62	4.52	0.00	0.00	25.62	98.53	4.52
0_T	78.51	13.86	0.00	0.00	78.51		13.86
0_R	17.80	3.14	0.00	0.00	17.80	96.30	3.14
2_T	73.38	12.95	0.00	0.00	73.38		12.95
2_R	20.34	3.59	0.00	0.00	20.34	93.72	3.59
2_T	89.41	15.78	0.00	0.00	89.41		15.78
2_R	6.64	1.17	0.00	0.00	6.64	96.05	1.17
4_T	83.24	14.69	3.14	0.55	86.39		15.25
4_R	9.01	1.59	0.00	0.00	9.01	95.40	1.59
4_T	66.64	11.76	0.00	0.00	66.64		11.76
4_R	30.73	5.42	0.00	0.00	30.73	97.37	5.42
7_T	67.63	11.93	4.56	0.81	72.19		12.74
7_R	26.50	4.68	0.00	0.00	26.50	98.69	4.68
7_T	66.85	11.80	2.73	0.48	69.59		12.28
7_R	24.90	4.39	0.00	0.00	24.90	94.48	4.39
10_T	77.91	13.75	6.39	1.13	84.30		14.88
10_R	15.22	2.69	0.00	0.00	15.22	99.52	2.69
10_T	74.00	13.06	4.58	0.81	78.58		13.87
10_R	16.62	2.93	0.00	0.00	16.62	95.20	2.93
15_T	63.02	11.12	8.86	1.56	71.88		12.68
15_R	21.82	3.85	0.00	0.00	21.82	93.70	3.85
15_T	51.04	9.01	14.37	2.54	65.41		11.54
15_R	24.91	4.40	0.00	0.00	24.91	90.32	4.40

[a] T or R presented sample in tube or residual in tube.
[b] Sum of any individual peaks containing less than 5% of applied radioactivity.
[c] Total recovery as detected by LSC.

Table 7.6-2: Distribution of radioactivity in the irradiated buffer treated with Picolinafen (fluoroaniline-label)

Aniline-label pH7 Interval (days) [a]	Picolinafen 21.6-min		Others		Total	Total mean	Conc.
	% AR	AQ Conc. (µg/L)	(%AR) [b]	Conc (µg/L)	(% AR)	(% AR)[c]	(µg/L)
0_T	72.12	12.95	0.00	0.00	72.12		12.95
0_R	22.11	3.97	0.00	0.00	22.11	94.23	3.97
0_T	69.22	12.43	0.00	0.00	69.22		12.43
0_R	25.22	4.53	0.00	0.00	25.22	94.45	4.53
2_T	74.34	13.35	0.00	0.00	74.34		13.35
2_R	19.81	3.56	0.00	0.00	19.81	94.15	3.56
2_T	63.75	11.45	0.00	0.00	63.75		11.45
2_R	31.80	5.71	0.00	0.00	31.80	95.55	5.71
4_T	73.92	13.27	0.00	0.00	73.92		13.27
4_R	24.83	4.46	0.00	0.00	24.83	98.75	4.46
4_T	68.72	12.34	0.00	0.00	68.72		12.34
4_R	28.85	5.18	0.00	0.00	28.85	97.57	5.18
7_T	74.18	13.32	0.00	0.00	74.18		13.32
7_R	19.92	3.58	0.00	0.00	19.92	94.10	3.58
7_T	83.21	14.94	2.93	0.53	86.14		15.47
7_R	7.84	1.41	0.00	0.00	7.84	93.98	1.41
10_T	71.04	12.76	0.00	0.00	71.04		12.76
10_R	21.89	3.93	0.00	0.00	21.89	92.93	3.93
10_T	52.57	9.44	3.94	0.71	56.51		10.15
10_R	35.86	6.44	0.00	0.00	35.86	92.37	6.44
15_T	64.84	11.64	4.75	0.85	69.59		12.50
15_R	21.27	3.82	0.00	0.00	21.27	90.86	3.82
15_T	69.47	12.48	6.75	1.21	76.23		13.69
15_R	13.58	2.44	0.00	0.00	13.58	89.81	2.44

[a] T or R presented sample in tube or residual in tube.
[b] Sum of any individual peaks containing less than 5% of applied radioactivity.
[c] Total recovery as detected by LSC.

No degradation was observed for the dark control samples

B. MASS BALANCE

Total average recoveries for the irradiated samples were 96.8% ± 1.5% for the pyridine label and 95.1% ± 1.8% for the fluoroaniline label. The corresponding dark control values were 97.5% ± 0.2% and 96.3 ± 1.8%, respectively.

C. TRANSFORMATION OF THE PARENT COMPOUND

Approximately 17.5% and 10.3% of the radioactivity from the samples treated with the pyridine and fluoroaniline, respectively, was degraded after 15 days of continuous exposure to artificial sunlight. No radioactive fraction was observed at greater than 5% of the applied radioactivity in the irradiated aqueous samples. No degradation was observed in the dark control samples.

For [Pyridine-^{14}C]Picolinafen, using single-first order a continuous Suntest photodegradation half-life of 64 days was calculated. This is equivalent to 182 days of summer natural sunlight. For the [Fluoroaniline-^{14}C]Picolinafen, a Suntest half-life of 89 days was calculated corresponding to approximately summer 253 days natural sunlight at latitude 40ºN.

D. FORMATION OF VOLATILES / MINERALISATION

The accumulated quantities of pyridine-^{14}C and fluoroaniline-^{14}C detected in the NaOH volatiles traps were 3.9% and 3.1%, respectively. Negligible quantities of volatile organic compounds were detected in the ethylene glycol volatiles traps.

III. CONCLUSION

This study demonstrated that Picolinafen degrades slowly by photolysis in pH 7 buffer at 25 ± 2 °C with a mean half-life of 76.4 days of continuous irradiation, corresponding to 217 days of natural summer sunlight at latitude 40 °N. Aqueous photolysis is not a significant route of degradation of picolinafen in the environment.

7.7 Ready biodegradability of the active substance

Adequate data to assess the ready biodegradability of picolinafen and its metabolites were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the first EU review (DAR dated September 2000).

Picolinafen was shown to be not readily or inherently biodegradable.

7.8 Degradation in aquatic systems

7.8.1 Aerobic biodegradation in aquatic systems

Data not required under Directive 91/414/EEC or Regulation (EC) No. 1107/2009.

7.8.2 Anaerobic biodegradation in aquatic systems

Data not required under Directive 91/414/EEC or Regulation (EC) No. 1107/2009.

7.8.3 Water/sediment studies

Adequate data to assess the degradation of picolinafen in water/sediment systems were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

The degradation of picolinafen and the carboxylic acid soil metabolite (CL 153815) in two water/sediment systems was investigated in a flow-through test system using ^{14}C-labelled picolinafen and ^{14}C-CL 153815 (radiolabel at the pyridine ring). Separate sets of experiments were carried out for both test compounds. Picolinafen was rapidly partitioned into the sediment and degraded to the acid metabolite CL 153815 and represented < 2 % after 100 days. CL 153815 represented up to 92.4% AR including the released NaOH harsh extractables. Mineralisation was negligible and sediment non-extractable residues increased up to a maximum value of 83 % AR after 100 days. In the separate water/sediment study with the metabolite CL 153815 it was shown to be only slowly degraded but with the major part strongly bound to the sediment. For both compounds, the bound residue was shown to be mainly due to CL 153815 which could be released by basic NaOH harsh extractions.

The rates of degradation of picolinafen and its metabolite in the water/sediment systems in the study of Yan (1999) have been re-evaluated according to the recommendations of the FOCUS Kinetics Group (FOCUS 2006). Details of the calculations are given below.

Report: II A 7.8.3/1
Mamouni A., Jarvis T. 2012(a)
Determination of rate of decline for Picolinafen and its metaboite CL 153815 in laboratory degradation studies according to the guidance within the FOCUS Kinetics Guidance Document
BASF DocID 2012/1206414
Guidelines: None
Testing Laboratory and dates: Exponent International Ltd.; Harrogate North Yorkshire HG2 8RE; United Kingdom 01-Aug-2012 - 01-Aug-2012
GLP: No, not subject to GLP regulations

Executive Summary

The degradation of picolinafen and its metabolite CL 153815 was examined separately at 20°C in two aquatic systems (river and pond) in one study (Yan Z., 1999). The decline of picolinafen was modelled according to the recommendations of the FOCUS Kinetics Guidance document. P-I approaches for the water dissipation phase of picolinafen showed a very good SFO fit with DT_{50} values of 1.9 to 4.0 days and DT_{90} values of 6.3 to 13.4 days. In the overall system, SFO kinetics showed a good fit and DT_{50} values of 5.3 - 5.4 days were obtained for picolinafen.

In the overall system for CL 153815, DFOP kinetics showed a good fit and DT_{50} values of 9.0 - 33.7 days were obtained.

I. MATERIAL AND METHODS

Experimental details for Yan Z. (1999) are summarised in the DAR dated September 2000, Point B.8.1 and in the following Table 7.8.3-1.

Table 7.8.3-1: Picolinafen water sediment studies: Experimental design

Study report	system	sediment type	sediment properties		appl. rate	temperature
			% Corg	pH [a/b]	mg/L	°C
Yan Z. (1999)	river	sandy loam	3.1	7.4/7.8	0.04	20
	pond	loam	5.2	4.4/5.2	0.04	20

[a] KCl / [b] water

Values used for the kinetics
The values used for the kinetics were taken from the DAR (September 2000) and are presented in Table 7.8.3-2 for the systems treated with picolinafen and in Table 7.8.3-3 for the systems treated with CL 153815.

Table 7.8.3-2: Residues of picolinafen and its metabolite in water sediment (Yan (1999))

% AR	Water layer		Sediment layer		Total system	
Day	Picolinafen	CL 153815	Picolinafen	CL 153815*	Picolinafen	CL 153815*
River system						
0	52.2	1.0	39.0	0.1	91.2	1.1
1	52.1	11.3	34.8	0	86.9	11.3
2	43.2	15.6	36.5	0	79.7	15.6
3	33.3	25.3	31.6	0.1	64.9	25.3
7	16.8	41.3	26.3	1.8	43.1	43.1
14	0.3	36.8	0	55.2	0.3	92.0
30	0	28.4	1.8	61.7	1.8	90.0
62	0	21	0.2	68.6	0.3	89.6
100	0	9.3	0	83.1	0	92.4
Pond system						
0	22.7	0.3	68.6	0	91.3	0.3
1	37.4	7.6	55.0	0.1	92.3	7.7
2	26.0	21	46.6	0.3	72.6	21.3
3	19.6	16.7	56.1	1.9	75.7	18.6
7	2.3	31.5	24.6	10.0	26.8	41.5
14	0.4	18.6	22.5	30.3	22.9	48.9
30	0	14.6	10.3	41.0	10.3	55.5
62	0	1.4	2.4	47.9	2.4	49.2
100	0	0	1.9	32.2	1.9	32.2

* including NaOH extracts / Note: duplicate samples showed similar values

Table 7.8.3-3: Residues of CL 153815 in water sediment (Yan (1999))

Days after application	Water layer	Sediment layer	Total system	Total system (bioavailable)*
River System (CL 153815)				
0	99.3	0	99.3	99.3
1	99.8	1.2	101	101
2	91.7	10.2	101.8	95.4
3	70.6	28.7	99.2	78.1
7	39.9	53.5	93.4	54.1
14	37.9	60.3	98.2	66.3
30	25.2	70.0	95.1	58.2
62	12.8	79.7	92.4	43.9
100	5.1	83.1	88.2	33.5
Pond System (CL 153815)				
0	98.1	0	98.1	98.1
1	88.4	3.1	91.4	91.4
2	80.9	6.6	87.5	87.5
3	67.9	16.1	83.9	74.7
7	39.2	25.3	64.5	50.0
14	19.3	34.8	54.0	41.7
30	15.4	42.4	57.8	43.5
62	1.6	52.5	54.1	22.8
100	Not analysed	55.4	55.4	20.4

* The extractable CL 153815 not including the NaOH extracts.

Rates of degradation were calculated according to the guidance of the FOCUS Degradation Kinetics Workgroup, using CAKE 1.3 (Prepared by Tessla for Syngenta).

For water sediment studies, the determination of kinetic endpoints in the FOCUS guidance follows a step-wise approach for deriving the simulation modelling end-point at P-I (overall system) and the approach for deriving the simulation modelling endpoint at P-II (individual compartments).

The approach used followed that given in Chapter 10 of the FOCUS Kinetics Guidance Document. The suitability of the fit of the models was evaluated both visually and statistically by calculating; (1) the minimum % error required to pass the χ^2 test at a probability of 0.05 (acceptability criteria χ^2 error < 15%), and (2) a t-test to evaluate whether the determined parameters were significantly different to 0 (acceptability criteria $P \leq 0.1$, according to the FOCUS Kinetics report).

The current kinetic assessment concentrates more on the process of determining endpoints for use as inputs for simulation models (Persistence endpoints are nonetheless proposed). Determination of the P-II modelling end-point was not attempted.

II. RESULTS AND DISCUSSION

Generally the visual fit of the SFO model to the decline of picolinafen and DFOP o the decline of CL 153815 were good. The statistical fit to the data was very good. The results are summarised in the Table 7.8.3-4.

Table 7.8.3-4: Persistence and modelling degradation endpoints of picolinafen and CL 153815 in aquatic systems

Water sediment / Picolinafen

Water sediment	System	Compartment	Model	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)
Yan Z. (1999)	River	water (persistence).	SFO	4.0	13.4	10.27
		whole system (pers. and model.)	SFO	5.4	17.9	11.58
	Pond	water (persistence)	SFO	1.9	6.3	6.36
		whole system (pers. and model.)	SFO	5.3	17.7	13.09

Water sediment / CL 153815

Water sediment system	system	Compartment	Model	DT_{50} (days)	DT_{90} (days)	χ^2 error (%)
Yan Z. (1999)	River	water (persistence).	DFOP	6.2	73.6	10.04
		whole system (pers. and model.)	DFOP	33.7	292.5	8.51
			DFOP	111.5	370.3	
	Pond	water (persistence).	DFOP	5.3	30.6	5.74
		whole system (pers. and model.)	DFOP	9.0	173.7	6.58
			DFOP	78.8	261.9	

III. CONCLUSION

The decline of picolinafen was modelled according to the recommendations of the FOCUS Kinetics Guidance document. P-I approaches for the water dissipation phase of picolinafen showed a very good SFO fit DT_{50} values of 1.9 to 4.0 days and DT_{90} values of 6.3 to 13.4 days. This confirmed that the **DT_{50} in the water column was >2 days**.

In the overall system for picolinafen, SFO kinetics showed a good fit and DT_{50} values of 5.3-5.4 days were obtained. It is clear that the majority of picolinafen occurs in the sediment and hence for simulation values, the whole system **DT_{50} of 5.3 days** (geometric mean) should be used for the **sediment** phase. The default DT_{50} of 1000 days is then used for the water phase.

In the overall system for CL 153815, DFOP kinetics showed a good fit and DT_{50} values of 9.0-33.7 days were obtained. It is clear that the majority of CL153815 occurs in the sediment and hence for simulation values, the whole system **DT_{50} of 93.7 days** (geometric mean of slow phase) should be used for the sediment phase. The default DT_{50} of 1000 days is then used for the water phase.

Summary of Route and Rate of Degradation in Aquatic Systems

Picolinafen is stable to hydrolysis and aqueous photolysis. Picolinafen is not readily or inherently biodegradable.

In sediment/water systems picolinafen was rapidly partitioned into the sediment where it was degraded to CL 153815. Picolinafen represented less than 2% after 100 days of incubation. The non-extractable residue was shown to be mainly due to bound CL 153815. With harsh extractions (including basic NaOH) CL 153815 represented over 92% AR in the whole system. Mineralisation was not significant and did not exceed 2.5% AR. DT_{50}s for picolinafen, calculated according to FOCUS (2006), were 5.3 to 5.4 days (mean 5.4 days) for the whole system and 1.9 to 4.0 days (mean 3.0 days) in water for picolinafen. For CL 153815 DT_{50}s were calculated to be 9.0 to 33.7 days (mean 21.4 days) for the whole system and 5.3 to 6.2 days (mean 5.8 days) in water.

Only pyrimidine labelled material was used in the sediment water study and the evaluation of this study in the DAR stated that no comment can be made regarding the aniline moiety of the active substance which will be released upon cleavage of the amide bond (CL7693). In the pyridine water sediment study, the analysed harsh extractions which released almost all bound radioactivity showed the presence of only CL 158315, representing over 92% in the whole systems at the end of the incubation (day 100). This was also confirmed in the samples treated with radioactive CL 153815. Therefore, picolinafen is expected to form CL 153815 and CL 7693 (4-fluoroaniline) in aquatic systems. Taking into account the results of studies investigating aerobic and anaerobic (flooded system) degradation of picolinafen in soil, it is anticipated that on formation 4-flouroaniline (CL7693) will instantaneously degrade under aerobic conditions to form mainly carbon dioxide and bound residues. CL 7693 was detected only in the anaerobic study with amounts not exceeding 7.6% AR, but only by using very harsh acidic and basic extractions.

Considering the behaviour of CL 7693 in the soil studies, the case previously presented in the DAR should be sufficient and a new study with the aniline label will not give any new results. The metabolic pathway in aquatic systems is therefore similar to the metabolic pathway in soil (see Figure 7.1/1).

7.9 Degradation in the saturated zone

Based on the simulation modelling submitted under chapter IIIA 9.6 picolinafen and its metabolite CL 153815 are predicted to have a low risk of leaching. Studies on its behaviour in the saturated zone are therefore not necessary.

7.10 Rate and route of degradation in air

Adequate data to assess the route and rate of degradation of picolinafen in air were evaluated during the first EU review and no further data are considered necessary. For further details, please refer to the DAR dated September 2000.

The results from a study on volatilisation from soil and leaf surfaces have shown that picolinafen exhibits no significant volatilisation (i.e. < 10% from both matrices) over the 24-hour period of the laboratory experiment.

These findings are in good agreement with its vapour pressure of 1.66 x 10^{-7} Pa at 20°C and its Henry's law constant of 1.6 x 10^{-3} Pa m^3 mol^{-1}. Volatility from soil and plants is therefore not expected to be a major entry route into air after application of picolinafen. Insignificant amounts of residues that might reach the air either via volatilisation or during the spraying are considered to have a short persistence in the atmosphere due to their degradation by OH-radicals (Atkinson method: DT_{50} = 1 day).

7.11 Definition of the residue

Soil

In aerobic metabolism studies only CL 153815 metabolite was detected at >10% AR at maximum of 66.4% AR. Soil photolysis is not an important route of degradation for picolinafen.

For risk assessment: Picolinafen and CL 153815
For monitoring: Picolinafen

Groundwater

In aerobic metabolism studies only CL 153815 metabolite was detected at >10% AR at maximum of 66.4% AR. Soil photolysis is not an important route of degradation for picolinafen.

For risk assessment: Picolinafen and CL 153815
For monitoring: Picolinafen

Surface water

In aerobic metabolism studies only CL 153815 metabolite was detected at >10% AR at maximum of 66.4% AR. The other part of the molecule following degradation of picolinafen will form CL 7693 (4-fluoroaniline). Taking into account the results of studies investigating aerobic and anaerobic (flooded system) degradation of picolinafen in soil and literature data, it is anticipated that on formation, 4-fluoroaniline (CL7693) will instantaneously degrade under aerobic conditions to form mainly carbon dioxide and bound residues. Aqueous photolysis is not an important route of degradation for picolinafen.

For risk assessment: Picolinafen and CL 153815
For monitoring: Picolinafen

Air

For risk assessment: Picolinafen
For monitoring: Picolinafen

7.12 Monitoring data concerning fate and behaviour

No data submitted.

7.13 Other/special studies

No other studies are submitted.

The Chemical Company

DOSSIER FOR THE EVALUATION OF THE ACTIVE SUBSTANCE

Picolinafen (BAS 700 H)

Data requirement according to Regulation (EU) No. 544/2011 and (EU) No. 545/2011 of 10 June 2011 (formerly Annex II and III of Directive 91/414/EEC)
using OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substance
(Dossier Guidance)
and Commission Regulation (EC) No 1141/2010 of 7 December 2010 (AIR procedure)

Document M-II

Summary and evaluation (Tier II)

Section 6

Ecotoxicological studies on the active substance

BASF DocID 2012/1208880

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Date: 30 August 2012

8 Ecotoxicological Studies on the Active Substance

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8 Ecotoxicological Studies on the Active Substance

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8.1 Avian toxicity

Avian toxicity data submitted for the previous EU review of picolinafen consisted of acute, dietary and reproductive toxicity studies. This supplemental dossier to the original Annex II dossier does not include any new avian toxicity studies. For completeness a brief summary of the studies is provided from the DAR (September 2000).

8.1.1 Acute oral toxicity to quail species, mallard duck or other bird

The acute oral toxicity of technical picolinafen (97.8 % purity) was tested in bobwhite quail according to EPA guideline 71-1. The test material was applied by gelatine capsule without the use of solvents at dose levels of 0/292/486/810/1350/2250 mg/kg body weight. Five males and five females, 20 weeks old, were treated per dose level. There were no mortalities and no signs of intoxication. Food consumptions was reduced at dose levels of 1350 and 2250 mg/kg, body weight was reduced at 2250 mg/kg bw.

LD_{50}: >2250 mg a.s./kg bw; **NOED**: 810 mg a.s./kg bw.

(Ref: AVS1999-62)

The acute oral toxicity of technical picolinafen (97.8 % purity) was tested in mallard duck according to EPA guideline 71-1. The test material was applied by gelatine capsule without the use of solvents at dose levels of 0/292/486/810/1350/2250 mg/kg body weight. Five males and five females, 20 weeks old, were treated per dose level. There were no mortalities and no signs of intoxication. Food consumptions and body weight was not different from the control up to the top dose level.

LD_{50}: >2250 mg a.s./kg bw; **NOED**: 2250 mg a.s./kg bw.

(Ref: AVS1999-63)

8.1.2 Avian dietary toxicity (5-day) test in quail species or mallard duck

The 5-day-dietary toxicity of technical picolinafen (97.8 % purity) was tested in bobwhite quail according to OECD guideline 205 and EPA guideline 71-2. The test material was mixed into the feed with corn oil at nominal concentrations of 0/100/270/729/1968/5314 ppm. Analysis of the feed showed deviations from nominal concentrations being -13 to -6 %; homogeneity and stability were proven to be sufficient. At each concentration level, a group of twelve 14-day-old birds of undetermined sex was used. There was one mortality in one of the control groups, and 3/0/4/1/1 mortalities in the five treatment groups. According to the pathological examination, mortalities in the lower three groups (up to 729 ppm) were considered unrelated to treatment. Body weight was affected at concentrations of 729 ppm and higher; food consumption was affected at 5314 ppm.

LC_{50}: >5314 ppm; **NOEC**: n.d.

(Ref: AVS1999-65]:

8.1.3 Avian dietary toxicity (5-day) test in a second unrelated species

The 5-day-dietary toxicity of technical picolinafen (97.8 % purity) was tested in mallard duck according to OECD guideline 205 and EPA guideline 71-2. The test material was mixed into the feed with corn oil at nominal concentrations of 0/100/270/729/1968/5314 ppm. Analysis of the feed showed deviations from nominal concentrations being -13 to -6%; homogeneity and stability were proven to be sufficient. At each concentration level, a group of twelve 8-day old birds of undetermined sex was used. There was mortality of one bird at 729 ppm, which was considered unrelated to treatment. Apart from that, no signs of intoxication were observed. Body weight and feed consumption were affected at 1968 and 5314 ppm.

LC_{50}: >5314 ppm; **NOEC**: 729 ppm

(Ref: AVS1999-64)

8.1.4 Subchronic and reproductive toxicity to birds

A one-generation reproduction study with bobwhite quail was conducted according to OECD guideline 206 and EPA guideline 71-4. Technical picolinafen (97.8 % purity) was mixed into the feed with corn oil at nominal concentrations of 0/216/432/864 ppm for an exposure period of 22 weeks. Analysis of the feed showed deviation from nominal concentrations being -16 to -14 %; homogeneity and stability were proven to be sufficient. At each concentration level 16 pairs were tested. The birds were 18 weeks old at the onset of exposure. There were observed no parental effects, nor effects on reproduction and chick development up to the top concentration.

NOEC: 864 ppm.

(Ref: AVS1999-68)

A one-generation reproduction study with mallard duck was conducted according to OECD guideline 206 and EPA guideline 71-4. Technical picolinafen (97.8 % purity) was mixed into the feed with corn oil at nominal concentrations of 0/216/432/864 ppm for an exposure period of 20 weeks. Analysis of the feed showed deviation from nominal concentrations being -6.8 to -5.5 %; homogeneity and stability were proven to be sufficient. At each concentration level 16 pairs were tested. The birds were 21 weeks old at the onset of exposure. There were observed no parental effects, nor effects on reproduction and chick development up to the top concentration.

NOEC: 864 ppm.

(Ref: AVS1999-67)

8.2 Fish toxicity

Fish toxicity data submitted for the previous EU review of picolinafen consisted of acute toxicity data to two species and a 28-day chronic toxicity study and early life stage study both conducted with the rainbow trout. This supplementary dossier to the original Annex I dossier does not include any new fish toxicity studies conducted with picolinafen, however it does contain an acute toxicity study with the metabolite CL 7693 (see Annex Point AIII 8.2.1.3).

For completeness a brief summary of the original studies submitted for the first review of picolinafen is provided from the DAR (September 2000).

8.2.1 Acute toxicity of the active substance to fish

8.2.1.1 Rainbow trout (*Oncorhynchus mykiss*)

According to the DAR (September 2000), a valid 96h acute toxicity study (flow-through) conducted in accordance with accepted international guidelines and GLP requirements was submitted. The 96h EC_{50} value was 0.68 mg/L and the NOEC was 0.68 mg/L.

(Ref: WAT1999-514)

8.2.1.2 Warm water fish species

According to the DAR (September 2000), a valid 96h acute toxicity study (flow-through) conducted with the Bluegill sunfish (*Lepomis macrochirus*) was submitted. The study was conducted in accordance with accepted international guidelines and GLP requirements. The 96h EC_{50} value was 1.0 mg a.s./L and the NOEC was 1.0 mg a.s./L.

(Ref: WAT1999-515)

8.2.1.3 Acute toxicity of metabolites to the more sensitive of fish species

Report:	II A 8.2.1.3/1 [redacted], [redacted] 2011(a) Acute toxicity of CL 7693 to rainbow trout (Oncorhynchus mykiss) in a 96-hour static test BASF DocID 2010/1159916
Guidelines:	OECD 203 (1992); EC 440/2008 C.1 Acute Toxicity for Fish
Deviations:	none
GLP:	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

In a static acute toxicity study, rainbow trout (*Oncorhynchus mykiss*) were exposed to CL 7693. The test substance was applied at concentrations of 4.3, 9.4, 21, 45 and 100 mg/L. In controls, test water was used without the addition of the test substance.

The test fish were observed after approximately 2, 24, 48, 72 and 96 hours of exposure for sublethal effects and mortality. Died fish were removed at least once daily and discarded.

In the control and at the nominal test concentrations up to and including 9.4 mg test item/L all fish survived until the end of the experiment and no signs of intoxication occurred. At the nominal test concentration of 100 mg/L all fish showed tumbling during swimming shortly after introduction in the test aquaria. After 2 h, four fish were dead and the remaining three fish showed dark colouration, tumbling during swimming and were lying on the side or the back on the bottom of the aquarium at the test concentration of nominal 100 mg test item/L. At the nominal test concentration of 45 mg/L, 2 fish were dead after 2 hours of test duration and 5 fish showed dark colouration and tumbling during swimming. After 24 h all fish were dead at the nominal test concentrations of 45 and 100 mg test item/L. At the nominal test concentration of 21 mg/L two fish were dead after 48 h but no further mortality or sublethal effects occurred until the end of the test.

The quantification of the test item CL 7693 was performed using liquid chromatography (HPLC-method). At the start of the test just before introduction of the fish 80 % of the nominal test concentrations were found. After 96 hours test duration 82 % of the nominal values were determined. Thus, during the test period of 96 hours the fish were exposed to a mean of 81 % of nominal. Therefore, all reported results were related to nominal concentrations of the test item.

Based on the test results the 96-hour LC_{50} of CL 7693 for Rainbow Trout (*Oncorhynchus mykiss*) was determined to be nominal 22.7 mg test item/L. The no observed effect concentration (NOEC) was determined to be 9.4 mg test item/L and the LOEC was determined to be 21 mg test item/L; all values being based on nominal test concentrations.

I. MATERIAL AND METHODS

1. **Test Material:** CL 7693
   Description: Orange liquid (purity 99.7%)
   Lot Batch #: AC12214-129
   Stability of test compound: Considered to be sufficiently stable for purpose of study

2. **Vehicle and/ or positive control:** Deionised water

3. **Test animals:**
   Species: Rainbow trout (*Oncorhynchus mykiss*); mean length: 5.08 ± 0.38 cm; mean weight 1.26 ± 0.34 g
   Strain: not reported
   Source: Forellenzuchtbetrieb Störk, 88348 Bad Saulgau, Germany
   Food: None during study
   Environmental conditions –
   Temperature: 13 – 15°C
   Oxygen concentration: 92 – 100% air saturation value
   Photoperiod: 16:8 L:D (30 min/dawn/dusk period; 480 – 1060 lux)
   pH: 7.6 – 8.0

   In-life dates: 22 – 26 November 2010

   Experimental treatments: From a stock solution (nominal 500 mg/L), adequate volumes were mixed into the test water to prepare the test concentrations (4.3, 9.4, 21, 45 and 100 mg/L). Following application of the test item, 7 fish were introduced into each aquarium (12 L glass aquaria containing 10 L test medium). Fish were not fed during the 96 hours of the test.

   Observations: Test conditions were recorded with suitable instruments. Mortality and sublethal effects in the different treatment groups were assessed after approximately 2, 24, 48, 72 and 96 hours following introduction to the test aquaria. Analysis of the test item concentrations in the test media from the four highest test concentrations was made after 0, 24 and 96 hours of test duration. Quantification was performed using liquid chromatography (HPLC-method).

   Statistics: The LC_{50} at the observation times was calculated by Probit analysis. The NOEC, LOEC, LC_0 and LC_{100} were determined directly from the raw data. Statistical analysis was performed performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH).

II. RESULTS AND DISCUSSION

All validity criteria were met.

The biological results from the study are summarised in Table 8.2.1.3-1. The 96 hour LC_{50} was 22.7 mg /L (nominal) with a 96 hour NOEC of 9.4 mg/L (nominal).

Table 8.2.1.3-1: Mortality of rainbow trout (*O. mykiss*) exposed to CL 7693 in a 96 h static acute toxicity test

Nominal concentration (mg/L)	Mortality					
	Exposure time (hours)					
	0	2	24	48	72	96
Control	0	0	0	0	0	0
4.3	0	0	0	0	0	0
9.4	0	0	0	0	0	0
21	0	0	1	2	2	2
45	0	2	7	7	7	7
100	0	4	7	7	7	7
LC_{50} (mg/L)	n.d.	81.1	24.2	22.7	22.7	22.7
95% C.I.	n.d.	49.8 – 443.6	n.d.	n.d.	n.d.	n.d.

n.d.:Could not be determined
C.I.: Confidence intervals

Analysis of the test concentrations showed at the start of the test (just before fish introduction) 80% of the nominal test concentrations was found. At the end of the study 82% of nominal values was determined. Mean exposure was calculated as 81% of nominal during the duration of the study and all results were reported as nominal concentrations of test item.

III. CONCLUSION

The 96 hour LC_{50} of CL 7693 for rainbow trout (*Oncorhynchus mykiss*) was determined to be 22.7 mg/L. The 96 hour NOEC and LOEC values were determined to be 9.4 and 21 mg test item/L, respectively.

8.2.2 Chronic toxicity to fish

See Annex Point AIII 8.2.3.

8.2.3 Chronic toxicity (28 day exposure) to juvenile fish

According to the DAR (September 2000), a valid 28 day chronic toxicity study (flow-through) conducted with the rainbow trout (*O. mykiss*) was submitted. The study was conducted in accordance with accepted international guidelines and GLP requirements. The 28 day NOEC value for mortality, growth and behaviour was 0.1 mg a.s./L.

(Ref: WAT1999-516)

8.2.4 Fish early life stage toxicity test

According to the DAR (September 2000), a valid fish early life-stage study (flow-through) conducted with the rainbow trout (*O. mykiss*) was submitted. The study was conducted in accordance with accepted international guidelines and GLP requirements. The NOEC values for mortality, hatch, growth and behaviour were 0.023, 0.042, 0.0064 and 0.023 mg a.s./L, respectively.

(Ref: 1999-517)

8.2.5 Fish life cycle test

Not required.

8.2.6 Bioconcentration potential in fish

8.2.6.1 Bioconcentration potential of the active substance in fish

Picolinafen has a Log P_{ow} of 5.43. Consequently a flow-through bioconcentration study conducted with the Bluegill sunfish (*L. macrochirus*) was evaluated in the DAR (September 2000). The resulting BCF was 580 and there was 95% depuration within 14 days.

(Ref: WAT1999-519)

8.2.6.2 Bioconcentration potential of the metabolites, degr. & react. products

No data submitted. No relevant metabolites have been identified in aquatic test systems.

8.2.7 Aquatic bioavailability/ biomagnification / depuration

Not required.

8.3 Toxicity to aquatic species other than fish, aquatic field tests

Toxicity data for aquatic invertebrates submitted for the previous EU review of picolinafen consisted of acute (48 hour) and chronic (21 day) studies conducted with *Daphnia magna*. This supplemental dossier to the original Annex I dossier does not include any new aquatic invertebrate toxicity studies conducted with picolinafen, however it does contain an acute toxicity study with the metabolite CL 7693 (see 8.3.1.1).

8.3.1 Acute toxicity to aquatic invertebrates

According to the DAR (September 2000), a valid 48h acute toxicity study (static) conducted in accordance with accepted international guidelines and GLP requirements was submitted. The 48h EC_{50} value was >0.45 mg a.s./L and the NOEC was 0.45 mg a.s./L.

(Ref: 1999-521)

8.3.1.1 Acute toxicity (24 and 48 hour) for Daphnia preferably (Daphnia magna)

Report:	II A 8.3.1.1/1 Kley, A, Deierling, T. 2011(b) Acute toxicity of 4-fluoroaniline (CL7693) to *Daphnia magna* in a semi-static 48-hour immobilisation test. BASF DocID 2010/1159917
Guidelines:	OECD 202 (2004); EC 440/2008 C.2 Daphnia sp. Acute Immobilisation Test
Deviations:	Storage of the test item: According to study plan; store in original container, in the refrigerator (approx. +4°C or cooler), in the dark. Deviation: Storage temperature was 11 - 15°C for 5 days. No presumed effect on study.
GLP:	Yes (Laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

In a static acute toxicity study, female *Daphnia magna* were exposed to CL 7693. The test substance was applied at concentrations of 0.019, 0.042, 0.093, 0.20 and 0.45 mg/L and renewed every 24 hours. In controls, test water was used without the addition of the test substance. The mobility of the test organisms was observed after 24 and 48 hours of exposure.

After 48 hours of exposure no immobilisation of the test animals was observed in the control and the test item concentration up to and including nominal 0.042 mg/L. At the nominal test concentration of 0.093 mg test item/L one *Daphnia* was immobile. Two immobile *Daphnia* were observed at the nominal test concentration of 0.20 mg test item/L. At the highest nominal test concentration of 0.45 mg test item/L, 20 animals were immobile.

The quantification of the test item CL 7693 was performed using liquid chromatography (HPLC-method). At the start of the test and at test medium renewal 96 % of the nominal test concentration was found (average of all test concentrations). After 24 and 48 hours test duration, 93 % of the nominal value was determined (average of all test concentrations). During the test the *Daphnia* were exposed to a mean of 95 % of nominal. Therefore, all reported results refer to nominal concentrations.

Based on the test results the 48-hour LC_{50} of CL 7693 for *Daphnia magna* was determined to be nominal 0.254 mg test item/L. The no observed effect concentration (NOEC) was determined to be 0.042 mg test item/L and the LOEC was determined to be 0.093 mg test item/L. All values were based on nominal test concentrations.

I. MATERIAL AND METHODS

1. **Test Material:** CL 7693
   Description: Orange liquid (purity 99.7%)
   Lot Batch #: AC12214-129
   Stability of test compound: Considered to be sufficiently stable for purpose of study

2. **Vehicle and/ or positive control:** Reconstituted water/ potassium dichromate

3. **Test animals:**
   Species: *Daphnia magna* (Straus); age: 3.75 to 19.5 hours old
   Strain: Clone 5
   Source: In-house culture
   Food: None during study
   Environmental conditions –
   Temperature: 20°C
   Oxygen concentration: 8.2 – 9.1 mg/L
   Photoperiod: 16:8 L:D (650 – 830 lux)
   pH: 7.9 – 8.0

   In-life dates: 05 – 07 July 2011

   Experimental treatments: From a stock solution (nominal 20 mg/L), adequate volumes were mixed into the test water to prepare the test concentrations (0.019, 0.042, 0.093, 0.20 and 0.45 mg/L) before the introduction of the test organisms. The test units consisted of glass beakers (100 mL) containing 60 mL test media and covered with a lid to reduce evaporation. 20 *Daphnia* per control and test item concentration (divided into 4 groups of five animals) used in the study. The test item media was renewed after 24 hours of exposure to maintain the test concentrations.

   Observations: Test conditions were recorded with suitable instruments. Assessment of immobility was determined by visual observations after 24 and 48 hours. Animals not able to swim within 15 seconds after gentle agitation of the test beaker were considered immobile. Analysis of the test item concentrations in the test media was made in freshly prepared samples (day 0 and day 1) and in the aged media after 24 and 48 hours. Quantification was performed using liquid chromatography (HPLC-method). The 24 and 48 hour LC_{50} and 95% confidence limits were calculated by Probit analysis. The 48 hour NOEC and LOEC values were determined directly from the raw data. Statistical analysis was performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH).

II. RESULTS AND DISCUSSION

All validity criteria were met.

The biological results from the study are summarised in Table 8.3.1.1-1. The 96 hour LC_{50} was 0.254 mg test item/L (nominal) with a 96 hour NOEC of 0.042 mg/L (nominal).

Table 8.3.1.1.-1: Immobility of *Daphnia magna* exposed to CL 7693 in a 48 h semi-static acute toxicity test

Nominal concentration (mg test item/L)	% of immobilised *Daphnia* after 24 or 48 hours	
	24 hours	48 hours
Control	0	0
0.019	0	0
0.042	0	0
0.093	0	5
0.20	0	10
0.45	10	100
EC_{50} (mg/L)	n.d.	0.254
95% confidence values (mg/L)	n.d.	n.d.
NOEC (mg/L)	0.20	0.042
LOEC (mg/L)	0.45	0.093

Values refer to nominal test concentrations
n.d. = not detected
NOEC and LOEC were determined directly from the raw data

At the start of the test and at test medium renewal 96 % of the nominal test concentration was found (average of all test concentrations). After 24 and 48 hours test duration, 93 % of the nominal value was determined (average of all test concentrations). During the test the *Daphnia* were exposed to a mean of 95 % of nominal. Therefore, all reported results refer to nominal concentrations.

III. CONCLUSION

The toxic effect of the test item CL 7693 to *Daphnia magna* was assessed in a semi-static dose-response test. The 48 hour NOEC was determined to be 0.042 mg test item/L. The 48 hour LOEC was determined to be 0.093 mg test item/L. The 48 hour EC_{50} value was calculated to be 0.254 mg test item/L.

(Kley A., Deierling T. 2011(b))

8.3.1.2 Acute toxicity (24/48 h) for representative species of aquatic insects

No data submitted. No data are required as picolinafen is not intended to be applied to surface water or intended for use as an insecticide.

8.3.1.3 Acute toxicity for representative species of aquatic crustaceans

No data submitted. No data are required as picolinafen is not intended to be applied to surface water or intended for use as an insecticide.

8.3.1.4 Acute toxicity for representative species of aquatic gastropod molluscs

No data submitted. No data are required as picolinafen is not intended to be applied to surface water or intended for use as an insecticide.

8.3.2 Chronic toxicity to aquatic invertebrates

See 8.3.2.1

8.3.2.1 Chronic toxicity in *Daphnia magna* (21-day)

According to the DAR (September 2000), a valid 21 day chronic toxicity study (flow-through) conducted with *D. magna* was submitted. The study was conducted in accordance with accepted international guidelines and GLP requirements. The 21 day NOEC value for mortality, growth and reproduction was 0.007 mg a.s./L.

(Ref: 1999-535)

8.3.2.2 Chronic toxicity for representative species of aquatic insects

No data submitted. No data are required as picolinafen is not intended to be applied to surface water or intended for use as an insecticide.

8.3.2.3 Chronic toxicity for representative species of aquatic gastropod molluscs

No data submitted. No data are required as picolinafen is not intended to be applied to surface water or intended for use as an insecticide.

8.3.3 Aquatic field testing

Report:	II A 8.3.3/1 Taylor S. 2012(b) The effect of Picolinafen on phytoplankton, periphyton and macrophytes in freshwater microcosms BASF DocID 2011/1078035
Guidelines:	OECD (2006) Guidance Document on Simulated Freshwater Lentic Field Tests (Outdoor Microcosms and Mesocosms)
Deviations:	No major deviations considered to impact the integrity of the study
GLP:	Yes (laboratory certified by Department of Health of the Government of the United Kingdom, United Kingdom)

Executive Summary

The purpose of this study was to assess the potential biological effects of the herbicide picolinafen (BAS 700 03 H) on algal biomass (phytoplankton), periphyton and macrophytes within aquatic mesocosms by analysis of species abundance and diversity following a single application of an aqueous dilution of the test item to give the following nominal treatment concentrations: 0.20, 0.45, 1.3, 2.8 and 7.5 µg a.s./L. The microcosms were evaluated for a period from approximately four weeks before, to 16 weeks after treatment with the test item. Secondary effects on zooplankton were also evaluated as part of this study.

The concentrations of picolinafen were measured in samples taken from the water column and sediment at intervals during the study using a LC-MS/MS method of analysis. Samples taken approximately one hour after treatment confirmed that the intended concentrations of picolinafen had been achieved in the water column, with mean measured levels ranging from 84 to 91% of their nominal values.

The No Observed Effect Concentration (NOEC) and No Observed Ecologically Adverse Effect Concentrations (NOEAEC) for each group were estimated according to the effects categories as published by de Jong *et al* (2008).

The algal class Zygnematophyceae were the most sensitive algal taxa to treatment with picolinafen as statistically significant effects were observed in both phytoplankton and periphyton samples in microcosms treated at 7.5 µg a.s./L. Statistically significant indirect effects were also observed for the zooplankton taxon *Daphnia longispina* on Day 84 to 98. In addition, clear treatment related effects on dissolved oxygen production were observed in microcosms treated at 7.5 µg a.s./L in the period shortly after treatment. However, these effects were transient and rapid recovery was observed.

The overall class 1 NOEC from this study was estimated to be 2.8 µg a.s./L. The NOEAEC class 5A (recovery by the end of the test) was estimated to be 7.5 µg a.s./L.

I MATERIALS AND METHODS

A TEST ITEM

Name:	Picolinafen (BAS 700 03 H)
Active substance:	Picolinafen
Description:	Pale brown granules
Lot/Batch no.:	1030
Purity:	77.2%

B TEST SYSTEMS

The microcosms used for this study comprised fibreglass tanks 1.8 m long x 0.9 m wide x 0.8 m deep, located in the ground to a depth of approximately 0.6 m with approximately 0.2 m remaining above ground. Each microcosm contained approximately 10 cm of sediment (7 cm of a clay loam and 3 cm of overlying mature lake sediment) and 60 cm of overlying water (volume *ca*. 972 L). The water in each microcosm comprised a mixture of tap water and mature pond water (50:50 v/v) collected from a nearby mesocosm reservoir facility, and was allowed to stand for approximately four months before the application of the test item. During this time, zooplankton and benthic invertebrates were collected from the mesocosm reservoir using nets and distributed to each microcosm. In addition, dried alder leaves were added to each microcosm to provide a food source for aquatic organisms.

C STUDY DESIGN

1 In life dates

12 May to 30 September 2011.

2 EXPOSURE REGIME AND TEST ITEM APPLICATION

Picolinafen was applied as an aqueous dilution of the formulation BAS 700 03 H on a single occasion to achieve nominal concentrations of 0.20, 0.45, 1.3, 2.8 and 7.5 µg a.s./L. Three microcosms were used for each treatment level and the control group.

The test item was then applied on 10 June 2011 by pouring dilutions of the test item (1 L) onto the surface of the water from a volumetric flask into each microcosm in a figure of eight pattern. On each occasion, the flask was refilled with deionised water and poured into the microcosm in the same way to rinse the flask. After each microcosm was dosed, the water was gently mixed with a stainless steel paddle for one minute to ensure the test item was homogenously distributed throughout the water column. Controls were treated identically to treated microcosms, except deionised water was used in place of dilutions of the test item.

Samples of the microcosm water were then taken using Depth Integrated Water Samples (DIWS) whereby aliquots (1.5 L) of the treated water were removed from five areas (each corner and one from a central position) in each microcosm and pooled. Sub-samples (40 mL) were taken from the pooled water approximately 1, 3 and 24 hours after treatment and stored frozen prior to analysis. Additional analytical samples were also taken from later time points.

The microcosms were evaluated for a period of approximately four weeks before to 16 weeks after treatment (112 days after the last application) of the test item. During this time, samples of water and sediment were taken and analysed to provide information on the concentration of the test item in these matrices and also to provide information on the fate of the test item.

3 OBSERVATIONS

The effects of the test item on the populations of phytoplankton, periphyton, macrophytes and zooplankton were evaluated by periodic sampling and evaluation of their diversity and abundance in treated and control microcosms. In addition, the physico-chemical water parameters and the primary productivity (total chlorophyll) of phytoplankton and periphyton were evaluated, as well as the coverage of the sediment with macrophytes and filamentous algae.

4 STATISTICS

Statistical analysis was carried out for four data types (zooplankton depth integrated water samplers, periphyton, phytoplankton and macrophytes). The transformation factor, “a”, to be used in the log transformation of abundance for analysis (ln(a*abundance+1)) was calculated based on the lowest possible non-zero value "x(min)" of the data set using the formula (a=2/x(min)) or was set to a standard value of 2.0.

4.1 Principal Response Curves

CANOCO version 4.5 for Windows was used to produce Principal Response Curves (PRCs) for each main data type. This multivariate method displays time-dependent effects of test concentrations on a given response (log(a*abundance+1)) relative to the control community. In the PRC diagram, the principal component was plotted against time with the response for the control community at y=0 for all time points. A deviation from the control response indicated a difference between the control ponds and those for the test concentration in question; the larger the deflection from y = 0, the larger the difference in the structures of the two communities. The derived species weightings from the PRC analysis indicated the relative influence of the different taxonomic groups on any apparent differences.

The existence of a relationship between the organism classification and the whole set of environmental variables (dose concentrations), given the co-variables (days after application), was evaluated using Monte Carlo permutational tests.

4.2 No Observed Effect Concentration (NOEC)

Where sufficient individuals were present to enable statistical analysis, the NOEC was evaluated for all sampling dates post application using the following procedure. For zooplankton, macroinvertebrates, periphyton and phytoplankton, a Williams’ test for a concentration-response of ln(a*abundance+1) on concentration rank was performed for all test concentrations using the software “Community Analysis 4.3.07”.

As macrophyte toxicity data can suggest a stimulatory effect at low concentrations no assumption of monotonicity was made. Where there were a high number of tied values (>30% of observations with one value, >50% of observations with one of two values or >65% of observations with one of three values) no assumptions were made regarding the distribution of the data. These data were analysed using a non-parametric Mann-Whitney test. For all other macrophyte data, a Dunnett’s test for a concentration-response of ln(a*abundance+1) was performed for all test concentrations using the software “Community Analysis 4.3.07”.

The NOEC was reported as the highest test concentration which did not show a significant concentration-response. The consistent NOEC was reported as the highest test concentration which did not show a significant concentration-response on two consecutive sampling occasions. When the consecutive NOECs differed, the highest value was taken, unless the lowest value was found on two or more consecutive sampling dates.

4.3 Community No Observed Effect Concentration ($NOEC_{community}$)

Redundancy Analysis (RDA) was performed to determine a Monte Carlo p-value for each individual sampling date. Log(a*abundance+1) was fitted as the response, with 'ln transformed nominal concentration' as the environmental factor. A p-value of <0.05 may indicate a systematic pattern that cannot be attributed to chance alone. Where significant effects were observed CANOCO version 4.5 for Windows was used to perform a Principal Component Analysis (PCA). The sample scores, derived from the first principal component, were subjected to a Williams' test in order to obtain a $NOEC_{community}$ for each day. These community NOECs and the P-values calculated for each sampling date are used to determine the overall $NOEC_{community}$.

4.4 Determination of Effect Classes

Effect Classes were reported for each occasion for which NOEC values were found to be less than 7.5 µg a.s./L. In accordance with De Jong *et al* (2008) effect classes were applied where statistically significant effects were observed on consecutive sampling occasions (see Table 8.3.3-1). The overall NOEC was defined as the lowest concentration that had no significant effect on the population or community on one or more consecutive sampling date. In addition, when consecutive statistically significant effects differed, the highest value was taken.

Table 8.3.3-1: Effect classes to evaluate the treatment-related responses observed in aquatic micro- and mesocosm tests (*de Jong et al*, 2008[a])

Effect class	***Description***	***Criteria***
1	Effects could not be demonstrated ($NOEC_{micro/mesocosm}$)	No (statistically significant) effects observed as a result of treatment Observed differences between treatment and control show no clear causal relationship
2	Slight and transient effects	Effects reported as 'slight' or 'transient', or other similar description Short-term and/or quantitatively restricted response of one or a few sensitive endpoints, and only observed at individual samplings
3A	Pronounced effects; recovery within 8 weeks after the first application or total period of effects <8 weeks	Clear response of sensitive endpoints, but full recovery within 8 weeks after the first application, or total period of effects < 8 weeks Effects reported as 'temporary effects on several sensitive species', 'temporary effects on less sensitive species/endpoints' or other similar descriptions Effects observed at some subsequent sampling instances
3B	Pronounced effects; recovery within 8 weeks after the last application	Clear effects of sensitive endpoints, but full recovery within 8 weeks following the last application. In the case of repeated treatments, a total duration of the effects of > 8 weeks is possible Effects reported as 'temporary effects on several sensitive species', 'temporary effects on less sensitive species/endpoints' or other similar descriptions Effects observed at some subsequent sampling instances
4	Pronounced effects; study too short to demonstrate recovery within 8 weeks after the last application	Clear effects observed as in Effect class 3, but the study is too short to demonstrate complete recovery within 8 weeks after the (last) application
5A	Pronounced effects; total period of effects >8 weeks and no recovery within 8 weeks after the last application; full recovery within the test period	Clear response of sensitive endpoints and recovery time is longer than 8 weeks after the last application Full recovery is reported before the end of the study Effects reported as 'long-term effects followed by recovery on several sensitive and less sensitive species/endpoints or other similar descriptions On consecutive time points
5B	Pronounced effects; total period of effects >8 weeks and no recovery within 8 weeks after the last application; and no full recovery within the test period	Clear response of sensitive endpoints and recovery time is longer than 8 weeks after the last application Full recovery is not reported before the end of the study Effects reported as 'long-term effects followed by recovery on several sensitive and less sensitive species/endpoints or other similar descriptions On consecutive time points

[a] de Jong, F.M.W., Brock, T.C.M., Foekema, E.M., & Leeuwangh, P. (2008) Guidance for summarising and evaluating aquatic micro and mesocosm studies, RIVM Report 601506009/2008.

II RESULTS AND DISCUSSION

A CHEMICAL ANALYSIS

The concentrations of picolinafen were measured in samples taken from the water column and sediment at intervals during the study using a LC-MS/MS method of analysis. Samples taken approximately one hour after treatment confirmed that the intended concentrations of picolinafen had been achieved in the water column, with mean measured levels ranging from 84 to 91% of their nominal values.

Samples taken three hours after application showed that concentrations of picolinafen had decreased slightly with measured levels ranging from 69 to 82% of their nominal values. A low level of picolinafen was also detected in one control replicate at this time point although this was below the LOQ of the analytical method (0.02 µg a.s./L). This was attributed to the use of contaminated equipment used to take aqueous chemistry samples on day 0 of the test. Due to the very low levels detected and the absence of any detectable residues on subsequent sampling occasions, the measured residues in the control group on day 0 of the test are not considered to have affected the integrity or validity of the study.

On Day 7 of the test measured levels of picolinafen in the test water were below the LOQ in the 0.2 and 0.45 µg a.s./L dose groups. At the remaining levels mean measured residues ranging from 5 to 7% were found. On Day 14 of the test mean measured residues equivalent to 3% of the nominal concentration were found at the highest treatment level (7.5 µg a.s./L); no quantifiable residues were found at any other level and no residues were detected at any level on subsequent sampling occasions.

No residues of picolinafen were found in samples of the microcosm sediment in the control group or in microcosms treated at 0.2 and 0.45 µg a.s./L. On Day 14 of the test, picolinafen was found at quantifiable levels (1.12 ng/g) in one replicate (M69) at 1.3 µg a.s./L and in all replicates in the 2.8 and 7.5 µg a.s./L dose groups, giving mean measured levels of 4.68 and 4.40 ng/g in each, respectively. Measurable levels (1.07 ng/g) were also detected in one replicate (M66) on Day 28 and one replicate (M73) on Day 56 of the test where residues of 4.81 ng/g were detected. No other quantifiable residues were found in any other samples taken during the test.

These data confirm that the majority of the active substance remained in the water column and did not have a high affinity to partition into the sediment during the study. The times for 50% disappearance (DT_{50}) from water were not calculated as this was not an objective of the study; however, it was estimated to be approximately one day.

B BIOLOGY

1 Zooplankton

The overall abundance of zooplankton was dominated by *Keratella quadrata* and Nauplia comprising 52.7% and 23.2% of the total abundance, respectively. Statistically significant indirect effects were observed for *Daphnia longispina* on Days 84 and 98 giving a NOEC of 2.8 µg a.s./L for this taxon. Recovery was demonstrated by Day 111 and no effects were observed at any other time point.

At the community level, the PRC for zooplankton samples showed no clear effects following treatment and as a result, the $NOEC_{community}$ derived from the PRC was 7.5 µg a.s./L.

2 Periphyton

For periphyton, the most sensitive class for which effects were observed following treatment with picolinafen was the green alga Zygnematophyceae which showed a consistent NOEC of 2.8 µg a.s./L from Day 35 to Day 42. Full recovery of this taxa was observed by Day 56 giving a NOEC of 7.5 µg a.s./L from this time point onwards.

At the community level, the PRC for periphyton showed no clear effects following treatment and as a result, the $NOEC_{community}$ derived from the PRC was 7.5 µg a.s./L.

3 Phytoplankton

For phytoplankton, the most sensitive class for which effects were observed following treatment with picolinafen was the green alga Zygnematophyceae which showed a consistent NOEC of 2.8 µg a.s./L from Day 42 to Day 70. Full recovery of this taxa was observed by Day 84 giving a NOEC of 7.5 µg a.s./L from this time point onwards.

At the community level, the PRC for phytoplankton showed no clear effects following treatment and as a result, the $NOEC_{community}$ derived from the PRC was 7.5 µg a.s./L.

As the most sensitive taxa was observed to be Zygnematophyceae for both phytoplankton and periphyton, a clear and consistent dose response is evident.

4 Macrophytes

Consistent NOECs were only observed for *Sparganium* (number of stems) giving a derived consistent NOEC of 2.8 µg a.s./L on days -1 and 7, however as the period of effect included pre-treatment measurements, it is clear that this cannot be a treatment related effect.

Some statistically significant effects were also observed for *Lemna minor*, however, these results have been disregarded as *Lemna* need high phosphorous and nitrogen concentrations for growth and although sediment rooted plants can assimilate nutrients directly from the sediment, floating plants can only assimilate nutrients from the water column. The author states that Portielje *et al*. (1995) demonstrated that *Lemna* could only grow in competition with macrophytes rooted within the sediment of experimental ditches when dissolved nutrients (principally dissolved phosphorous and nitrogen) were no longer limiting, due to *Lemna* deriving its nutrient requirements solely from the water column. These arguments are also applicable to *Ceratophyllum demersum* which failed to establish in the study.

The authors also demonstrate that Kufel *et al.* (2010) reported that growth rates of *Lemna minor* are significantly correlated with *in situ* concentrations of all dissolved nutrients; stating that although the plant is known to grow in waters of a broad range of nutrient concentrations it is not typically found in oligotrophic habitats which are defined as water bodies with the following characteristics (US EPA, 2000):

- Sestonic chlorophyll (µg/L): <10
- Total nitrogen (µg/L): <700
- Total phosphorous (µg/L): <25

When considering the majority of the sestonic chlorophyll levels were <10 µg/L and the nutrient levels were significantly lower than those required for mesotrophic nutrient status, then it is unsurprising that under these conditions, normal growth of *Lemna* could not be achieved. Consequently, the *Lemna* data should be discounted from the derivation of the overall NOEAEC from this study. These conclusions are supported by (Brock et al, 2011) who states that in micro/mesocosm studies, the growth of *Lemna* minor/gibba is often poor due to low nutrient levels in water.

As no treatment related effects were observed, the NOEC for macrophytes was 7.5 µg a.s./L. No PRC was calculated for macrophytes as community data were not collected.

5 Secondary effects

Water quality measurements made routinely during the study showed that concentrations of dissolved oxygen were reduced in the highest treatment group (7.5 µg a.s./L) in the period shortly after treatment. On Day 4, 7 and 14 of the test, mean dissolved oxygen levels in microcosms treated at 7.5 µg a.s./L were 10.32, 10.62 and 10.72 mg/L, respectively. By comparison, mean values in the control group were 12.25, 12.35 and 11.81 mg/L on the same sampling occasions, respectively. Less pronounced effects were also observed in the 2.8 µg a.s./L treatment group for the same period (Day 4 to 14), however a clear dose response was not evident at this concentration as the levels of dissolved oxygen in one of the replicates at this level was above or similar to the maximum range of the controls. By Day 21 of the test, dissolved oxygen levels in treated microcosms at all treatment levels were comparable with the range of the controls showing rapid recovery of photosynthetic activity had occurred. No effects on dissolved oxygen were observed for any subsequent sampling occasion.

6 Diurnal oxygen measurements

Although there was some evidence of a treatment related effect on diurnal dissolved oxygen measurements in microcosms treated at 2.8 and 7.5 µg a.s./L on Day 13 to 14, measured levels of dissolved oxygen in some replicates treated at these concentrations were within the range of the controls. As a result, a clear dose response could not be identified. No treatment related effects were observed on later sampling occasions.

7 Overall NOEC

Statistically significant indirect effects were observed on *Daphnia longispina,* and statistically significant direct effects Zygnematophyceae in microcosms treated at 7.5 µg a.s./L. Although not statistically evaluated, clear treatment related effects were also observed for the levels of dissolved oxygen in the period shortly after treatment in microcosms dosed at 7.5 µg a.s./L.

The class 1 NOEC was estimated to be 2.8 µg a.s./L.

8 NOEAEC

Based on the effect classifications as published by de Jong *et al* (2008) the class 5A NOEAEC was estimated to 7.5 µg a.s./L due to recovery of all affected populations and the levels of dissolved oxygen at this level by the end of the test.

C DEFICIENCIES

None

III CONCLUSIONS

The concentrations of picolinafen measured in samples taken from the water column approximately one hour after treatment confirmed that the intended concentrations of picolinafen had been achieved with mean measured levels ranging from 84 to 91% of their nominal values.

Statistically significant indirect effects were observed on *Daphnia longispina,* and statistically significant direct effects Zygnematophyceae in microcosms treated at 7.5 µg a.s./L. Although not statistically evaluated, clear treatment related effects were also observed for the levels of dissolved oxygen in the period shortly after treatment in microcosms dosed at 7.5 µg a.s./L.

The class 1 NOEC was estimated to be 2.8 µg a.s./L BAS 700 H

The class 5A NOEAEC was estimated to be 7.5 µg a.s./L due to recovery of all affected populations at this level by the end of the test.

(Taylor S., & Priestly S., 2012)

References

Brock, T., Crum, S., Bruns, E., and Hartmut, G. (2011): Impact of the herbicide indaziflam in freshwater microcosms including macrophyte bioassays. SETAC, Milano.

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Kufel, L., Strzalek, M., Konieczna, A. and Izdebska, K. (2010): The effect of *Stratiotes aloides* L. and nutrients on the growth rate of *Lemna minor* L. *Aquatic Botany*, 92: 168-172.

Portiejle, R. and Roijackers, R.M.M. (1995): Primary succession of aquatic macrophytes in experimental ditches in relation to nutrient input. *Aquatic Botany*, 50: 127-140.

8.4 Effects on algal growth and growth rate (2 species)

Toxicity data for algae were submitted for the previous EU review of picolinafen (see 8.4.1). This supplementary dossier to the original Annex I dossier does not contain any new laboratory studies assessing the toxicity of picolinafen to algae, however it does contain additional aquatic field testing data (microcosm study) addressing the effects of picolinafen on phytoplankton, periphyton and macrophytes (see Annex Point AIII 8.3.3) and additional laboratory toxicity data for algae, which consists of a short-term toxicity study with the metabolite CL 7693 (see Annex Point AIII 8.4.1.1).

8.4.1 Effects on algal growth and growth rate

In the Addendum 1 to the DAR (August 2001) data on the effects of picolinafen on a range of algal species were submitted (B9.2). The most sensitive species tested was *Ankyra judayi* with a 72h EC_{50} = 0.000025 mg a.s./L for effects based on biomass.

(Ref: WAT2001-202).

8.4.1.1 Effects on algal growth and growth rate (72h)

Report: II A 8.4/1
Kley A., Deierling T. 2011(c)
Toxicity of CL 7693 to Pseudokirchneriella subcapitata in an algal growth inhibition test
BASF DocID 2010/1159918

Guidelines: OECD 201 (2006); (EC) No 761/2009 laying down test methods pursuant to (EC) No 1907/2006 of European Parliament and of Council on the REACH 2009 - Part C.3: Algal Inhibition Test

Deviations:
(i) Test concentrations: According to study plan - 10, 3.2, 1.0, 0.32 and 0.10 mg test item/L and a control should be tested. Deviation to study plan – due to calculation error 20, 3.2, 1.0, 0.32 and 0.10 mg test item/L and a control were tested. No effect presumed on study since the actual concentrations were used for the evaluations and calculation of endpoints.
(ii) Storage of the test item: According to study plan - In original container, in the refrigerator (approx. +4 °C or cooler), in the dark. Deviation to study plan – For technical reasons the test item was stored in original container, in the refrigerator (≤ +5 °C), in the dark. No effect presumed on study since deviation was slight.

GLP: Yes
(laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

An algal growth inhibition study the toxicity of CL 7693 to *Pseudokirchneriella subcapitata* was investigated. The test substance was applied at concentrations of 0.10, 0.32, 1.0, 3.2 and 20 mg/L. These nominal concentrations corresponded to geometric mean measured concentrations of 11.98, 1.57, 0.487, 0.157 and 0.049 mg test item/L. In controls, test water was used without the addition of the test substance.

The study encompassed 6 treatment groups (5 dose rates of the test item and a control) with three replicates per test concentration and six replicates for the control. At the start of the test 50 mL of the test concentrations were inoculated with 5000 algal cells/mL test medium and defined volumes of the algal suspensions were sampled after 24, 48 and 72 hours for determination of cell densities by spectrophotometrical measurement.

The quantification of the test item CL 7693 was performed using liquid chromatography (HPLC-method). At the start of the test 82 % of the nominal test concentrations was found (average of all test concentrations above the NOEC). After 72 hours test duration, 34 % of the nominal value was determined (average of all test concentrations above the NOEC). Since the test item concentrations were not stable during the test duration, all reported results refer to geometric mean measured concentrations

Based on the test results, the 72-hour E_rC_{50} value was calculated to be 14.0 mg test item/L (extrapolated) and the 72-hour E_yC_{50} was calculated to be 1.84 mg test item/L. The 72-hour NOE_rC and the 72-hour NOE_yC were determined to be 0.487 mg test item/L and the associated 72-hour LOE_rC and LOE_yC is 1.57 mg test item/L.

I. MATERIAL AND METHODS

1. **Test Material:** CL 7693
   Description: Orange liquid (purity 99.7%)
   Lot Batch #: AC12214-129
   Stability of test compound: Considered to be sufficiently stable for purpose of study

2. **Vehicle and/ or positive control:** Reconstituted water (OECD medium)/ potassium dichromate

3. **Test animals:**
   Species: *Pseudokirchneriella subcapitata*
   Strain: Strain No.: 61.81 SAG
   Source: Sammlung von Algenkulturen, Pflanzenphysiologisches Institut der Universität Göttingen", 37073 Göttingen, Germany
   Environmental conditions –
   Temperature: 22 – 23°C
   Photoperiod: Continuous illumination
   Light intensity: Mean: 5725 lux (Range: 5610 – 5930 lux)
   pH: 8.0 – 9.4

   In-life dates: 8 – 11 November 2010

Experimental treatments:

The study was conducted using uniquely identified Erlenmeyer flasks (50 mL volume) containing 50 mL of test medium. From a stock solution (nominal 20 mg/L), adequate volumes were mixed into the test water to prepare the test concentrations (0.1, 0.32, 1.0, 3.2 and 20 mg/L). The pH of this stock solution was adjusted with1 N NaOH from 7.9 to 8.1. The test media was prepared just before introduction of the algae. The test was started (0 hours) by inoculation of a biomass of 5000 algal cells per mL test medium. There were three replicates per test concentration and six replicates in the control. Volumes of 50 mL of algal suspension per replicate were continuously stirred with magnetic stirrers and the flasks were covered with glass dishes and incubated in a water bath. Additionally, one replicate of each test concentration and of the control was prepared without algae to provide a "blank" for the spectrophotometrical measurements. The additional replicates were incubated under the same conditions as described above

Observations:

Test conditions were recorded with suitable instruments. Cell density was determined by spectrophotometrical measurement after 24, 48 and 72 hours of exposure. Inhibition of algal growth was determined by calculating average specific growth rate (increase in cell density per unit time) and yield (actual number of cells per volume of medium (cells/mL) at the end of exposure minus the cell number at the start of the study). Concentrations of the test item were analysed in the duplicate test media samples from all test concentrations above the NOEC determined in this test and both sampling times (0 and 72 hours). Quantification was performed using liquid chromatography (HPLC-method).

Statistics:

Based on the calculated cell densities, the 72-hour E_rC_{50} and the 72-hour E_yC_{50}, the corresponding EC_{10} values and where possible their 95 %-confidence limits were calculated by Probit analysis. For the determination of the 72-hour LOEC and the 72-hour NOEC, the calculated growth rates and yields at each test concentration were tested for significant differences compared to the control values by the Williams t-test (growth rate, yield), respectively. Statistical analysis was performed performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH).

II. RESULTS AND DISCUSSION

All validity criteria were met.

Results are summarised in Table 8.4.1.1-1. Based on the geometric mean measured concentrations of the test item the 72-hour E_rC_{50} was calculated to be 14.0 mg test item/L and the 72-hour E_yC_{50} was calculated to be 1.84 mg test item/L. The corresponding 72-hour E_rC_{10} was calculated to be 1.48 mg test item/L and the 72-hour E_yC_{10} was calculated to be 0.504 mg test item/L.

The 72-hour NOE_rC and the 72-hour NOE_yC were determined to be 0.487 mg test item/L based on geometric mean measured concentrations of the test item and the associated 72-hour LOE_rC and LOE_yC is 1.57 mg/L, respectively.

Table 8.4.1.1-1: Effects on growth rate and yield of *Pseudokirchneriella subcapitata* following exposure to CL 7693

Parameter (0 – 72 hours)	Growth rate (mg test item/L)	Yield (mg test item/L)
72 hour EC_{50}:	14.0*	1.84
95% confidence limits	11.6 – 17.7	1.55 – 2.31
72 hour EC_{10}:	1.48	0.504
95% confidence limits	0.937 – 2.04	0.313 – 0.664
72 hour NOEC:	0.487	0.487
72 hour LOEC:	1.57	1.57

Values refer to geometric mean measured concentrations
* Value extrapolated

The microscopic examination of the shape of the algal cells after 72 hours of test duration did not show any difference between the algae that had been growing at a nominal test concentration of 20 mg test item/L and the algal cells in the control.

At the start of the test 82 % of the nominal test concentrations was found (average of all test concentrations above the NOEC). After 72 hours test duration, 34 % of the nominal value was determined (average of all test concentrations above the NOEC). Since the test item concentrations were not stable during the test duration, all reported results refer to geometric mean measured concentrations.

III. CONCLUSION

The influence of CL 7693 on the growth of the freshwater green algae *Pseudokirchneriella subcapitata* was assessed in a static dose-response test. The 72-hour E_rC_{50} value was calculated to be 14.0 mg test item/L (extrapolated) and the 72-hour E_yC_{50} was calculated to be 1.84 mg test item/L. The 72-hour NOE_rC and the 72-hour NOE_yC were determined to be 0.487 mg test item/L and the associated 72-hour LOE_rC and LOE_yC is 1.57 mg test item/L.

8.5 Effects on sediment dwelling organisms

The effect of picolinafen on sediment dwelling organisms was addressed for the previous EU review (see DAR September 2000). In the DAR, a 28 day chronic toxicity study was conducted. For completeness a brief overview of this study is provided in AIII 8.5.2. The supplemental dossier does not contain any additional data for sediment dwelling organisms.

8.5.1 Acute test

No data submitted. Acute toxicity studies on sediment dwelling organisms are not required.

8.5.2 Chronic test

According to the DAR (September 2000), a valid 28 day chronic (water spiked) toxicity study conducted in accordance with accepted international guidelines and GLP requirements was submitted. The 28 day NOEC values for development and emergence were 0.18 and 0.48 mg a.s./L, respectively.

(Ref: WAT1999-513)

8.6 Effects on aquatic plants

Data examining the effects of picolinafen on aquatic plants were presented in the DAR dated September 2000. The most sensitive endpoint from a 14 day *Lemna* study was for frond number with an EC_{50} of 0.057 mg a.s./L and a NOEC of 0.0072 mg a.s./L. The EC_{50} and NOEC for biomass were 0.08 mg a.s./L and 0.027 mg a.s./L, respectively.

(Ref: WAT1999-527)

8.7 Effects on bees

To address the toxicity of picolinafen to bees an acute oral and contact study conducted in accordance with accepted international guidelines and GLP requirements was submitted during the first EU review.

(Ref: BIE2000-05)

8.7.1 Acute oral toxicity

According to the DAR (September 2000), an acute oral toxicity study conducted in accordance with EPPO-Guideline 170 resulted in an acute oral LD_{50} >200 µg a.s./bee.

8.7.2 Acute contact toxicity

According to the DAR (September 2000), an acute contact toxicity study conducted in accordance with EPPO-Guideline 170 resulted in an acute contact LD_{50} >200 µg a.s./bee.

8.7.3 Toxicity of residues on foliage to honey bees

No data submitted – not required.

8.7.4 Bee brood feeding test

No data submitted – not required.

8.8 Effects on non-target terrestrial arthropods

In the DAR (September 2000), the toxicity of formulated picolinafen to the two standard species (the phytoseiid mite *Typhlodromus pyri* and the braconid wasp *Aphidius rhopalosiphi*), the ground dwelling carabid beetle (*Poecilus cupreus)* and the ground dwelling spider (*Pardosa sp.*) was determined in laboratory tests based on IOBC Guidelines. For completeness a short summary of the individual studies is provided below. This supplementary dossier only contains additional data for other terrestrial invertebrates.

8.8.1 Effects on non-target terrestrial arthropods, artificial substrates

8.8.1.1 Parasitoid

BBA-Reference:	Nienstedt, K. M., Maise, S., Strnd, S. P., 1999
Species:	*Aphidius rhopalosiphi*
Guideline:	Aphidius, Lab (Mead-Briggs 1992)
Test substance:	Formulation: AC 900001 750 g/kg WG (SF09617) (WG) BBA-Reg. Nr. 4796 (Picolinafen 747 g/kg)
Developmental stage:	Adults
Substrate:	Glass plate
Route of exposure:	deposit
Duration of exposure:	24 h

Results:

Field rate tested	Mortality	Sublethal effects	Total effects
0.134 kg/ha	0%	6% (Parasitisation)	
0.0008 kg/ha	0%	24% (Parasitisation)	

Valid: yes

(Ref: ANA1999-156)

8.8.1.2 Predatory mites

BBA-Reference:	Nienstedt, K. M., Ott, U., Strnd, S. P., 1999
Species:	T*yphlodromus pyri*
Guideline:	Typhlodromus (Overmeer 1988)
Test substance:	Formulation: AC 900001 750 g/kg WG (SF09617) (WG) BBA-Reg. Nr. 4796 (Picolinafen 747 g/kg)
Developmental stage:	Protonymphs
Substrate:	Glass plate
Route of exposure:	deposit
Duration of exposure:	14 d (7 + 7)

Results:

Field rate tested	Mortality	Sublethal effects	Total effects
0.134 kg/ha	0%	10% (Fertility)	
0.0008 kg/ha	2.1%	43.5% (Fertility)	

Notes:	Mortality: Dead and escapers
Valid:	yes

(Ref: ANA1999-157)

8.8.1.3 Ground dwelling predatory species

8.8.1.3-1:

BBA-Reference:	Nienstedt, K. M., Reder, E., Ott, U., Strnd, S. P., 1999
Species:	*Pardosa spp.*
Guideline:	Pardosa (Wehling 1998)
Test substance:	Formulation: AC 900001 750 g/kg WG (SF09617) (WG) BBA-Reg. Nr. 4796 (Picolinafen 747 g/kg)
Developmental stage:	Adults
Substrate:	Quartz sand
Route of exposure:	overspray
Duration of exposure:	14 d

Results:

Field rate tested	Mortality	Sublethal effects	Total effects
0.134 kg/ha	0%	+1% (Food uptake)	
0.0008 kg/ha	5%	7% (Food uptake)	

Notes: In treatment "0.0008 kg/ha" food uptake was reduced significantly by 38% (4 d to 7 d) as compared to the control.

Valid: yes

(Ref: ANA1999-159)

8.8.1.3-2:

BBA-Reference:	Nienstedt, K.M., Reeder, E., Ott, U., Strnd, S.P., 1999,
Species:	*Poecilus cupreus*
Guideline:	Poecilus (Heimbach 1992)
Test substance:	Formulation: AC 900001 750 g/kg WG (SF09617) (WG) BBA-Reg. Nr. 4796 (Picolinafen 747 g/kg)
Developmental stage:	Adults
Substrate:	Quartz sand
Route of exposure:	overspray + oral
Duration of exposure:	14 d

Results:

Field rate tested	Mortality	Sublethal effects	Total effects
0.134 kg/ha	0%	0% (Food uptake)	
0.0008 kg/ha	0%	0% (Food uptake)	

valid: yes

(Ref: ANA1999-158)

8.8.1.4 Foliage dwelling predatory species

No data submitted or required.

8.8.2 Effects on non-target terrestrial arthropods in lab/semi-field test

No data submitted or required.

8.8.2.1 Parasitoid

See 8.8.2 above

8.8.2.2 Predatory mites

See 8.8.2 above

8.8.2.3 Ground dwelling predatory species

See 8.8.2 above

8.8.2.4 Foliage dwelling predatory species

See 8.8.2 above

8.8.2.5 Other terrestrial invertebrates

If the results of the repeated chronic earthworm study had resulted in a TER_{LT} < 5, this may have triggered a requirement for the risk assessment for soil macro-invertebrates to be re-assessed. Therefore, it was considered justifiable to conduct a chronic collembolan study with picolinafen.

Report:	II A 8.8.2.5/1 Luehrs U. 2011(a) Effects of BAS 700 H on reproduction of the collembola Folsomia candida in artificial soil with 5% peat BASF DocID 2010/1159926
Guidelines:	OECD 232 (2009); ISO 11267 (1999)
Deviations:	none
GLP:	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

In a laboratory 28 day chronic toxicity study the effects of BAS 700 H on mortality and reproduction of the Collembola *Folsomia candida* (Isotomidae) were investigated. Five concentrations of the test item (31.25, 62.5, 125, 250 and 500 mg BAS 700 H/kg soil dry weight) were incorporated into the soil; 5% peat only) with four replicates per treatment (each containing 10 Collembola). An untreated control with 8 replicates was included. The reference item was tested in a separate study.

Assessment of mortality and reproduction was carried out after 28 days. BAS 700 H did not show any statistically significant effects on mortality and reproduction up to and including 250 mg test item/kg soil dry weight. At the concentration of 500 mg test item/kg soil dry weight mortality and reproduction were statistically significantly different compared to the control. No behavioural abnormalities were observed in any of the treatment groups.

In a 28 day Collembola reproduction study with BAS 700 H, no adverse effects on survival and reproduction could be determined at concentrations up to and including 250 mg test item/kg soil dry weight. The overall NOEC was equivalent to 250 mg test item/kg soil dry weight.

I. MATERIAL AND METHODS

1. **Test Material:** BAS 700 H
   Description: Cream solid (Purity: 97.8%)
   Lot Batch #: CA 14113
   Stability of test compound: Sufficient for purposes of study

2. **Vehicle and/ or positive control:** Untreated (same amount of acetone treated sand per g substrate as in test item groups, moistened with deionised water) / Boric acid

3. **Test animals:**
   Species: *Folsomia candida* (Willem 1902); juveniles, adults; 10 – 12 days old)
   Source: In-house culture
   Food: Granulated dry yeast
   Environmental conditions –
   Temperature: 18 – 22°C
   WHC: Start: 19.0% to 19.5% (48.7% to 49.9% of maximum water holding capacity (WHC))
   Finish: 15.3% to 17.4% (39.2% to 44.6% of the maximum WHC)
   pH: Start: 6.3 – 6.4
   End: 6.0
   Photoperiod: 16:8 L:D (Light intensity: 400 – 800 lux)

   In-life dates: 24 January 2011 – 23 February 2011

   Experimental treatments: The 28 day test was conducted in treated artificial soil based on OECD 232 (5% sphagnum peat only). The test units consisted of glass containers (volume 100 mL, 5 cm diameter) closed tightly to avoid water evaporation and filled with 3.0 g ± 1.0 g artificial soil fresh weight.

   A stock solution was prepared by dissolving 400.0 mg of BAS 700 H in 20 mL acetone. A 1:2 dilution series was prepared by adding 10 mL of acetone to 10 mL of the stock solution or the corresponding dilutions. Then 5 mL of the stock solution and the corresponding dilutions were added to 50 g fine quartz sand. Different concentrations of the test item were incorporated into the soil; 6 treatment groups (5 test item concentrations (31.25, 62.5, 125, 250 and 500 mg BAS 700 H/kg soil dry weight), control); There were 4 replicates for the test item treatments and 8 replicates for the control with 10 individuals per replicate. One additional container per treatment was prepared to check the pH and water content of the test substrate after 28 days.

Observations: Assessment of mortality, behavioural effects and reproduction was carried out after 28 days exposure of adult worms in treated artificial soil. Reproduction rate (number of offspring) was assessed after additional 28 days (assessed 56 days after application).

Statistics: Mortality data were statistically analysed using Fisher's Exact Test ($\alpha = 0.05$, one-sided greater). Reproduction data were tested for normal distribution and homogeneity of variance using Kolmogoroff-Smirnov test and Levene's test ($\alpha = 0.05$). Further statistical evaluation was performed using Dunnett's t-test (multiple comparison, $\alpha = 0.05$, one-sided smaller). The determination of the NOEC and LOEC values was based on the results of the statistical evaluation. The EC_{50} for reproduction was calculated by Probit Analysis (Finney 1971). Statistical analysis was performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH.

II. RESULTS AND DISCUSSION

All validity criteria were met. The results are summarised in Table 8.8.2.5-1.

Mortality of up to 20% was observed in the test item treated groups up to and including 250 mg test item/kg soil dry weight, which was not statistically significantly different compared to the control, where 16% of the Collembola died (Fisher's Exact test, $\alpha = 0.05$). At the concentration of 500 mg test item/kg soil dry weight a statistically significant mortality of 45 % was observed.

Reproduction of the collembolans exposed to BAS 700 H was not statistically significantly different compared to the control up to and including 250 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$). At the concentration of 500 mg test item/kg soil dry weight a statistically significant reduction of reproduction was observed.

No behavioural abnormalities were observed in any of the treatment groups.

In a separate study (study code 61401016) the reference item Boric acid showed statistically significant effects on reproduction at concentrations of ≥ 59.3 mg/kg soil dry weight; the EC_{50} for reproduction was calculated to be 70.7 mg/kg soil dry weight. Mortality was statistically significantly higher compared to the control at 88.9 mg/kg soil dry weight and above.

Table 8.8.2.5-1: Effect of BAS 700 H on Collembola (*Folsomia candida)* in a 28-day reproduction study

BAS 700 H [mg/kg soil dry weight]	**Control**	**31.25**	**62.5**	**125**	**250**	**500**
Mortality (day 28) [%][1)]	16	13	18	20	15	45
Significance [1)]	-	n.s.	n.s.	n.s.	n.s.	*
No. of juveniles (day 28) [2)]	403	417	334	347	374	172
Significance [2)]	-	n.s.	n.s.	n.s.	n.s.	*
Reproduction in [%] of control (day 28)	--	103	83	86	93	43
Endpoints [mg test item/kg soil dry weight]						
NOEC (mortality)	250					
LC_{50} (mortality) [3)]	>500					
NOEC (reproduction)	250					
EC_{50} (reproduction) [4)]	489					

n.s. = not significantly different compared to the control
* = significantly different compared to the control
[1)] Fisher's Exact Test, $\alpha = 0.05$, one-sided greater
[2)] Dunnett's t-test, $\alpha = 0.05$, one-sided smaller
[3)] estimated value
[4)] Probit analysis

III. CONCLUSION

BAS 700 H had no significant effects on mortality or reproduction of *Folsomia candida* up to and including the concentration of 250 mg test item/kg soil dry weight. At the concentration of 500 mg test item/kg soil dry weight mortality and reproduction were statistically significantly different compared to the control.

The overall No Observed Effect Concentration (NOEC) was determined to be 250 mg test item/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was determined to be 500 mg test item/kg soil dry weight.

It was possible that the re-assessment of degradation rates using FOCUS kinetics for CL 153815 (Reg. No. 4037090) and the results of the chronic earthworm study with CL 153815 may have triggered the need to re-assess the risk assessment for soil macro-invertebrates for CL 153815. Therefore, it was considered justifiable to conduct a chronic collembolan study with CL 153815.

Report:	II A 8.8.2.5/2 Luehrs U. 2011(b) Effects of Reg.No. 4037090 on reproduction of the collembola Folsomia candida in artificial soil with 5% peat BASF DocID 2010/1159923
Guidelines:	OECD 232 (2009); ISO 11267 (1999)
Deviations:	none
GLP:	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

In a laboratory 28 day chronic toxicity study the effects of Reg. No. 4037090 on mortality and reproduction of the Collembola *Folsomia candida* (Isotomidae) were investigated. Five concentrations of the test item (62.5, 125, 250, 500 and 1000 mg Reg. No. 4037090/kg soil dry weight) were incorporated into the soil (5% peat only) with four replicates per treatment (each containing 10 Collembola). An untreated control with 8 replicates was included. The reference item was tested in a separate study.

Assessment of mortality and reproduction was carried out after 28 days. Reg. No. 4037090 did not show any statistically significant effects on mortality and reproduction up to and including 250 mg test item/kg soil dry weight. At the concentration of 500 mg test item/kg soil dry weight mortality and reproduction were statistically significantly different compared to the control. No behavioural abnormalities were observed in any of the treatment groups.

In a 28 day Collembola reproduction study with Reg. No. 4037090, no adverse effects on survival and reproduction could be determined at concentrations up to and including 250 mg test item/kg soil dry weight. The overall NOEC was equivalent to 250 mg test item/kg soil dry weight.

I. MATERIAL AND METHODS

1. **Test Material:** Reg. No.: 4037090
   Description: Faint beige solid (Purity: 100.0%)
   Lot Batch #: CA 16282
   Stability of test compound: Sufficient for purposes of study

2. **Vehicle and/ or positive control:** Untreated (same amount of acetone treated sand per g substrate as in test item groups, moistened with deionised water) / Boric acid

3. **Test animals:**
   Species: *Folsomia candida* (Willem 1902); juveniles, adults; 10 – 12 days old)
   Source: In-house culture
   Food: Granulated dry yeast
   Environmental conditions –
   Temperature: 18 – 22°C
   WHC: Start: 18.8% to 19.3% (48.1% to 49.5% of maximum water holding capacity (WHC))
   Finish: 15.3% to 16.7% (39.3% to 42.9% of the maximum WHC)
   pH: Start: 6.4 – 6.5
   End: 5.9 – 6.0
   Photoperiod: 16:8 L:D (Light intensity: 400 – 800 lux)

   In-life dates: 31 January 2011 – 02 March 2011

   Experimental treatments: The 28 day test was conducted in treated artificial soil based on OECD 232 (5% sphagnum peat only). The test units consisted of glass containers (volume 100 mL, 5 cm diameter) closed tightly to avoid water evaporation and filled with 3.0 g ± 1.0 g artificial soil fresh weight.

   A stock solution was prepared by dissolving 800.0 mg of Reg. No. 4037090 in 20 mL acetone. A 1:2 dilution series was prepared by adding 10 mL of acetone to 10 mL of the stock solution or the corresponding dilutions. Then 5 mL of the stock solution and the corresponding dilutions were added to 50 g fine quartz sand. Different concentrations of the test item were incorporated into the soil; 6 treatment groups (5 test item concentrations (62.5, 125, 250 and 500 mg Reg. No, 4037090/kg soil dry weight), control); There were 4 replicates for the test item treatments and 8 replicates for the control with 10 individuals per replicate. One additional container per treatment was prepared to check the pH and water content of the test substrate after 28 days.

Observations: Assessment of mortality, behavioural effects and reproduction was carried out after 28 days exposure of adult worms in treated artificial soil. Reproduction rate (number of offspring) was assessed after additional 28 days (assessed 56 days after application).

Statistics: Mortality data were statistically analysed using Fisher's Exact Test ($\alpha = 0.05$, one-sided greater). Reproduction data were tested for normal distribution and homogeneity of variance using Kolmogoroff-Smirnov test and Levene's test ($\alpha = 0.05$). Further statistical evaluation was performed using Dunnett's t-test (multiple comparison, $\alpha = 0.05$, one-sided smaller). The determination of the NOEC and LOEC values was based on the results of the statistical evaluation. The EC_{50} for reproduction was calculated by Probit Analysis (Finney 1971). Statistical analysis was performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH.

II. RESULTS AND DISCUSSION

All validity criteria were met. The results are summarised in Table 8.8.2.5-2.

Mortality of *Folsomia candida* was not significantly different compared to the control up to and including the test concentration of 250 mg test item/kg soil dry weight. At the test concentrations of 500 and 1000 mg test item/kg soil dry weight a statistically significantly increased mortality was observed (Fisher's Exact test, $\alpha = 0.05$).

Reproduction of the collembolans exposed to Reg. No. 4037090 was not statistically significantly different compared to the control up to and including the concentration of 250 mg test item/kg soil dry weight. At the concentration of 500 mg test item/kg soil dry weight and above a statistically significant decrease of reproduction was observed (Dunnett's t-test, $\alpha = 0.05$, one-sided smaller).

No behavioural abnormalities were observed in any of the treatment groups.

In a separate study (study code 61401016) the reference item Boric acid showed statistically significant effects on reproduction at concentrations of $\geq$ 59.3 mg/kg soil dry weight; the EC_{50} for reproduction was calculated to be 70.7 mg/kg soil dry weight. Mortality was statistically significantly higher compared to the control at 88.9 mg/kg soil dry weight and above.

Table 8.8.2.5-2: Effect of Reg. No. 4037090 on Collembola (*Folsomia candida)* in a 28-day reproduction study

Reg. No. 4037090 [mg/kg soil dry weight]	**Control**	**62.5**	**125**	**250**	**500**	**1000**
Mortality (day 28) [%][1)]	14	10	18	18	35	100
Significance [1)]	-	n.s.	n.s.	n.s.	*	*
No. of juveniles (day 28) [2)]	396	408	509	422	245	0
Significance [2)]	-	n.s.	n.s.	n.s.	*	*
Reproduction in [%] of control (day 28)	--	103	129	107	62	0
Endpoints [mg test item/kg soil dry weight]						
NOEC (mortality)	250					
LC_{50} (mortality) [3)]	541.7					
NOEC (reproduction)	250					
EC_{50} (reproduction) [4)]	512.4					

n.s. = not significantly different compared to the control
* = significantly different compared to the control
[1)] Fisher's Exact Test, $\alpha = 0.05$, one-sided greater
[2)] Dunnett's t-test, $\alpha = 0.05$, one-sided smaller
[3)] Probit value

III. CONCLUSION

Reg. No. 4037090 caused no significant effects on mortality or reproduction of *Folsomia candida* up to and including the concentration of 250 mg test item/kg soil dry weight.

Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be 250 mg test item/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was determined to be 500 mg test item/kg soil dry weight.

8.9 Effects on earthworms

8.9.1 Acute toxicity to earthworms

For the first EU review, the acute toxicity of the technical substance AC900001 (picolinafen), metabolite CL 153815 and a formulation of AC 900001 in a 750 g/kg water dispersible granulate formulation (75WG) to earthworms was tested in the laboratory according to OECD-Guideline No.: 207. The results are presented in the DAR (September 2000) and reported below.

Table 8.9-1 shows that the LC_{50} of the technical substance was > 1000 mg a.s./kg. The LC_{50} of the formulation was > 1000 mg/kg and the LC_{50} of the metabolite CL 153815 was > 476.5 mg/kg.

Table 8.9-1: Acute toxicity of the technical substance AC 900001, the metabolite CL 153815 and a formulation of AC 900001 (75 WG) to *Eisenia fetida* in the laboratory

Test substance	Species	LC_{50} (mg/kg)	NOEC (mg/kg)	LOEC (mg/kg)	Reference
Technical substance AC900001	*Eisenia fetida*	>1000	111	>333	Nienstedt, K. M.; Reder, E. and S. P. Strnad (1999) [ARW 2000-24]
Metabolite CL 153815	*Eisenia fetida*	476.5	125	250	Gossmann, A. and J. Wisk (1999) [ARW 2000-23]
AC 900001 75 WG formulation	*Eisenia fetida*	>1000	333	1000	Nienstedt, K. M. et al. (1999) [ARW 2000-26]

8.9.2 Sublethal effects on earthworms

The reproduction study with picolinafen was repeated because in the original study the CV in control reproduction was > 30%. It is therefore considered necessary to repeat the study to robustly support the long-term risk assessment for earthworms.

Report:	II A 8.9.2/1 Luehrs U. 2011(c) Effects of BAS 700 H on reproduction and growth of earthworms Eisenia fetida in artificial soil with 5% peat BASF DocID 2010/1159925
Guidelines:	OECD 222 (2004); ISO 11268-2 (1998)
Deviations:	none
GLP:	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

The effects of BAS 700 H on mortality, biomass development and reproduction of the earthworm *Eisenia fetida* (Annelida: Oligochaeta) were investigated in a laboratory study over 56 days. Five concentrations 0.54, 0.67, 0.84, 1.68 and 3.35 mg BAS 700 H/kg soil dry weight were incorporated into the soil (5% peat only) with four replicates per treatment (each containing 10 worms). An untreated control with 8 replicates was included. The reference item was tested in a separate study.

Assessment of worm mortality, body weight and feeding activity was carried out after 28 days. Assessment of reproduction (number of juveniles) was carried out after 56 days.

BAS 700 H did not show any statistically significant effects on mortality and body weight. No mortality was observed at any test item concentration or in the control. The body weight changes were not significantly different compared to the control in any test item treated group (Dunnett's t-test, $\alpha = 0.05$, two-sided).

The reproduction rates were not statistically different compared to those in the control up to and including the highest concentration of 3.35 mg BAS 700 H/kg soil dry weight. No behavioural abnormalities were observed in any of the treatment groups. The feeding activity in all the treated groups was comparable to the control.

In a 56-day earthworm reproduction study with BAS 700 H, no adverse effects on survival and biomass development could be determined at concentrations up to and including 3.35 mg/kg soil dry weight. The NOEC for mortality, biomass, reproduction and feeding activity was equivalent to 3.35 mg/kg soil dry weight, the highest concentration tested.

I. MATERIAL AND METHODS

1. Test Material: BAS 700 H
Description: Cream solid (Purity: 97.8%)
Lot Batch #: CA 14113
Stability of test compound: Sufficient for purposes of study

2. Vehicle and/ or positive control: Deionised water; Luxan Carbendazim FC (500 g/L carbendazim)

3. Test animals:
Species: *Eisenia fetida* (with clitellum and weight range 300 to 600 mg; approximately 12 months old)
Source: In-house culture
Food: Finely ground cattle manure (10%)
Environmental conditions –
Temperature: 18 – 22°C
WHC: Start: 19.7% to 22.0% (49.3% to 55.0% of maximum water holding capacity (WHC))
Finish: 23.7% to 25.0% (59.3% to 62.5% of the maximum WHC)
pH Start: 6.3 – 6.4
End: 6.4 – 6.5
Photoperiod: 16:8 L:D (Light intensity: 400 – 800 lux)

In-life dates: 14 December 2010 – 11 January 2011

Experimental treatments: The 56-day test was conducted in treated artificial soil prepared according to OECD 222 (5% peat only). The test units consisted of plastic boxes (18.3 cm 13.6 cm x 6 cm; with a soil surface of approx. 189.75 cm^2 (16.5 cm x 11.5 cm) with perforated lids to enable air exchange. Each container was filled with 615.1 g of prepared soil (500 g dry weight plus 110.1 g water plus 5 g food).

Different concentrations of the test item were incorporated into the soil; 6 treatment groups (5 test item concentrations (0.54, 0.67, 0.84, 1.68 and 3.35 mg BAS 700 H/kg soil dry weight), control); 4 replicates for the test item treatments and 8 replicates for the control with 10 worms each.

Observations:	Assessment of adult worm mortality, behavioural effects (feeding) and biomass development was carried out after 28 days exposure of adult worms in treated artificial soil. Reproduction rate (number of offspring) was assessed after additional 28 days (assessed 56 days after application).
Statistics:	Dunnett's t-test (weight changes and reproduction) was performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH.

II. RESULTS AND DISCUSSION

All study validity criteria were met. No mortality was observed in any treatment group.

The body weight change of the earthworms after 4 weeks exposure to BAS 700 H was not statistically significantly different compared to the control up to and including the highest test concentration of 3.35 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$).

The reproduction rates were not significantly different compared to the control up to and including the highest test concentration of 3.35 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$). No behavioural abnormalities were observed in any of the treatment groups. The feeding activity in all the treated groups was comparable to the control (see Table 8.9.2-1).

Table 8.9.2-1: Effect of BAS 700 H on earthworm (*Eisenia fetida*) in a 56-day reproduction study.

BAS 700 H [mg/kg soil dry weight]	**Control**	**0.54**	**0.67**	**0.84**	**1.68**	**3.35**
Mortality (day 28) [%]	0.0	0.0	0.0	0.0	0.0	0.0
Significance	--	-	-	-	-	-
Weight change (day 28) [%]	23.1	29.7	26.4	24.2	25.8	30.6
Significance [1)]	--	n.s.	n.s.	n.s.	n.s.	n.s.
No. of juveniles (day 56)	292	308	310	363	285	358
Significance[1)]	--	n.s.	n.s.	n.s.	n.s.	n.s.
Reproduction in [%] of control (day 56)	--	105.3	106.3	124.1	97.4	122.4
Food consumption [g]	25.0	25.0	25.0	25.0	25.0	25.0
Endpoints [mg/kg soil dry weight]						
NOEC (day 28 mortality and weight)	3.35					
NOEC (day 56 reproduction)	3.35					

- = not relevant -- = not applicable
n.s. = not significantly different compared to the control
[1)] Dunnett´s t-test, $\alpha = 0.05$, two-sided for weight changes and one-sided smaller for reproduction

III. CONCLUSION

In an earthworm reproduction and growth study with BAS 700 H the No Observed Effect Concentration (NOEC) for mortality, growth, reproduction and feeding activity of the earthworm *Eisenia fetida* was determined to be 3.35 mg test item/kg soil dry weight, *i.e.* the highest concentration tested.

In the original submission, CL 153815 (Reg. No.: 4037090) was shown to be more acutely toxic than the parent. Therefore, it was considered necessary to conduct a chronic earthworm study with CL 153815.

Report:	II A 8.9.2/2 Luehrs U. 2011(d) Effects of Reg.No. 4037090 on reproduction and growth of earthworms Eisenia fetida in artificial soil with 5% peat BASF DocID 2010/1159922
Guidelines:	OECD 222 (2004); ISO 11268-2 (1998)
Deviations:	none
GLP:	Yes (laboratory certified by Hessisches Ministerium fuer Umwelt, Energie, Landwirtschaft und Verbraucherschutz, Wiesbaden)

Executive Summary

The effects of Reg. No.: 4037090 on mortality, biomass development and reproduction of the earthworm *Eisenia fetida* (Annelida: Oligochaeta) were investigated in a laboratory study over 56 days. Five concentrations (0.25, 0.5, 1.0, 2.0 and 4.0 mg Reg. No.: 4037090/kg soil dry weight) were incorporated into the soil (5% peat only) with four replicates per treatment (each containing 10 worms). An untreated control with 8 replicates was included. The reference item was tested in a separate study.

Assessment of worm mortality, body weight and feeding activity was carried out after 28 days and assessment of reproduction (number of juveniles) was carried out after 56 days.

Reg. No.: 4037090 did not show any statistically significant effects on mortality and body weight. No mortality was observed at any test item concentration or in the control. The body weight changes were not significantly different compared to the control in any test item treated group (Dunnett's t-test, $\alpha = 0.05$, two-sided).

The reproduction rates were not statistically different compared to those in the control up to and including the highest concentration of 4.0 mg Reg. No.: 4037090/kg soil dry weight. No behavioural abnormalities were observed in any of the treatment groups. The feeding activity was comparable to the control up to and including the concentration of 2.0 mg test item/kg soil dry weight and appeared slightly reduced (<10%) at 4.0 mg test item/kg soil dry weight.

In a 56-day earthworm reproduction study with Reg. No.: 4037090, no adverse effects on survival and biomass development could be determined at concentrations up to and including 4.0 mg/kg soil dry weight. The NOEC for mortality, biomass and reproduction was equivalent to 4.0 mg/kg soil dry weight, the highest concentration tested.

I. MATERIAL AND METHODS

1. **Test Material:** Reg. No.: 4037090
   Description: Faint beige solid (Purity: 100.0%)
   Lot Batch #: CA 16282
   Stability of test compound: Sufficient for purposes of study

2. **Vehicle and/ or positive control:** Deionised water; Luxan Carbendazim FC (500 g/L carbendazim)

3. **Test animals:**
   Species: *Eisenia fetida* (with clitellum and weight range 300 to 600 mg; approximately 12 months old)
   Source: In-house culture
   Food: Finely ground cattle manure (10%)
   Environmental conditions –
   Temperature: 18 – 22°C
   WHC: Start: 19.7% to 20.8% (48.5% to 52.0% of maximum water holding capacity (WHC))
   Finish: 21.6% to 24.9% (54.1% to 62.3% of the maximum WHC)
   pH Start: 6.3 – 6.4
   End: 6.4 – 6.5
   Photoperiod: 16:8 L:D (Light intensity: 400 – 800 lux)

   In-life dates: 14 December 2010 – 11 January 2011

   Experimental treatments: The 56-day test was conducted in treated artificial soil prepared according to OECD 222 (5% peat only). The test units consisted of plastic boxes (18.3 cm 13.6 cm x 6 cm; with a soil surface of approx. 189.75 cm^2 (16.5 cm x 11.5 cm) with perforated lids to enable air exchange. Each container was filled with 615.1 g of prepared soil (500 g dry weight plus 110.1 g water plus 5 g food).

   Different concentrations of the test item were incorporated into the soil; 6 treatment groups (5 test item concentrations (0.25, 0.5, 1.0, 2.0 and 4.0 mg Reg. No.: 4037090/kg soil dry weight), control); 4 replicates for the test item treatments and 8 replicates for the control with 10 worms each.

Observations:	Assessment of adult worm mortality, behavioural effects (feeding) and biomass development was carried out after 28 days exposure of adult worms in treated artificial soil. Reproduction rate (number of offspring) was assessed after additional 28 days (assessed 56 days after application).
Statistics:	Dunnett's t-test (weight changes and reproduction) was performed with ToxRat Professional (Version 2.10.05, ToxRat® Solutions GmbH.

II. RESULTS AND DISCUSSION

The body weight change of the earthworms after 4 weeks exposure to Reg. No.: 4037090 was not statistically significantly different compared to the control up to and including the highest test concentration of 4.0 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$).

The reproduction rates were not significantly different compared to the control up to and including the highest test concentration of 4.0 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$). No behavioural abnormalities were observed in any of the treatment groups. The feeding activity was comparable to the control up to and including the concentration of 2.0 mg test item/kg soil dry weight and appeared slightly reduced at 4.0 mg test item/kg soil dry weight (see Table 8.9.2-2).

Table 8.9.2-2: Effect of Reg. No.: 4037090 on earthworm (*Eisenia fetida*) in a 56-day reproduction study.

Reg. No.: 4037090 [mg/kg soil dry weight]	**Control**	**0.25**	**0.5**	**1.0**	**2.0**	**4.0**
Mortality (day 28) [%]	0.0	0.0	0.0	0.0	0.0	0.0
Significance	-	-	-	-	-	-
Weight change (day 28) [%]	41.6	39.3	40.3	37.5	36.8	39.9
Significance [1)]	-	n.s.	n.s.	n.s.	n.s.	n.s.
No. of juveniles (day 56)	283	295	291	287	263	286
Significance[1)]	-	n.s.	n.s.	n.s.	n.s.	n.s.
Reproduction in [%] of control (day 56)	-	104.2	102.8	101.3	93.0	101.0
Food consumption [g]	25.0	25.0	24.0	24.0	24.0	23.5
Endpoints [mg/kg soil dry weight]						
NOEC (day 28 mortality and weight)	4.0					
NOEC (day 56 reproduction)	4.0					

- = not applicable
n.s. = not significantly different compared to the control
[1)] Dunnett´s t-test, $\alpha = 0.05$, two-sided for weight changes and one-sided smaller for reproduction

III. CONCLUSION

In an earthworm reproduction and growth study with Reg. No.: 4037090, the No Observed Effect Concentration (NOEC) for mortality, growth, reproduction and feeding activity of the earthworm *Eisenia fetida* was determined to be 4.0 mg test item/kg soil dry weight, *i.e.* the highest concentration tested.

8.10 Effects on soil microbial activity

The DAR (September 2000) summarised laboratory tests that were performed to examine the effects of picolinafen on microbial activities in soil. The tests were carried out with the active ingredient, a WG formulation containing 75 % picolinafen and with CL 153815 (a metabolite of picolinafen). The test with CL 153815 was conducted according to BBA-guideline 1-1, part VI, March 1990 and the tests with the active ingredient and the WG formulation were conducted according to BBA-guideline and to SETAC-guideline. The respective summaries from the DAR are reproduced below.

8.10.1 Nitrogen transformation

The effects on nitrogen mineralisation were tested with all substances in two different soils and the results summarised in the tables below.

Table 8.10.1-1: Effects of picolinafen on nitrogen conversion

Type of soil	Application rate (g a.s./ha)	Comparison with untreated (%)	Test duration (days)	influence tolerable (Y/N)	Ref.
Loamy sand	97.5	103.6	28	Y	van der Kolk, J. (1999) [BMF 1999-34]
	97.5	102.6	42	Y	
	502.5	129.2	28	N	
	502.5	107.7	42	Y	
Sandy loam	97.5	88.3	28	Y	
	502.5	95.3	28	Y	

Table 8.10.1-2: Effects of WG formulation (75 % picolinafen) on nitrogen conversion

Type of soil	Application rate (g product/ha) [g a.s./ha]	Comparison with untreated (%)	Test duration (days)	influence tolerable (Y/N)	Ref.
loamy sand	130 (97.5)	91.6	28	Y	van der Kolk, J. (1999) [BMF 1999-35]
	670 (502.5)	93.9	28	Y	
sandy loam	130 (97.5)	105.7	28	Y	
	670 (502.5)	110.5	28	Y	

Table 8.10.1-3: Effects of CL 153815 (a metabolite of picolinafen) on nitrogen conversion

Type of soil	Application rate (g a.s./ha)	Comparison with untreated (%)	Test duration (days)	influence tolerable (Y/N)	Ref.
Loamy sand	42	122.2	28	Y	Keirs, D.C. (1998) [BMF 1999-33]
	42	98.0	60	Y	
	221	114.4	28	Y	
	221	102.7	60	Y	
Clay silt	42	120.3	28	Y	
	42	105.3	60	Y	
	221	122.6	28	Y	
	221	106.9	60	Y	

8.10.2 Carbon mineralization

The effects on short-term respiration were tested with all substances in two different soils and the results summarised in the tables below.

Table 8.10.2-1: Effects of picolinafen on carbon conversion

Type of soil	Application rate (g a.s./ha)	Comparison with untreated (%)	Test duration (days)	influence tolerable (Y/N)	Ref.
Loamy sand	97.5	101.9	28	Y	van der Kolk, J. (1999) [BMF 1999-34]
	502.5	98.4	28	Y	
Sandy loam	97.5	106.1	28	Y	
	502.5	97.6	28	Y	

Table 8.10.2-2: Effects of WG formulation (75% picolinafen) on carbon conversion

Type of soil	Application rate (g product/ha) [g a.s./ha]	Comparison with untreated (%)	Test duration (days)	influence tolerable (Y/N)	Ref.
loamy sand	130 (97.5)	99.1	28	Y	van der Kolk, J. (1999) [BMF 1999-35]
	670 (502.5)	99.5	28	Y	
sandy loam	130 (97.5)	97.0	28	Y	
	670 (502.5)	105.2	28	Y	

Table 8.10.2-3: Effects of metabolite CL 153815 on carbon conversion

Type of soil	Application rate (g a.s./ha)	Comparison with untreated (%)	Test duration (days)	influence tolerable (Y/N)	Ref.
Loamy sand	42	95.0	28	Y	Keirs, D.C. (1998) [BMF 1999-33]
	221	95.6	28	Y	
Clay silt	42	103.3	28	Y	
	221	97.6	28	Y	

8.10.3 Rates of recovery following treatment

No data submitted.
The available data shows picolinafen to have no effect on microbial processes at the levels tested. Therefore, no further studies are required.

8.11 Effects on marine and estuarine organisms

8.11.1 Marine or estuarine organisms acute toxicity LC50/EC50

No data submitted. Toxicity data on marine or estuarine organisms is not relevant to the proposed uses of picolinafen.

8.11.2 Marine/Estuarine fish - salinity challenge

No data submitted. Toxicity data on marine or estuarine organisms is not relevant to the proposed uses of picolinafen.

8.12 Effects on terrestrial vascular plants

According to Addendum 1 to the DAR (August 2001) and the Review Report (SANCO /1418/2001-final 18 September 2002) the most sensitive species tested in seedling emergence and vegetative vigour studies were *Beta vulgaris* and *Brassica vulgaris* with ED_{50} values between 5 – 10 g a.s./ha.

8.13 Effects on terrestrial. vertebrates other than birds / wild mammal toxicity

This is not a data requirement under Directive 91/41/EEC / Reg. (EC) No. 1107/2009.

8.14 Effects on other non-target organisms believed to be at risk

No additional data are available. The information provided in the preceding annex points is considered sufficient to assess the potential toxicity of picolinafen to non-target organisms.

8.14.1 Summary of preliminary data: biological activity & dose range finding

Please refer to chapter 8.14 above.

8.14.2 Assessment of relevance to potential impact on non-target species

Please refer to chapter 8.14 above.

8.15 Effects on biological methods for sewage treatment

Please refer to the DAR dated September 2000, Point B.9.10 for further details.
Exposure of sewage treatment plants was not considered relevant.

8.16 Other/special studies

8.16.1 Other/special studies - laboratory studies

No data submitted. Not considered necessary.

8.16.2 Other/special studies - field studies

No data submitted. Not considered necessary.

8.17 Summary and evaluation of points IIA 7 and IIA 8.1 to 8.16

Environmental fate

Route and rate of degradation in soil:

The DAR (September 2000) concluded that the degradation of picolinafen in soil under aerobic conditions occurs by cleavage of the amide bond to form the degradates CL 153815, 6-(3-trifluoromethylphenoxy)-2-pyridine carboxylic acid (max 44%) and CL 7693, 4- fluoroaniline (detected only in the NaOH harsh extractions). These compounds are incorporated into the soil matrix where they are further metabolized under aerobic conditions. Mineralisation was significant from the aniline and pyridine label, with 16 – 50% AR identified as CO_2 after 122 to 152 days of incubation in the aerobic degradation studies. Between 20 and 61 % AR was found as bound residues after 122 – 152 days. In the soil degradation and metabolism study (Steinführer, 1998a); AIIA-7.1.1.1.1/01), non-identified radioactivity reached a maximum of 5.6% at two consecutive timepoints. However, this was due to TLC origin radioactivity bound to the extractable organic matter as well as integrated background non resolved radioactivity. The background non resolved radioactivity was due to the high binding of picolinafen and its metabolites to the extractable soil organic matter. However, no single fraction exceeded 5% AR. In the soil degradation study (Steinführer, 1997) the non identified unknown radioactivity amounted to a maximum of 17% AR. However, this was only due to the integrated background non resolved radioactivity.

According to the DAR (September 2000) in the soil degradation (Steinführer (1998b)) performed at low temperature (8 ºC) picolinafen was degraded to only CL 153815 as a metabolite. The differences between the amounts of extractable radioactivity (% AR) and the sum of picolinafen and CL 153815 (% TAR) was 8 % AR on day 0 and increased to amounts of 19 % AR on day 100. Similarly, in the studies performed at 20 ºC, unknown radioactivity was only due to the non-resolved background radioactivity. The amounts of $^{14}CO_2$ increased to 9.6 % on day 100 and to 12.7 % AR on day 160. dThe non-extractable residues increased to 32.8 % AR after 160 days of incubation.

The new aerobic route and rate of degradation study in three soils using the fluoro-phenoxy-ring labelled picolinafen confirms the results of the previously evaluated studies, with picolinafen rapidly degrading to CL 153815 (maximum 66.4%). No other fraction exceeded 5% AR. The non-extractable radioactivity and $^{14}CO_2$ reached the maximum of 42.0 – 45.3% and 40.7 – 50%, respectively, within the 89 days of incubation. The proposed route of degradation is summarised in Figure 7.1/1 (see Section MIIA 7.1.1).

Soil photolysis of picolinafen is not considered to be a significant route of degradation in the environment. The extractable minor photodegradates were composed of several products; none exceeded 5 % AR.

Under anaerobic incubation conditions in soil, the rate of degradation of picolinafen (pyridine and aniline label) was not affected and the pattern of degradates remained identical to that under aerobic conditions. The amount of CL 153815 (including its methyl ester CL 197393) increased continuously to a maximum of 87.5% AR after two months and remained at that level until the end of the test period after four months. The methyl ester CL 197393 is expected to degrade rapidly to the acid CL 153815 under aerobic conditions. CL 7693 (4-fluoroaniline) was formed at maximum of 7.6% AR. However, due to its volatility and the low observed recovery, CL 7693 might have been formed at up to 29% AR based on the lowest recovery of 71% AR. CL 7693 will however be rapidly degraded under aerobic conditions. Mineralisation was low and amounted to maximum 0.4% (pyridine label) and 5.1% (aniline label) within 120 days. The amount of non-extractable residues was lower, when compared to the aerobic degradation, i.e. maximum of 2.6% for the pyridine label and 46.1% for the aniline label.

In the DAR (September 2000) for picolinafen, reported laboratory DT_{50}s were 46 - 51 days (n = 4, SFO) and laboratory DT_{50}s for CL 153815 were 30 – 77 days (n = 4).

DT_{50}s have been re-calculated for the studies presented in the DAR according to the recommendations of the FOCUS kinetics workgroup (FOCUS 2006) and ranged from 3.2 to 16 days for picolinafen and from 15.3 to 104.6 for CL 153815 metabolite. The new study performed with the fluoro-phenoxy label confirmed the rapid degradation of picolinafen with DT_{50}s ranging from 2.2 to 2.6 days. CL 153815 was degraded with DT50 values ranging from 19.3 to 34.6 days. The obtained persistence DT_{50}s as well as the modelling normalised values to pF 2 and 20 ºC are summarised in Tables 7/1 to 7/3 in MIIA 7.3.3.

Eight field dissipation studies are available (see DAR, September 2000) and in the first review calculated field DT_{50}s were 9 to 64 days for picolinafen and 19 to 107 days for the metabolite CL 153815. DT_{50}s from these field studies have been recalculated according the recommendations of FOCUS (2006). The visual fit of the SFO model to the decline of picolinafen and its metabolite was adequate and the statistical fit was acceptable. The DT_{50}s for picolinafen were 4.5 to 64.5 days and the DT_{50}s for CL 153815 were 32.6 to 104.7 days.

<u>Mobility in soil:</u>

Picolinafen is immobile in soil based on its very high Koc value (15000 – 31800 mL/g) as well as the column and aged leaching studies in various soils summarised in the DAR (September 2000).

Picolinafen major soil metabolite, CL 153815 is classified as having medium to low mobility according to the McCall scale with a Koc value of 160 – 783 mL/g and was not detected in the leachates of the column and aged leaching studies. CL 7693 was not detected in any soil metabolism study under aerobic conditions (field or laboratory studies). Its detections at very low levels following very harsh extractions showed that it will be immobile in soil.

Route and rate of degradation in aquatic systems:

Picolinafen is stable to hydrolysis and aqueous photolysis. Picolinafen is not readily or inherently biodegradable.

In sediment/water systems picolinafen was rapidly partitioned into the sediment, where it was degraded to CL 153815. Picolinafen represented less than 2% AR after 100 days of incubation. The non-extractable residue was shown to be mainly due to bound CL 153815. With harsh extractions (including basic NaOH) CL 153815 represented over 92% AR in the whole system. Mineralisation was not significant and did not exceed 2.5% AR. DT_{50}s for picolinafen, calculated according to FOCUS (2006), were 5.3 to 5.4 days (mean 5.4 days) for the whole system and 1.9 to 4.0 days (mean 3.0 days) in water for picolinafen. For CL 153815 DT_{50}s were calculated to be 9.0 to 33.7 days (mean 21.4 days) for the whole system and 5.3 to 6.2 days (mean 5.8 days) in water.

Only pyrimidine labelled material was used in the sediment water study and the evaluation of this study in the DAR (September 2000) stated that no comment can be made regarding the aniline moiety of the active substance which will be released upon cleavage of the amide bond (CL7693). In the pyridine water sediment study, the analysed harsh extractions which released almost all bound radioactivity showed the presence of only CL 158315, representing over 92% in the whole systems at the end of the incubation (day 100). This was also confirmed in the samples treated with radioactive CL 153815. Therefore, picolinafen is expected to form CL 153815 and CL 7693 (4-fluoroaniline) in aquatic systems. Taking into account the results of studies investigating aerobic and anaerobic (flooded system) degradation of picolinafen in soil, it is anticipated that on formation 4-fluoroaniline (CL7693) will instantaneously degrade under aerobic conditions to form mainly carbon dioxide and bound residues. CL 7693 was detected only in the anaerobic study with amounts not exceeding 7.6% AR, but only by using very harsh acidic and basic extractions.

Considering the behaviour of CL 7693 in the soil studies, the case previously presented in the DAR should be sufficient and a new study with the aniline label will not give any new results. The metabolic pathway in aquatic systems is therefore similar to the metabolic pathway in soil.

Fate and behaviour in air:

The results from a study on volatilisation from soil and leaf surfaces have shown that picolinafen exhibits no significant volatilisation (i.e. < 10% from both matrices) over the 24-hour period of the laboratory experiment (DAR, September 2000).

These findings are in good agreement with its vapour pressure of 1.66×10^{-7} Pa at 20°C and its Henry's law constant of 1.6×10^{-3} Pa m^3 mol^{-1}. Volatility from soil and plants is therefore not expected to be a major entry route into air after application of picolinafen. Insignificant amounts of residues that might reach the air either via volatilisation or during the spraying are considered to have a short persistence in the atmosphere due to their degradation by OH-radicals (Atkinson method: DT_{50} = 1 day).

Ecotoxicology

Terrestrial vertebrates:

Two GLP studies using the Bobwhite quail and Mallard duck were reported in the DAR and, in the interests of animal welfare, no additional studies have been provided. The lowest acute oral LD_{50} value was >2250 mg/kg bw indicating picolinafen to be of low acute oral toxicity to birds.

Short-term dietary toxicity studies conducted in accordance with GLP were conducted with the Bobwhite Quail and Mallard duck and included in the DAR (2000). These studies resulted in LC_{50} values >5,314 ppm feed for both species tested, indicating picolinafen to be of low dietary toxicity to birds.

Two avian reproduction studies, conducted with the Bobwhite quail and Mallard duck were reported in the DAR (September 2000). The results of both studies were the same; the NOEC from these studies reported in the DAR was 864 ppm (equivalent to 86.1 mg/kg bw/day).

Picolinafen has a low acute oral toxicity in mammals (LD_{50}: > 5000 mg/kg bw). In addition, long-term toxicity was addressed by a two-generation study conducted with the rat (NOAEL = 4 mg/kg bw/d; revised NOAEL = 43.0 mg a.s./kg bw/d). No further vertebrate studies are required

Aquatic organisms:

The DAR (September, 2000) included acute fish toxicity studies conducted with *Oncorhynchus mykiss* and *Lepomis macrochirus* and a chronic (28 day exposure) fish toxicity study conducted with juvenile *O. mykiss*. In addition, a fish early life stage study conducted with *O. mykiss* was also performed and reported.

The toxicity of picolinafen to aquatic invertebrates was addressed in acute and chronic *Daphnia* toxicity studies reported in the DAR (September 2000).

Studies conducted with the algal species *Selenastrum capricornutum* and *Anabaena flos-aquae* were reported in the DAR (September 2000). An additional study on *Ankyra judayi* was reported in Addendum 1 (August 2001) to the DAR. The higher tier plant *Lemna gibba* was also tested. The available studies indicate the most sensitive aquatic species tested were algae (*A. judayi*) with an EC_{50} of 0.000025 mg a.s./L.

An additional higher tier study addressing recovery of algal was summarised in Addendum 1 to the DAR (2001) and this study has been supplemented with an additional higher tier study (see Annex Point AII 8.3.3). The NOEAEC for phytoplankton, periphyton and macrophytes was 0.0075 mg a.s./L.

Bees:

The DAR (September 2000) included the results of oral and contact bee toxicity tests conducted with technical material. From both exposure routes the 48 hour LD_{50} values were in excess of 200 µg/bee, indicating picolinafen to be non-toxic to bees. No further data are provided

Non-target arthropods:

In the DAR (September 2000), the acute toxicity of formulated picolinafen (750 g a.s./l WG) was tested against the two standard species (the phytoseiid mite *Typhlodromus pyri* and the braconid wasp *Aphidius rhopalosiphi*), the ground dwelling carabid beetle *Poecilus cupreus* and the lycosid spider *Pardosa* spp. based on IOBC Guidelines. The results indicate that picolinafen is of low toxicity to non-target arthropods

Earthworms:

The DAR (September 2000) included acute studies addressing the toxicity of picolinafen and the soil metabolite CL 153815 to the earthworm *Eisenia foetida*. The subsequent evaluation of the available data resulted in an acute (14d) LC_{50} for picolinafen to earthworms of > 1000 mg/kg dry soil. This indicates picolinafen to be of low acute toxicity to earthworms.

With respect to chronic toxicity, the supplementary dossier contains a reproduction study conducted to address concerns highlighted following evaluation of a study in the DAR (September 2000). No adverse effects on survival and biomass development were observed at concentrations up to and including 3.35 mg/kg soil

Soil micro-organisms:

It was concluded from the DAR (September 2000) that picolinafen at 97.5 – 502.5 g a.s./ha did not affect soil microbial activities determined as carbon (soil respiration) and nitrogen turnover. No additional data are considered necessary since these rates cover 1 x and 5x the proposed application rate of 100 g a.s./ha.

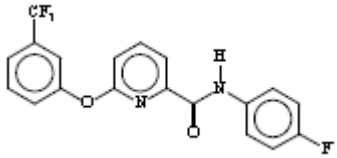
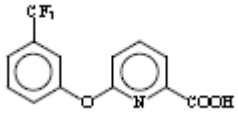
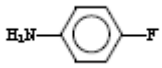
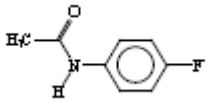
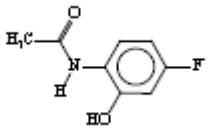
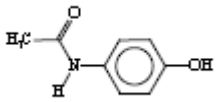
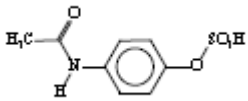
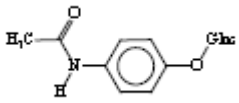
Non-target plants:

According to Addendum 1 to the DAR (August 2001) and the Review Report (SANCO /1418/2001-final 18 September 2002) the most sensitive species tested were *Beta vulgaris* and *Brassica vulgaris* with ED50 values between 5 – 10 g a.s./ha.

Biological methods for sewage treatment:

The DAR (September 2000) concluded that exposure of sewage plants to picolinafen was not considered relevant. It is reasonable to conclude therefore that picolinafen, as no exposure is anticipated, will not impair the function of waste-water treatment plants and no further data are necessary.

Appendix: Metabolites in wheat, lactating goat, soil and surface water

Code (CL Number)	Chemical Structure	Chemical Name	Matrices of Metabolism Studies
AC 900 001 (Picolinafen)		N-(4-fluorophenyl)-6-[3-(trifluoromethyl)phenoxy]-2- pyridinecarboxamide	Wheat plant and straw; goat fat, urine, faeces, soil, water
CL 153815 (Picolinic acid)		6-[(3-trifluoromethyl-phenoxy)picolinic acid	Wheat plant and straw; goat liver, kidney, milk, urine, faeces, soil, water
CL 7693		4-fluoroaniline	Intermediate
CL 44167		4-fluoroacetanilide	Goat fat, liver, kidney, milk, urine
CL 410142		4-fluoro-2-hydroxyacetanilide	Goat kidney, urine
CL 6497		4-hydroxyacetanilide	Goat liver, kidney, milk, urine
CL 1009639		4-acetamidophenyl sulfate	Intermediate in goat liver and kidney
CL 1009718		1-O-[4-acetamidophenyl)-ß- D-glucuronic acid	Goat liver, kidney, urine