European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance bispyribac (unless otherwise stated all data evaluated refer to the variant bispyribac-sodium)[1]

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SUMMARY

Bispyribac-sodium is a new active substance for which in accordance with Article 6(2) of Council Directive 91/414/EEC[3] Italy received an application from Bayer CropScience AG for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/305/EC[4].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State Italy made the report of its initial evaluation of the dossier on bispyribac-sodium, hereafter referred to as the draft assessment report (DAR), available on 1 August 2003.

The peer review was initiated on 14 October 2003 by dispatching the DAR (Italy, 2003) for consultation of the Member States and the applicant. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in September 2004. Remaining issues as well as further data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in June – July 2005.

A final discussion of the outcome of the consultation of experts took place in a written procedure with the Member States in February/March 2009 leading to the conclusions as laid down in this report.

This conclusion was reached on the basis of the evaluation of the representative use as a herbicide on rice. Full details of the GAP can be found in the list of end points. The representative formulated product for the evaluation was 'Nominee 400 SC', a suspension concentrate (SC). In the formulation the active substance is present as the sodium salt.

Adequate methods are available to monitor all compounds given in the respective residue definitions for plants, soil, ground water and air. With the inclusion of M01 and M02 and their salts in the residue definition for surface water some new data requirements have been identified.

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[1] On request from the European Commission. Question No. EFSA-Q-2009-00310, issued on 12 July 2010

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[3] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19

[4] OJ No L 112, 6.5.2003, p.10

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Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

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

With regard to its toxicological properties, bispyribac-sodium is almost completely absorbed from the gastro-intestinal tract, does not bioaccumulate in the organism and is mainly excreted as bispyribac-sodium. It is of low acute toxicity and presents skin sensitisation properties. The proposed classification is Xi, R43 "May cause sensitisation by skin contact". In repeated dose studies, the main target organ was the liver in all species, and the red blood cells in rats. No genotoxic potential was shown *in vitro* or *in vivo*, and no evidence of carcinogenicity was observed in long term studies. In the reproductive toxicity studies, the fertility parameters and the embryo-foetal development were not affected. Mechanistic studies have confirmed that bispyribac-sodium has an effect on the excretory biliary system at the high dose. Several metabolites were also tested and shown to be of low acute oral toxicity and without mutagenic properties. The agreed **Acceptable Daily Intake** (**ADI**) is **0.01 mg/kg bw/day** based on the 2-generation and 2-year rat studies. The agreed **Acceptable Operator Exposure Level** (**AOEL**) is **0.072 mg/kg bw/day** based on the subchronic rat study. An Acute Reference Dose (ARfD) was not considered necessary due to the lack of effects after acute exposure. In the absence of experimental data, the default value of 100% was agreed for the dermal absorption. The operator exposure estimates according to the German model are below the AOEL without the use of personal protective equipment.

The metabolism studies with bispyribac-sodium in dry-seeded and water-seeded rice demonstrated that the metabolic pathway was similar under the two cultivation conditions investigated. Bispyribac-sodium was incorporated to a large extent into plant components. Of the extractable residues, unchanged parent bispyribac-sodium was always the largest component and was thus defined as the relevant residue for risk assessment and MRL setting purposes. Metabolism studies and residue trials results indicate that under practical conditions, residues of bispyribac-sodium are not expected to exceed the LOQ of 0.02 mg/kg in rice grain. In a confined rotational crop study total residues in the rotated wheat, radish, soybean did not exceed 0.01 mg/kg and thus no significant residues are expected in crops planted in soil previously treated with bispyribac-sodium. No significant residues occur in commodities to be processed or used in livestock diet, and therefore no further investigation in processing studies and livestock studies was required to support the representative use in rice.

In a chronic consumer exposure risk assessment it could be demonstrated that the maximum estimated dietary intake of residues of bispyribac-sodium is well below (<1%) the toxicological reference value ADI. As no ARfD was allocated an acute risk assessment is not necessary.

The route and rate of degradation of bispyribac-sodium in drained and flooded paddy rice soils was investigated under aerobic and anaerobic conditions at 20°C. Bispyribac-sodium was low to moderately persistent in aerobic drained paddy soils and moderately persistent in aerobic flooded paddy soils. It degraded to form the major metabolite M06 (DesMe-2023) that was further degraded to M05 (Na-BX-180; major metabolite only under drained conditions). Metabolite M06 (DesMe-2023) was low to moderately persistent and metabolite M05 (Na-BX-180) was moderately persistent in aerobic paddy soils both under drained or flooded conditions. Under anaerobic conditions, bispyribac-sodium is moderately to highly persistent in anaerobic flooded paddy soils. Metabolite M06 (DesMe-2023) and an additional metabolite M04 (MeBA) were identified as major metabolites under anaerobic conditions.

During the peer review some concerns were expressed regarding the lack of information in the DAR on the multi-compartmental model assumed on the fitting of data to calculate kinetic parameters for metabolites. The RMS has made available to EFSA a new addendum in March 2008 (dated July 2007).

No soil photolysis study is available based on the use in paddy rice just before flooding.

Dissipation of bispyribac-sodium in soil was also investigated in four rice field sites replicating the proposed intended use. Bispyribac-sodium was low persistent in these field trials ($DissT_{50}$ = 2.1 – 9.1 d). Metabolites M03 (Me2BA: max. <1µg /kg soil; < 13.9 %), M05 (NaBX-180: max. 1.88 µg /Kg soil; 21.8 % parent equivalents).M06 (DesMe-2023: max. 5.44 µg /Kg ; 45.3 % parent equivalents) and M10 (Na-DesMe-180: max.0.3µg /L < 7.74 % parent equivalents) were found in these trials.

PEC soil of bispyribac-sodium and its major soil metabolites M06 (DesMe-2023) and M05 (Na-BX-180) were calculated with MED-Rice tools (European Commission, 2003).

According to the available studies, bispyribac-sodium and metabolite M05 (Na-BX-180) are expected to exhibit medium mobility in soil whereas metabolite M06 (DesMe-2023) may be considered highly mobile.

Bispyribac-sodium is slowly hydrolysed at pH 5 and may be considered stable at pH 7 and 9. Bispyribac-sodium was found to be stable to direct aqueous photolysis. Bispyribac-sodium is considered not to be readily biodegradable.

In water sediment systems, bispyribac-sodium was converted to a number of metabolites through demethylation and breakage of ether bridges ($DT_{50\ whole\ system}$ = 10.7 – 59.9 d). The only major metabolite found in the water phase of one of the systems was M06 (DesMe-2023). In the sediment layer M10 (Na-DesMe-180) occurred as a major metabolite in one of the systems. The MED-Rice scheme was used to calculate PEC_{SW} and PEC_{SED} for bispyribac-sodium and its metabolites. The aerobic flooded soil study and the aerobic water sediment study were used to calculate geometric mean $DissT_{50\ water}$ (16.2 d) and geometric mean $DT_{50\ whole\ system}$ (22.1 d) used in the calculations. The application rate was reduced assuming a DT_{50} = 8.7 d for the drained soil period. PEC_{SW} and PEC_{SED} for metabolites were calculated according to the MED-Rice scheme. DT_{50} from the whole aerobic flooded soil experiments were used for M05 (Na-BX-180; $DissT_{50}$ = 25.9 d) and M06 (DesMe-2023; $DissT_{50}$ = 28.3 d) were used to represent dissipation in both the sediment and the water phase. Maximum amounts of M05 (Na-BX-180; 21.8 % AR) and M06 (DesMe-2023; max. 45.3 % AR) observed in the field dissipation study were used to simulate a pseudo application of the metabolite.

Potential ground water contamination by bispyribac-sodium and its soil metabolites was assessed by calculating PEC_{GW} with the MED-Rice scheme.

Predicted environmental concentrations for the two rice scenarios were calculated to be < 0.001 µg / L for bispyribac-sodium and metabolite M05 (Na-BX-180) and 0.08 µg / L for M06 (DesMe-2023) in the sandy scenario. However, the presumed minor non transient metabolites M04 and M10 and major metabolite M03 in field studies need to be addressed for potential ground water contamination.

Due to the low potential of volatilization and the estimated rapid photochemical transformation, the environmental concentrations in air and the transport through air are considered negligible for bispyribac-sodium.

The first-tier TER values for insectivorous and herbivorous birds and mammals were above the Annex VI trigger values indicating a low risk. The risk from contaminated drinking water was considered low both for birds and mammals. Secondary poisoning was considered to be of no concern, given the hydrophilic properties of bispyribac-sodium.

Bispyribac-sodium is very toxic to aquatic organisms and should be classified as R50. Annex VI trigger values were met for all aquatic organisms in an “off-crop” risk assessment for both the active substance and all the metabolites, based on PEC_{pw} values derived in accordance with the MED-Rice guidance document. Following the MED-Rice guidance document the “in-crop” aquatic risk assessment focused on aquatic animals. Annex VI triggers were met for bispyribac-sodium and all metabolites, indicating a low risk to aquatic animals “in-field”. Bioconcentration was not considered an issue as bispyribac-sodium is hydrophilic.

The risk to bees and not-target arthropods and biological methods of sewage treatment was assessed as low. Additionally the risk to soil dwelling organisms, i.e. earthworms, *Folsomia* and micro-organisms was assessed as low, both for the active substance and the major soil metabolites MO6 (DesMe-2023)

and MO5 (Na-Bx-180). The tier 1 risk assessment to non-target plants indicated a need for risk mitigation, e.g. no-spray buffer zones of 30 m.

KEY WORDS

bispyribac, bispyribac-sodium peer review, risk assessment, pesticide, herbicide

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC[5] Italy received an application from Bayer CropScience AG for inclusion of the active substance bispyribac-sodium in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/305/EC[6].

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State Italy submitted the report of its initial evaluation of the dossier on bispyribac-sodium, hereafter referred to as the draft assessment report (DAR, Italy, 2003), to the ECCO team at the Federal Biological Research Center for Agriculture and Forestry (BBA) in Braunschweig on 1 August 2003. The DAR was distributed for consultation to the Member States and the applicant on 14 October 2003.

The comments received on the DAR were evaluated and addressed by the rapporteur Member State (RMS). Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 27 September 2004 on data requirements to be addressed by the applicant as well as issues for further detailed discussion at expert level. A representative of the applicant attended this meeting.

Taking into account the information received from the applicant addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team in June – July 2005. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure in February/March 2009 leading to the conclusions as laid down in this report.

During the peer review of the DAR and the consultation of technical experts no critical issues were identified for consultation of the Panel on Plant Protection Products and their Residues (PPR).

Following the agreement between the EU Commission and EFSA regarding the peer review of new active substances, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period. A list of the relevant end points for the active substance as well as the formulation is provided in appendix A.

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

the comments received,

the resulting reporting table rev. 1-1 of 15 October 2004

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

the reports of the scientific expert consultation,

the evaluation table (rev.2-1 of 27 March 2009)

Given the importance of the DAR including its addendum (compiled version of July 2009 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

[5] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19
[6] OJ No L 112, 6.5.2003, p.10

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Bispyribac-sodium is the ISO common name for sodium 2,6-bis(4,6-dimethoxypyrimidin-2-yloxy) benzoic acid (IUPAC). Due to the fact that the bispyribac-sodium, a variant of bispyribac, is used in the formulated product, it should be noted that the evaluated data belong to the variant bispyribac-sodium, unless otherwise specified.

Bispyribac-sodium, belongs to the class of pyrimidinyloxybenzoic acid herbicides. The only other compound in this class is pyriminobac. Its mode of action is by branched chain amino acid synthesis inhibition. It is a selective, systemic post-emergence herbicide, absorbed by foliage and roots.

The representative formulated product for the evaluation was 'Nominee 400 SC', a suspension concentrate (SC).

The evaluated representative uses were as a post-emergence herbicide on rice. Full details of the GAP can be found in the list of end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of bispyribac-sodium as manufactured should not be less than 930 g/kg. At the moment no FAO specification exists. The technical material contains no relevant impurities.

The content of bispyribac-sodium in the representative formulation is 408 g/L (pure). A question was raised during the peer review and the applicant confirmed that this is the correct value.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of bispyribac-sodium or the respective formulation.

The main data regarding the identity of bispyribac-sodium and its physical and chemical properties are given in appendix A.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Adequate analytical methods are available for the determination of bispyribac-sodium in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Therefore, sufficient data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, for food of plant origin (rice), soil, ground water and air. For surface water, as metabolites M01 and M02 and their salts have been included in the residue definition for surface water data requirements have been identified for methods of analysis for these compounds. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Rice, soil and water can be analysed for bispyribac and its salts by HPLC-MS/MS with an LOQ of 0.02 mg/kg (rice), 1 µg/kg (soil) and 0.05 µg/L (water). Air is analysed by HPLC-DAD with a LOQ of 0.003 mg/m^3.

An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2). A method for body fluids and tissues is not required as the active substance is not classified as toxic or highly toxic.

2. Mammalian toxicology

Bispyribac-sodium was discussed by the experts in mammalian toxicology in June 2005 (EPCO meeting 28).

EFSA notes after the expert meeting: The representativeness of the toxicological batches with regard to the technical specification has not been discussed during the EPCO expert meeting. In the DAR (Volume 4), no information was available on the identity of the impurities and their levels in the toxicological batches. Considering that the purity of the toxicological batches (up to 99%) was higher than the proposed technical specification (max 93%), a data requirement has been set for the assessment of the equivalence of the toxicological batches with the technical specification.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Rapidly and almost completely absorbed by the gastro-intestinal tract (based on an excretion >90% within 48h), bispyribac-sodium is widely distributed but does not bioaccumulate in the organism. The proposed metabolic pathway includes demethylation, hydroxylation, hydrolysis and conjugation reactions. The major route of elimination is the faeces (63-81%, primarily biliary excretion) followed by the urine (11-28%). The main compound excreted is the unchanged bispyribac-sodium (60-85%) and the primary metabolite in all excreta was a salt of M01 (<10%).

2.2. Acute toxicity

Bispyribac-sodium showed low acute toxicity after oral, dermal or inhalative administration (oral LD_{50} >2000 mg/kg bw, dermal LD_{50} >2000 mg/kg bw, LC_{50} >4.48 mg/L air). It was not a skin irritant but was slightly irritating to the eyes (not sufficient to warrant classification). Positive results of skin sensitisation were observed in a Magnusson/Kligman test. Therefore, the proposed classification is **Xi, R43 May cause sensitisation by skin contact**.

2.3. Short term toxicity

In repeated oral administration in rats, mice and dogs (4-week and 90-day studies in the three species, 52-week study in the dog), the liver was the main target (with increased enzyme activities, increased organ weight, and proliferation of the bile duct or gall bladder mucosa). However, effects on the red blood cells were the most critical endpoints in rats.

The relevant NOAEL in rats was 7.2 mg/kg bw/day based on an increased transaminase activity in males and effects on the red blood cells in females. The relevant NOAEL in mice was 6.8 mg/kg bw/day based on epithelial hyperplasia of the gall-bladder mucosa. Based on the hyperplasia of intrahepatic bile ducts, the relevant NOAEL in dogs was 10 mg/kg bw/day (52-week study).

No systemic or local effect was observed in a 21-day dermal study in rats, giving a NOAEL of 1000 mg/kg bw/day.

2.4. Genotoxicity

Bispyribac-sodium was tested *in vitro* for the induction of gene mutations (reverse mutation in Ames test, forward mutations in V79 cells), of chromosomal aberrations in Chinese hamster ovary cells, and of DNA damage (UDS in rat hepatocytes). All *in vitro* results were negative. In the *in vivo* mouse micronucleus study, negative results were also obtained. It was concluded that bispyribac-sodium has no genotoxic potential.

2.5. Long term toxicity

Following chronic exposure to bispyribac-sodium, the liver was found to be the main target organ in both rodent species. In rats, increased liver weight, increased activity of transaminases and liver cell

hyperplasia were observed. Additionally, hyperplasia occurred in the intrahepatic bile ducts and in the common bile duct epithelium. In mice, centrolobular swelling of liver cells and sporadic appearance of multinuclear giant cells were found, with dilatation of the gall-bladder glands and eosinophilic changes in the epithelium. The relevant NOAELs were 1.1 mg/kg bw/day in the rat based on haematological changes, and 14.1 mg/kg bw/day in the mouse based on reduced body weight gain, reduced red blood cells parameters and dilated gall-bladder glands. No evidence of an oncogenic potential was observed.

2.6. Reproductive toxicity

In a rat 2-generation study, the reproductive parameters were not affected up to the highest dose tested, therefore the reproductive NOAEL was 500 mg/kg bw/day. Based on a reduced body weight at birth and body weight gain, the NOAEL for the offspring was 50 mg/kg bw/day. Finally the parental NOAEL was 1 mg/kg bw/day based on epithelial hyperplasia of the common bile duct.

In the rat teratogenicity study, the maternal NOAEL was 300 mg/kg bw/day based on ano-genital staining, whereas the developmental NOAEL was 1000 mg/kg bw/day (highest dose tested). In the rabbit teratogenicity study, the maternal effects were more marked with one death and reduced body weight gain at the high dose. Therefore the maternal NOAEL was 100 mg/kg bw/day and the developmental NOAEL was 300 mg/kg bw/day (highest dose tested). In both species, bispyribac-sodium was devoid of teratogenic properties.

2.7. Neurotoxicity

Specific neurotoxicity studies with bispyribac-sodium were not considered necessary based on the lack of evidence for neurotoxicity in the available studies and based on the chemical structure, which is different from the compounds known to induce delayed neuropathy.

2.8. Further studies

Mechanistic studies:

The effects of bispyribac-sodium on the excretory biliary system were confirmed in mechanistic studies with mice and rats, the rat being more susceptible. Strong increases in bile acid levels in the serum were found in rats, and morphological changes of the main bile duct were considered as an indication of an increased biliary secretion at high dose levels.

Metabolites

Several metabolites of bispyribac-sodium were tested for acute oral toxicity (in rats) and mutagenicity *in vitro* (Ames test): M03, M04, M08, M09, M02 and M06. All of them were shown to be of low acute toxicity (oral LD_{50} >4000 mg/kg bw) and without mutagenic properties in bacterial cells.

2.9. Medical data

No adverse effect has been observed in medical examinations of plant personnel, or in operators or workers during the experimental biological testing. No epidemiological studies for the general population are available, and no cases of human poisoning are known to the applicant.

Note: Due to the non-specific effect on bile acids, potentially associated with foetal effects in pregnant women, the experts agreed that the issue of monitoring the serum bile acid concentrations in female workers should be addressed at a Member State level.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

Based on the long term rat studies (2-year and 2-generation), and applying a safety factor of 100, the agreed **ADI is 0.01 mg/kg bw/day**.

Based on the sub-chronic feeding study in rats, and considering that no correction for oral absorption is needed, the agreed **AOEL is 0.072 mg/kg bw/day** with the use of a safety factor of 100.

Finally, taking into account the low acute toxicity of bispyribac-sodium, the setting of an **ARfD** was not considered necessary by the experts.

2.11. Dermal absorption

No dermal absorption studies were performed with bispyribac-sodium, and a default value of 100% was used for the calculations of exposure assessment.

2.12. Exposure to operators, workers and bystanders

The representative plant protection product 'Nominee 400 SC' is a soluble concentrate (SC) containing 408 g a.s./L for use in rice. The intended method of application is a single spray treatment by means of a tractor-mounted boom with hydraulic nozzles at a maximum application rate of 30.6 g a.s./ha in a minimum spray volume of 200 L water/ha.

Operator exposure

The operator exposure estimates give values below the AOEL without the use of personal protective equipment according to the German model (BBA, 1992), or with the use of gloves during mixing, loading and application according to the UK model (United Kingdom, MAFF, 1986/1992) (see recalculations provided in the addendum to Volume 3 from July 2007, p.83-84 of the final addendum (Italy 2009)).

Estimated exposure presented as % of AOEL (0.072 mg/kg bw/day), according to calculations with the German and UK POEM model is shown below. The default for body weight of the operator is 70 kg in the German model and 60 kg in the UK-POEM model.

Model	No PPE:	With PPE 1:	With PPE 2:
German	54	7	-
UK POEM	530	-	43

PPE (personal protective equipment) 1: gloves during mixing/loading (M/L), standard protective garment and sturdy footwear during M/L and application (A);

PPE 2: gloves during M/L and A.

Worker exposure

The proposed use of bispyribac-sodium involves a single application at an early growth stage. The only operation necessary in the period following treatment is re-flooding of paddies, which does not involve exposure of workers to residues.

Bystander exposure

The estimates of bystander exposure were calculated assuming spray drift as the most important source of exposure according to Ganzelmeier, 1995 (Italy 2007), and resulted in a worst case exposure level of 0.4% of the AOEL.

3. Residues

Bispyribac-sodium was discussed in the meeting of experts in residues (EPCO 29) in June 2005.

It is noted that the sodium salt, a variant of bispyribac, was used in the residue studies. Thus the evaluated data belong to the variant bispyribac-sodium and the reported residue levels are expressed as bispyribac-sodium, unless otherwise explicitly specified.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The behaviour and metabolism of bispyribac-sodium was investigated in dry-seeded and water-seeded rice using pyrimidine-[^{14}C]-labelled and benzene-[^{14}C]-labelled bispyribac-sodium applied at a rate that was only slightly exaggerated (1.3-1.9 N) compared to the representative GAP.

The studies demonstrated that the metabolic pathway of bispyribac in rice is similar under the different cultivation conditions investigated.

Metabolism in the plants was extensive, with a substantial part of the radioactivity recovered in the mature plant being incorporated into natural plant components such as starch, lignin, and cellulose. Residues in mature rice grain were always very low and no further analysis was conducted due to the low amount of radioactivity. Upon analysis of immature plants and/or straw and roots bispyribac-sodium was always the major component of the total residue, amounting to 77% TRR in the immature rice plant, to 8% TRR in straw and 3% TRR in the roots. Similar metabolites were identified in the examined materials, with M02 (BX-180) or its sodium salt M05 (Na-BX-180) being most prevalent in the mature crop (2-5%TRR in straw and roots). None of the identified and unidentified metabolites was present in significant amounts in the plants.

A metabolic pathway could be established for bispyribac-sodium in rice plants that involves hydroxylation of a pyrimidine ring at the 5 position (M11 or M08), or O-demethylation of a methoxy group on a pyrimidine ring (M01 or M06, M10, and M04) followed by glucoside conjugation at the demethylated position (M17) or hydrolytic cleavage of a pyrimidine ring from the benzyl moiety, yielding M02/M05, M03 and M04. All major metabolic steps observed in rice plants were common with those seen in the rodent metabolism studies.

Based on the studies conducted on rice under various cultivation conditions and with two different radiolabels it can be concluded that bispyribac-sodium was the major component of the residue. None of the metabolites are present in rice plants in significant amounts. In a confined rotational crop study (see 3.1.2 below) total residues in the rotated crops did not exceed 0.01 mg/kg. Therefore it was agreed in the meeting of experts that the residue definition in rice for risk assessment and monitoring purposes should be bispyribac and its salts expressed as bispyribac-sodium. The residue definition is only applicable to cereal crops.

To investigate the residue levels of bispyribac-sodium in treated rice, a total of eight residue trials were conducted in southern Europe with bispyribac-sodium formulated as 'Nomineé 400 SC'. The product was applied according to GAP criteria. The LOQs of the employed analytical methods were 0.02 mg/kg for all tested matrices (grain, straw, green forage). Grain and straw samples were taken at harvest at PHIs of 70 to 110 days. Residues of bispyribac expressed as bispyribac-sodium in grain and in straw at harvest were always below the LOQ of 0.02 mg/kg. The results are supported by valid freezer storage stability data in rice matrices and validated analytical methods.

As residue levels in rice grain were always below the LOQ of the analytical method no studies on the level and nature of residues in food of processed grain are required.

3.1.2. Succeeding and rotational crops

The residue behaviour of bispyribac-sodium in succeeding and rotational crops was investigated in a confined rotational crop study. Pyrimidine labelled bispyribac-sodium was applied at approximately 2.3 fold rate of the notified application rate. Model crops (wheat, radish and soybean) were planted 28-46 days and 120 days after treatment. The total radioactive residues in all crops and matrices sampled after the first planting were well below 0.01 mg/kg, ranging in the various matrices from 0.001-0.005 mg/kg. Due to the low residue levels, quantification of metabolites in the samples was not attempted, and the investigation of residues was not continued for crops with longer plant-back intervals of 120-days and 360 days. Based on the results of this study and particularly in consideration of the exaggerated application rate, no residues are expected in rotational crops in soil previously treated with bispyribac-sodium. Further studies, such as field rotational crop trials, are not necessary.

3.2. Nature and magnitude of residues in livestock

With regard to the representative use in rice no significant residues are expected to occur in livestock diet, and therefore the submission of livestock studies was not a requirement.

However studies on the metabolism of orally administered pyrimidine- or benzene-labelled bispyribac-sodium in lactating goats and in laying hens were submitted and summarised in the DAR for future reference.

3.3. Consumer risk assessment

The chronic dietary risk assessment for consumers is based on the proposed MRL of 0.02 mg/kg and on consumption data from the WHO/GEMS Food European diet and national consumption data from Germany and UK, respectively.

The TMDI from the consumption of rice grain for all considered consumer groups (adults, toddlers, and children) are all significantly below (< 1%) the allocated ADI of 0.01 mg/kg bw/day.

As no ARfD was allocated an acute risk assessment is not necessary.

3.4. Proposed MRLs

In supervised residue trials with bispyribac-sodium in rice residues were always below the LOQ of 0.02 mg/kg and thus the MRL proposed for rice grain is 0.02 mg/kg.

No MRLs are proposed for food of animal origin.

4. Environmental fate and behaviour

Bispyribac-sodium was discussed in the meeting of experts on fate and behaviour in the environment EPCO 26 (June 2005) on basis of the DAR (August 2003) and Addendum (May 2005) prepared by the RMS. An additional addendum has been provided to EFSA in March 2008 (dated July 2007). This latest addendum has not been peer reviewed. During the drafting of the conclusion the RMS provided an additional addendum in June 2009 (Italy, 2009) where the risk assessment for the metabolites was updated with the values obtained from the field studies. This addendum is also not peer reviewed but the results are considered to be in line with the peer reviewed data.

In this section parent bispyribac and its metabolites are reported as their sodium salts. However, it should be understood that in the environment a combination of salts and the acid form will coexist depending on the pH and the cat ions present in the particular media. Sodium salts are used therefore as representative of lead compounds of this family of substances. Since in other sections of the dossier and the DAR the acid forms are selected as lead compounds the equivalence is presented below for transparency:

M06 is the sodium salt of the acid M01

M05 is the sodium salt of the acid M02

M10 is the sodium salt of M09

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

Route of degradation of bispyribac-sodium (^{14}C labelled either at the bispyrimidine rings or at the phenyl ring) was investigated under aerobic dark conditions at 20 °C in two drained paddy soils (pH 8.4 – 8.5; OC 0.68 – 1.3 %; clay 8.7 % - 26.1 %; 49 % MWHC). After the initial demethylation of one of the pyrimidyl moieties to form the major metabolite **M06** (DesMe-2023; max 14.4 % AR after 3 d) the molecule was further degraded to **M05** (Na-BX-180; max 15 % AR after 15 – 119 d). Unextrated residues reached maximum amounts of 50 – 57 % AR for the bispyrimidine rings labelled and 62-66.3% AR for the phenyl-labelled material. Mineralization was higher for the bispyrimidine moieties (CO_2: 24.7 – 52.1 % AR) than for the phenyl labelled moiety (CO_2: 5.4 % – 29.4 % AR). Additionally, to assess the specific use in rice, route and rate of degradation was investigated in the same two soils in systems consisting of 100 g soil with a water layer of about 1.5-2.0 cm incubated in darkness at 20°C (stagnant systems simulating paddy conditions). Under these conditions bispyribac-sodium was translocated from water phase to soil. Metabolite M06 (DesMe-2023) was also found as a major metabolite in these experiments (max.: 10.4 – 22,6 % AR water layer; 6.0 – 9.1 % AR soil layer; 16.4 – 31.7 % AR entire system). M05 (Na-BX-180) was however a minor metabolite under these conditions (max. 6.5 % AR in the entire system). Unextracted residues amounted up to 62.6 – 87.3 % AR and mineralization was in the same range than under drained aerobic conditions (CO_2 max: 25.4 % – 48.7 % AR).

Degradation under dark anaerobic conditions at 20 °C was also investigated in the same two soils under flooded (stagnant) conditions. Under these conditions bispyribac-sodium was translocated from

water phase to soil. Metabolite MO6 (DesMe-2023) was also found as a major metabolite in these experiments (max.: 10.4 – 14.7 % AR water layer; 9.2 – 10.2 % AR soil layer; 19.6 – 24.9 % AR entire system). A major metabolite was identified under anaerobic conditions **M04** (MeBA: max. 15.8 % AR in the entire system). Unextracted residues amounted up to 25.7 – 78.3 % AR and mineralization was practically negligible (CO_2 max: 1.7 % AR).

No soil photolysis study is available and it is not required based on the use in paddy rice just before flooding.

Dissipation of bispyribac-sodium in soil was also investigated in four rice field sites (pH 7.5 – 7.7; OC 0.64 – 1.17 %; clay 13.5 – 38.6 %) replicating the proposed intended use. Bispyribac-sodium was applied at amounts of 25.2 g/ha (19.1 µg /L) on bare soils where rice had been planted and flooded six days after the application. At the end of the peer review, the RMS re-calculated the amounts of metabolites in relation to the applied bispyribac-sodium taking into consideration the LOD and LOQ of the analytical methods employed in the field studies. Metabolites M03 (Me2BA: max. <1µg /kg soil; < 13.9 % parent equivalents), M05 (NaBX-180: max. 1.88 µg /Kg soil; 21.8 % parent equivalents), M06 (DesMe-2023: max. 5.44 µg /Kg ; 45.3 % parent equivalents) M04 (<0.3 µg /kg soil; < 7.7 % parent equivalents) and M10 (Na-DesMe-180: max. 1µg /L; < 7.5 % parent equivalents) were found in these trials. Due to the analytical method quantification and detection limits metabolite M03 has to be considered a major metabolite in soil and metabolites M04 and M10 are presumed to be minor non-transient metabolite. Data requirements for these metabolites have therefore been identified during the finalisation of the EFSA conclusion.

The meeting of experts discussed the narrow range of pHs tested in the soil degradation studies. However, they agreed that for the assessment of the representative use proposed in rice no further data are needed taking into account that alkaline conditions could be considered conservative with respect to hydrolysis of bispyribac-sodium and that biological degradation was significantly faster than the hydrolysis rates.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

The rate of degradation in two soils under aerobic conditions was investigated in the same studies referred in the route section. Bispyribac-sodium is low to moderately persistent in aerobic drained paddy soils (DT_{50} = 6.0 – 19.6 d) and moderately persistent in aerobic flooded paddy soils (DT_{50} = 18.9 – 19.5 d). Degradation rates of the major aerobic metabolites were calculated on basis of the data obtained in the studies performed applying the parent compound. Metabolite M06 (DesMe-2023) was low to moderately persistent in aerobic drained paddy soils (DT_{50} = 1.9 – 15.4 d) and aerobic flooded paddy soils (DT_{50} = 7.4 – 13.5 d). Metabolite M05 (Na-BX-180) was moderately persistent in aerobic drained paddy soils (DT_{50} = 39.6 d) and aerobic flooded paddy soils (DT_{50} = 14.4 – 27.6 d).

The rate of degradation in two soils under anaerobic conditions was investigated in the same studies referred in the route section. Bispyribac-sodium is moderately to highly persistent in anaerobic flooded paddy soils (DT_{50} = 32.9 – 110 d). Degradation rates of the major anaerobic metabolites were calculated on the basis of the data obtained in the studies performed applying the parent compound. Metabolite M06 (DesMe-2023) was moderately persistent in anaerobic flooded paddy soils (DT_{50} = 33.8 d). It was not possible to determine degradation rate of metabolite M04 (MeBA) under anaerobic conditions, however, the applicant assumed that this metabolite would be rapidly degraded under aerobic conditions.

During the peer review some concerns were expressed with regard to the lack of information in the DAR on how the multi-compartmental model assumed on the fitting of data to calculate kinetic parameters for metabolites. No addendum was available for the discussions during the expert meetings (June 2005). The RMS has made available to EFSA a new addendum on March 2008 (dated July

2007). Further clarification of the model assumed in the fitting and the adjustments made in the raw data to consider the stoichiometry of the formation of the metabolites are provided in this addendum. Although not fully compliant with FOCUS kinetics recommendations, EFSA is of the opinion that the parameters derived from this modelling exercise could be used for environmental modelling needing kinetic degradation and formation input parameters. Based on the original study report EFSA has calculated formation fractions for the metabolites and reported them in the list of end points.

Bispyribac-sodium was low persistent in the field trials available ($DissT_{50}$ = 2.1 – 9.1 d).

PEC soil of bispyribac-sodium and its major soil metabolites M06 (DesMe-2023) and M05 (Na-BX-180) were calculated with MED-Rice tools (European commission, 2003). The geometric mean from the drained soil laboratory studies and the paddy field dissipation studies (DT_{50} = 8.7 d) was used in the PEC soil calculations for bispyribac-sodium in soil under drained conditions and the geometric mean of the flooded studies and the water sediment study (DT50 = 16.2 for the water phase and DT50 = 22.1 d for the sediment phase under flooded conditions. Arithmetic mean Kfoc = 302 mL/ g was used for the calculations. At the time of writing the conclusion it was noted that in the original assessment kinetically derived half lives for the metabolites had been matched with the maximum observed in laboratory studies. This was considered incorrect since the formation fractions should have been used for PEC calculations. Additionally, it was noted that for some metabolites the maximum observed in the field studies was higher than the maximum observed in the laboratory studies. The RMS presented a new assessment in March 2009 (Italy, 2009) based on the maximum percentile of metabolites observed in the field studies and the dissipation (or decline) half lives measured from the maximum observed (M05: $DissT_{50}$ = 25.9 d; M06 $DissT_{50}$ = 28.3). Whereas this final assessment is not peer reviewed, it was considered acceptable by EFSA taking into account that it is more in line with current guidance and results in a more conservative risk assessment.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Batch soil adsorption / desorption studies were performed with bispyribac-sodium in five soils (pH 5.4 – 7.0; OC 0.1 – 1.4 %; clay 4 – 28 %) and major soil metabolites M05 (Na-BX-180) and M06 (DesMe-2023) in three soils (pH 7.1 – 8.5; OC 0.68 – 1.9; clay 8.7 – 26.1 %). According to these studies bispyribac-sodium and metabolite M05 (Na-BX-180) may be considered to be medium mobile (bispyribac-sodium: K_{fOC} = 143 – 604 mL/g; MO5 (Na-BX-180): K_{fOC} = 131 – 601 mL/g) and metabolite M06 (DesMe-2023) high mobile (K_{foc} = 60 - 106 mL/g).

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

The hydrolysis of bispyribac-sodium (^{14}C-labelled at the pyrimidine ring) was investigated at 25 ºC in sterile aqueous buffer solutions (pH 5, 7 and 9). An additional experiment was run at 50 ºC (pH 5). Bispyribac-sodium may be considered stable at pH 7 and 9 and it is slowly hydrolysed at pH 5 ($DT_{50\ 20\ C}$ = 167 d). The major hydrolysis metabolites at pH 5 were M03 (Me2BA: max. 59.4 % AR at 50 ºC) and M02 (BX-180, acidic form of the salt M05 [Na-BX-18]; max 34.7 % AR at 50 ºC). Metabolite is M03 (Me2BA) is not further hydrolysed at 50 ºC and therefore may be considered stable under normal environmental conditions.

Photolysis of bispyribac-sodium (^{14}C-labelled at the pyrimidine ring) was investigated in buffered water (pH 7) at 25 ºC. Test samples were exposed to simulated sun light (filtered xenon lamp) for 30 d of continuous irradiation. Under these conditions bispyribac-sodium was found to be stable to direct aqueous photolysis.

No ready biodegradation study is available for bispyribac-sodium. Bispyribac-sodium is considered not to be readily biodegradable.

Fate and behaviour of bispyribac-sodium (^{14}C-labelled either at the pyrimidine or phenyl ring) in aquatic environment under dark aerobic conditions at 20 ºC was investigated in one study with two water sediment systems (pH_{water} = 8.5 – 8.7; pH_{sed} = 8.1 – 8.3, OC 0.63 – 4.2 %).

Bispyribac-sodium partitioned with the sediment and was converted to a number of metabolites through demethylation and breakage of ether bridges ($DissT_{50\ water}$ = 7.7 – 56.4; $DT_{50\ whole\ system}$ = 10.7 – 59.9 d). The only major metabolite found in the water phase of one of the systems was M06 (DesMe-2023: max. 22.6 % AR after 90 d). In the sediment layer M10 (Na-DesMe-180) occurred as a major metabolite in one of the systems (M10. max. 13.4 % after 90 d). Unextracted radioactivity was lower for residues deriving from the pyrimidine-labelled moiety (13.1 – 61.5 % AR) than the phenyl labelled one (18.5 – 78.8 % AR) were the higher values being observed in the sediment with higher organic carbon content. Conversely, mineralization was higher for residues deriving from the pyrimidine labelled moiety (25.7 – 26.6 % AR) than the phenyl labelled one (9.9 – 19.0 % AR).

The MED-Rice scheme (European Commission, 2003) was used to calculate PEC_{SW} and PEC_{SED} for bispyribac-sodium and its metabolites. Aerobic flooded soil study and the aerobic water sediment study were used to calculate the geometric mean $DissT_{50\ water}$ (16.2 d) and the geometric mean $DT_{50\ whole\ system}$ (22.1 d) used in the calculations. The application rate was reduced assuming a DT_{50} = 8.7 d for the drained soil period. Also PEC_{SW} and PEC_{SED} values for the metabolites were calculated according to the MED-Rice scheme. As indicated above the assessment of the metabolites has been updated in the Addendum submitted in March 2009 (Italy 2009). DT_{50} from the whole aerobic flooded soil experiments were used for M05 (Na-BX-180; $DissT_{50lab}$ = 25.9 d) and M06 (DesMe-2023; $DissT_{50lab}$ = 28.3 d) were used to represent dissipation in both the sediment and the water phase. Maximum amounts of M05 (Na-BX-180, 21.8 %) and M06 (DesMe-2023, max. 45.3 %) observed in the field dissipation study were used to simulate a pseudo application of the metabolite. Although this final assessment is not peer reviewed, it was considered acceptable by EFSA taking into account that it is more in line with current guidance and results in a more conservative risk assessment.

4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

The potential ground water contamination by bispyribac-sodium and its soil metabolites was assessed by calculating PEC_{GW} with the MED-Rice scheme. The geometric mean of the half lives corresponding to drained paddy field situations (drained laboratory study and drained field studies) was used as the input parameter for bispyribac-sodium under drained periods (DT_{50} = 8.7 d). For flooded periods, the geometric mean half-life of the aerobic flooded soil study and the aerobic water sediment study were used as input half-live for bispyribac-sodium ($DissT_{50\ water}$ = 16.2 d; $DT_{50\ whole\ system}$ = 22.1 d).

Predicted environmental concentrations for the two rice scenarios were calculated to be < 0.001 µg / L for bispyribac-sodium and metabolite M05 (Na-BX-180) and 0.0893 µg / L for M06 (DesMe-2023) in the sandy scenario. For these metabolites the assessment was updated in March 2009 as indicated above. Whereas this final assessment is not peer reviewed, it was considered acceptable by EFSA taking into account that it is more in line with current guidance and results in a more conservative risk assessment. However, the presumed minor non-transient metabolites M04 and M10 and major metabolite M03 in field studies has not been addressed for potential ground water contamination. The RMS submitted an addendum during the finalisation of the EFSA conclusion to address potential ground water contaminations by metabolites M04, M10 and M03. This addendum has also not been peer reviewed. For informative purposes, EFSA notes that in this paper tentative groundwater calculation are presented for M04, M10 and M03 based on a worst-case half-life of 1000 d and the QSAR estimated Koc's. Whereas the use of QSAR and worst-case estimations has been accepted previously for some minor non transient metabolites, it is considered not acceptable for major metabolites (such it could be the case of M03). Furthermore, in this particular case, due to the ionisable nature of all three compounds, QSAR estimates of Koc are expected to be subject to a high degree of uncertainty. It is reasonable to expect that actual Koc measured values would result in more

unfavourable values than those calculated with QSAR. Without precluding the need for a more detailed examination and peer review of this position paper, under this first examination, it does not seem to fully address the potential ground water contamination by metabolites M04, M10 and M03.

4.3. Fate and behaviour in air

Due to the low potential for volatilization and the estimated rapid photochemical transformation, the environmental concentrations in air and the transport through air are considered negligible for bispyribac-sodium.

5. Ecotoxicology

Bispyribac-sodium was discussed at the EPCO 27 Experts Meeting on ecotoxicology in June 2005, based on the DAR (Italy 2003) and the Addenda to the DAR (Italy, 2009).

The proposed GAP for bispyribac-sodium is as a spray application as a rice herbicide in temporary drained rice paddy fields once per season at a dose of 4-30 g a.s./ha post emergence growth stage BBCH 25 of rice. The lead formulation bispyribac-sodium 400 SC (referenced to as Nomineé 400 SC in the GAP table) contains 400 g a.s./L.

The nominal active substance content of NOMINEE SC 400 was corrected from 400 g/L to 408 g/L in the addendum from July, 2007 (not peer reviewed). This difference of 2% has to be taken in to account when the nominal content of the active substance serves as basis for the risk assessment. This corresponds to a maximum application rate of 30.6 g a.s./ha rather than the 30 g a.s./ha used in the risk assessment. The impact of the increased active substance content is assessed in the end of the relevant sub-sections of the ecotox section. The list of endpoints was updated to reflect the correct values.

In this sections parent bispyribac and its metabolites are generally reported as their sodium salts. One exception is however the toxicity endpoints for *Lemna gibba* and *Chironomus riparius* exposed to the metabolite M09 (DesMe-180), which is the acid form or the sodium salt M10 (Na-DesMe-180) (see also the introduction to section 4).

5.1. Risk to terrestrial vertebrates

The risk to birds and mammals was assessed in accordance with the Guidance Document on Risk Assessment for Birds and Mammals (European Commission 2002a). The risk to birds was assessed for large herbivorous birds and insectivorous birds. The TER values for herbivorous birds were above the Annex VI triggers (TER_a>1067, TER_{st}>2057, TER_{lt}=217) as was the TER values for insectivorous birds (TER_a>1233, TER_{st}>2273, TER_{lt}=128) indicating a low risk. Similary the risk to herbivorous mammals (TER_a=445, TER_{lt}=29.8) and insectivorous mammals (TER_a=10135, TER_{lt}=521) was considered low.

The risk from contaminated drinking water was considered low both for birds and mammals, based on initial paddy surface water concentrations (PEC_{pw}) from the worst case sandy scenario and acute toxicity data. Additionally, the risk from secondary poisoning was assessed as low, based on the hydrophilic properties of bispyribac-sodium (log P_{ow} = -1.03) as well as substantially low logP_{ow} for the metabolites.

None of the conclusions in the risk assessment for terrestrial vertebrates would be affected by an increase in exposure of 2% (see previous paragraph).

5.2. Risk to aquatic organisms

The lowest end point value for technical bispyribac-sodium was obtained for the duckweed *Lemna gibba,* with an E_rC_{50} of 0.013 mg a.s./L. Bispyribac-sodium should be classified as very toxic to the

aquatic environment. Studies conducted with the lead formulation gave similar results of 0.011 mg a.s./L based on increase in biomass of duckweed. The TER calculations provided in the DAR for adjacent water bodies were updated in an addendum before the expert meeting (Italy, 2009), to include PECsw values based in the MED-Rice guidance document (see section 4.2). Annex VI trigger values were met for all aquatic organisms including *Chironimus* and higher plants. The aquatic risk assessment was agreed during the expert meeting. However, it was noticed that TER values should be provided for both the growth and biomass endpoint for algae and duckweed. Updated TER calculations were provided in an addendum (Italy 2009) without affecting the conclusion of the aquatic risk assessment.

In the DAR four metabolites were considered in the water phase of the aquatic risk assessment. The two metabolites M06 (DesMe-2003) and M04 (MeBA) were detected respectively in the water phase of a water-sediment study and in the water phase of an anaerobic paddy soil study. The major metabolite in sediment and its salt, M09 (DesMe-180)/M10 (Na-DesMe-180 were included in the risk assessment in addition to the major soil metabolite M05 (Na-BX-180) Metabolite toxicity testing was restricted to the duckweed *Lemna gibba* as it was >100 times more sensitive to bispyribac-sodium than other aquatic organisms. As M09 (DesMe-180) and its salt M10 (Na-DesMe-180) were major metabolites in the sediment phase, toxicity was tested with the sediment dwelling organism *Chironimus reparius* exposed to M09 (DesMe-180) in a water spiked system. For the Tier 1 risk assessment a generic worst-case scenario was assumed by taking the initial PEC_{sw} and PEC_{sed} of the parent compound resulting from rice paddy field outflow (worst-case sandy scenario) as being representative for the initial PEC of each metabolite. TER values were grater than 10 for all the tested metabolites, indicating a low risk to aquatic organisms from the intended uses. Ideally the TER calculation for M09 (DesMe-180) should have been based on the equivalent concentrations of the salt, i.e. M10 (Na-DesMe-180), to be equivalent to the exposure concentration. This calculation was not provided in the DAR. EFSA consider this to be of less importance, given the large margin of safety for this metabolite, indicated by TER values exceeding the Annex trigger by several orders of magnitude. After the peer review the soil metabolite M03 (Me2BA) was considered to be a relevant metabolite (see section 4.1.1). The risk to aquatic organisms from M03 was not considered in the DAR and no data on the effects for aquatic organisms were available. EFSA however notes that the effect data for the additional metabolites (M04, M05, M06 and M09) indicated similar or less toxicity to *Lemna* compared to the toxicity of bispyribac-sodium. EFSA therefore considers it very unlikely that M03 would be more toxic to aquatic organisms than the active substance and the risk to M03 was considered to be addressed by the aquatic risk assessment of bispyribac-sodium.

According to the MED-Rice guidance document (European Commission, 2003) an in-field aquatic risk assessment is generally not appropriate as the rice paddy falls dry after a certain period of time. The guidance document suggests that Member States should perform specific in-field aquatic risk assessments. An in-field aquatic risk assessment for bispyribac-sodium focusing on aquatic animals was provided in the DAR. Effects on plants (algae and higher plants) were not considered as bispyribac-sodium is a herbicide. TER values were calculated with initial PEC_{pw}, based on the MED-Rice guidance document, and Annex VI triggers were met for all aquatic animals.

The same metabolites were considered to be relevant in paddy water ("in-field") as in the adjacent water bodies. As a worst case, the maximum initial PEC_{sw} for the metabolites M04 (MeBA) and M09 (DesMe-180) was assumed identical to the initial PEC_{pw} of the parent compound. The initial PEC_{pw} for the metabolites M05 (Na-BX-180) and M06 (DesMe-2023), based on the MED-Rice guidance document, were updated after finalising the peer review (see section 4.2.1). In the DAR and in the addendum (March 2009) TER calculations were based on metabolite toxicity to *Lemna.* EFSA, however, revised the risk assessment for metabolites in paddy water after the peer review, to be in line with the in-field risk assessment of the parent substance, i.e. risk to plants (algae and higher plants) were not considered as bispyribac-sodium is a herbicide. TER values several order of magnitude above the Annex VI trigger for fish and daphnia (applying surrogate toxicity endpoints based on 10 times higher toxicity to fish and daphnia that for the parent substance) indicated a low risk from all metabolites in paddy water.

None of the conclusions in the aquatic risk assessment for the active substance and metabolites would be affected by an increase in exposure of 2%. The most critical TER value for *Lemna gibba* would decrease from 16.1 to 15.8.

Bio-concentration was not considered an issue as bispyribac-sodium is hydrophilic (log P_{ow} = -1.03).

Additional studies on the acute toxicity of the formulation to rainbow trout and daphnia was submitted by the applicant and assessed in an addendum (May 2005), to confirm that the formulation should be classified R52/R53. The expert meeting agreed that the classification should be based on both *Lemna* and algae endpoints and that this would result in R50/R53 classification.

5.3. Risk to bees

Oral and contact toxicity to bees was found to be low for technical bispyribac-sodium and the formulated product Nomineé SC 400. The hazard quotients were well below the Annex VI trigger indicating a low risk for both the active substance and the formulation. The risk to bees was considered to be low, even with an increase in exposure of 2%.

5.4. Risk to other arthropod species

Glass plate studies with the two indicator species *Aphidius rhopalosiphi* (parasitoid wasp) and *Typhlodromus pyri* (predatory mite) were conducted with the formulation Nomineé SC 400. The formulation has no significant effects on mortality and reproduction of *T. pyri* or *A. rhopalosiphi* up to 30.0 g a.s./ha. This conclusion was confirmed in the expert meeting. The effect on reproductive capacity of *T. pyri* was recalculated in an addendum (Italy 2009) and confirmed in the expert meeting, without changing the conclusion of the study. Further testing with *Pardosa spp.* (wolf spider) and *Chrysoperla carnea* (lacewing) on quartz sand and glass plate respectively, indicated no effects above the critical trigger of 50% at application rates up 30.0 g a.s./ha. No data on the effects of metabolites on non-target arthropods were submitted. In the absence of any effects on ground-dwelling predators as represented by Pardosa spp. with an exposure of 14 days no additional tests on the effects of metabolites on non-target arthropods were deemed necessary.

The highest application rates used in the dose response tests represent the maximum recommended field application rates used. Thus the risk from the use of Nomineé SC 400 to non-target arthropods was considered low both in-crop and off-crop.

The mortality was considered to be significantly below the trigger value of 50 %, even with an increase in exposure from 30 g a.s./ha to 30.6 g a.s./ha.

5.5. Risk to earthworms

The acute toxicity of bispyribac-sodium and the formulation Nomineé SC 400 to earthworms was low. A minor correction of the calculation to provide the endpoint for the acute toxicity of the formulation to earthworms on active substance basis was presented in an addendum (Italy, 2009). The risk assessment presented in the DAR was based on a initial PEC_{soil} of 0.04 mg a.s./kg dw, which was different from the PEC_{soil} of 0.0251 mg a.s./kg dw presented in the fate section of the DAR. The PEC_{soil} value was confirmed during the fate expert meeting. The TER calculations for earthworms were not re-calculated with correct PEC_{soil} values in any of the provided addenda. However, the correct TER values were provided in the final list of endpoints, and they are clearly above the Annex VI trigger.

The two metabolites M06 (DesMe-2023) and M05 (Na-BX-180) were included in the risk assessment for earthworms. The acute toxicity to earthworms was low. The risk assessment for the metabolites presented in the DAR was based on the conservative assumption that metabolites would appear at the same concentrations as the parent substance, i.e. PEC_{soil} values of 0.04 mg a.s./kg dw. However, actual PEC_{soil} values of 0.0062 mg a.s./kg and 0.0015 mg a.s./kg for M06 (DesMe-2023) and M05 (Na-BX-

180) respectively, were calculated in the fate section of the DAR. The latter metabolite PEC_{soil} values were confirmed during the fate expert meeting. The TER calculations for earthworms exposed to metabolites were not correct in any of the provided addenda. The correct TER values were provided in the final list of endpoints, and they were clearly above the Annex VI trigger. After the peer review the soil metabolite M03 (Me2BA) was considered to be a major metabolite in soil (see section 4.1.1). No data were available. However, assuming a 10-fold higher toxicity than the parent substance (same approach as for minor metabolites) and a formation rate of < 13.9% maximum, the TER-values should still be in the range of the parent substance. Therefore no risk to soil organisms was anticipated and testing should be not needed. In conclusion the risk to earthworms from the active substance and the metabolites was considered to be low. The conclusion would not be affected by an increase in exposure of 2 %.

5.6. Risk to other soil non-target macro-organisms

The effect of the major soil metabolites M06 (DesMe-2023) and M05 (Na-Bx-180) on non target macro-organisms were tested with *Folsomia candida*, as a representative species for soil dwelling non target arthropods. The NOEC endpoint of 3.08 mg M05 (Na-BX-180)/kg dw soil (corrected for purity) presented in the DAR was questioned by the applicant, who suggested a NOEC of 26.7 mg M05 (Na-BX-180)/kg dw soil. The RMS provided a revised risk assessment for *Folsomia* in an addendum using the NOEC suggested by Applicant. However, the expert meeting agreed to use the original NOEC of 3.08 mg M05 (Na-BX-180)/kg dw soil as information was lacking in support of the higher NOEC. The risk assessment for the metabolites presented in the DAR was based on the conservative assumption that metabolites would appear at the same concentrations as the parent substance, i.e. PEC_{soil} values of 0.04 mg a.s./kg dw. However, actual PEC_{soil} values of 0.0062 mg a.s./kg and 0.0015 mg a.s./kg for M06 (DesMe-2023) and M05 (Na-BX-180) respectively, were calculated in the fate section of the DAR. The latter metabolite PEC_{soil} values were confirmed during the fate expert meeting. The TER calculations for *Folsomia candida* exposed to metabolites were not correct in any of the provided addenda. The corrected TER values were provided in the final list of endpoints, and they were clearly above the Annex VI trigger. In conclusion the risk to non target macro-organisms from the metabolites was considered to be low, even with an increase in exposure of 2%.

5.7. Risk to soil non-target micro-organisms

Technical bispyribac-sodium had no effects >25% after 28 days on soil respiration or nitrogen transformation at the recommended application rate of 30 g a.s./ha or at 5 times the application rate of 150 g a.s./ha. Effects on the major soil metabolites M06 (DesMe-2023) and M05 (Na-Bx-180) on the soil micro-flora were only tested with respect to nitrogen transformation and no effects were identified. The RMS considered in the DAR the nitrogen transformation to be more sensitive than the carbon transformation test. The expert meeting confirmed that no adverse effects on carbon mineralization are to be expected. It was concluded that the risk from bispyribac-sodium and the metabolites M06 (DesMe-2023) and M05 (Na-Bx-180) is considered to be low.

The 2% increase in exposure to 30.6 g a.s./ha was covered by the maximum exposure of 150 g a.s./ha in the risk assessment.

5.8. Risk to other non-target-organisms (flora and fauna)

Bispyribac-sodium was tested as an SC 400 preparation against 6 species in a seedling emergence test and in a vegetative vigour test. Bispyribac-sodium was also tested as a WP80 preparation against 10 plant species. The most sensitive endpoints were vegetative vigour in radish (E_bC_{50} = 0.18 g a.s./ha) and seedling emergence in lettuce (E_bC_{50} = 1.9 g a.s./ha). The RMS provided a tier 1 risk assessment in the DAR assuming 50 % interception by surrounding vegetation. TER values were above 4 if no-spray buffer zones of 10 m were considered. RMS found TER values of 3-4 acceptable taking into account that toxicity values were available for 10 species. In a tier 2 deterministic risk assessment a

geometric mean of the endpoint from two studies with two formulations was used in addition to the assumption of 50 % interception. Furthermore, a probabilistic risk assessment based on the same geometric mean endpoints and 50 % interception was provided. Both approaches indicated low risk applying no-spray buffer zones of 5 m. However, documentation for the 50% intercept was requested during the peer-review. The applicant never submitted such documentation and the RMS provided a tier 1 and 2 risk assessment without interception in an addendum (Italy 2009). At tier 1 TER values > 5 were achieved with no-spray buffer zones of 30 m. In a tier 2 deterministic risk assessment TER value > 5 were achieved with no-spray buffer zones of 10 m. Tier 2 assessment based on HC5 value for all species gave EC50 values of 1.93 g/ha seedling emergence AND 0.44 g/ha vegetative vigour, proposing that 1m and 5 m no-spray buffer zones provide sufficient protection, i.e. TER > 5. The addendum was discussed in the expert meeting. The meeting agreed that it was not appropriate to combine the data for different formulation types. The meeting agreed to the 1 tier assessment indicating a concern but noted that appropriate risk mitigation would have to be addressed at national level.

All major soil and aquatic metabolites were screened for herbicidal activity against 11 plant species (5 monocotyledonous and 6 dicotyledonous) of 7 families, at pre-emergence and post-emergence stages. None of the metabolites caused phytotoxic effects > 50 % at the dose of intended use and the risk was considered to be low.

TER values indicated that the conclusion would not be affected by an increase in exposure of 2 %.

5.9. Risk to biological methods of sewage treatment

Data from an available test with technical Bispyribac-Sodium gave an EC_{50} of >10000 mg a.s./L for inhibition of respiration rate of activated sludge micro-organisms. The risk is considered to be low.

6. Residue definitions

Soil

Definition for risk assessment: bispyribac and their salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05, M03 (from field studies) and M04 (only under anaerobic conditions).

Definition for monitoring: Bispyribac and its salts expressed as bispyribac-sodium

Water

Ground water

Definition for exposure assessment: bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05, M03, M10 and M04.

Definition for monitoring: Pending final assessment of metabolites.

Surface water

Definition for risk assessment: bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06.

Definition for monitoring: Bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05.

Air

Definition for risk assessment: bispyribac and its salts expressed as bispyribac-sodium

Definition for monitoring: Bispyribac and its salts expressed as bispyribac-sodium

Food of plant origin

Definitions for risk assessment: bispyribac and its salts expressed as bispyribac-sodium

Definitions for monitoring: bispyribac and its salts expressed as bispyribac-sodium

Food of animal origin

Definitions for risk assessment: not required for the notified use

Definitions for monitoring: not required for the notified use

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
Bispyribac-sodium	$DT_{50\ drained}$ = 6.0 – 19.6 d $DT_{50\ flooded}$ = 18.9 -19.5 d	The risk was assessed as low for non-target arthropods, earthworms and soil non-target micro-organisms.
M06 (DesMe-2023, sodium salt of M01)	$DT_{50\ drained}$ = 1.9 – 15.4 d $DT_{50\ flooded}$ = 7.4 – 13.5 d	The risk was assessed as low for earthworms and soil non-target macro- and micro-organisms
M05 (Na-BX-180, sodium salt of M02)	$DT_{50\ drained}$ = 39.6 d $DT_{50\ flooded}$ = 14.4 – 27.6 d	The risk was assessed as low for earthworms and soil non-target macro- and micro-organisms
M03 (Me2BA)*	No data available	No data available.
M04 (MeBA, under anaerobic conditions)	No data available	No data available.

* Major metabolite in field studies

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Bispyribac-sodium	medium mobile (K_{foc} = 143 – 604 mL/g)	MED-Rice: no	Yes	Yes	Yes
M06 (DesMe-2023 sodium salt of M01)	high mobile (K_{foc} = 60 - 106 mL/g)	MED-Rice: no	No	Not relevant. low acute oral toxicity (LD_{50} >4000 mg/kg bw) Ames test negative	No
M05 (Na-BX-180 sodium salt of M02)	medium mobile (K_{foc} = 131 – 601 mL/g)	MED-Rice: no	Yes (based on toxicity to *Lemna)*	No data available.	No
M04 (MeBA)*	No data available	No data available Data required	No	Not relevant. low acute oral toxicity (LD_{50} >4000 mg/kg bw) Ames test negative	No
M03 (Me2BA)**	No data available	Data required	No data available.	Not relevant.	No data available.

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
				low acute oral toxicity (LD_{50} >4000 mg/kg bw) Ames test negative	
M10 (Na-DesMe180, sodium salt of M09)***	No data available	Data required.	No data available.	No data available	No data available.

* Presumed minor non-transient metabolite in field studies, major metabolite under anaerobic conditions.
** Major metabolite (> 10%) in field studies
*** Presumed minor non-transient metabolite in field studies

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Bispyribac-sodium (water and sediment phases)	Bispyribac-Sodium is very toxic to aquatic organisms. The risk was assessed as low for aquatic organisms (see section 5.2)
M06 (DesMe-2023 sodium salt of M01, surface water only)	The risk was assessed as low for aquatic organisms (see section 5.2)
M04 (MeBA, surface water only)	The risk was assessed as low for aquatic organisms (see section 5.2)

M09 (DesMe-180 acid of M10, surface water only)	The risk was assessed as low for aquatic organisms (see section 5.2)
M05 (Na-BX-180 sodium salt of M02, sediment only)	The risk was assessed as low for aquatic organisms (see section 5.2)
M03 (Me2BA)*	The risk was assessed as low for aquatic organisms (see section 5.2)

* Potential major metabolite (> 10%) in field studies.

Air

Compound **(name and/or code)**	**Toxicology**
Bispyribac-sodium	low acute toxicity (LC_{50} >4.48 mg/L air)

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

Methods for metabolites M01 and M02 and their salts in surface water with an appropriately validated LOQ (relevant for all uses evaluated, data requirement identified by EFSA January 2009, proposed submission date unknown, refer to section 1)

Assessment of the equivalence of the toxicological batches with the technical specification (with regard to purity and impurities) (relevant for all representative uses, data requirement identified by EFSA after the expert meeting EPCO 28 (June 2005), refer to section 2)

Presumed minor non-transient metabolites found in field studies M04 and M10 and major metabolite M03 need to be addressed for potential ground water contamination (relevant for all representative uses, data requirement identified by EFSA when writing the conclusion, not peer reviewed position paper to address these metabolites presented by the RMS is available; refer to section 4)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

This conclusion was reached on the basis of the evaluation of the representative use as a herbicide on rice. Full details of the GAP can be found in the list of end points. The representative formulated product for the evaluation was 'Nominee 400 SC', a suspension concentrate (SC). In the formulation the active substance is present as the sodium salt.

Adequate methods are available to monitor all compounds given in the respective residue definitions for plants, soil, ground water and air. With the inclusion of M01 and M02 and their salts in the residue definition for surface water some new data requirments have been identified. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

With regard to its toxicological properties, bispyribac-sodium is almost completely absorbed from the gastro-intestinal tract, does not bioaccumulate in the organism and is mainly excreted as bispyribac-sodium. It is of low acute toxicity and presents skin sensitisation properties. The proposed classification is Xi, R43 May cause sensitisation by skin contact. In repeated dose studies, the main target organ was the liver in all species, and the red blood cells in rats. No genotoxic potential was shown *in vitro* or *in vivo*, and no evidence of carcinogenicity was observed in long term studies. In the reproductive toxicity studies, the fertility parameters and the embryo-foetal development were not affected. Mechanistic studies have confirmed that bispyribac-sodium has an effect on the excretory biliary system at the high dose. Several metabolites were also tested and shown to be of low acute oral toxicity and without mutagenic properties. The agreed **Acceptable Daily Intake** (**ADI**) is **0.01** mg/kg bw/day based on the 2-generation and 2-year rat studies. The agreed **Acceptable Operator Exposure Level** (**AOEL**) is **0.072** mg/kg bw/day based on the subchronic rat study. An Acute Reference Dose (ARfD) was not considered necessary due to the lack of effects after acute exposure. In the absence of experimental data, the default value of 100% was agreed for the dermal absorption. The operator exposure estimates according to the German model are below the AOEL without the use of personal protective equipment.

In metabolism studies with bispyribac-sodium in dry-seeded and water-seeded rice it was demonstrated that the metabolic pathway was similar under the two cultivation conditions investigated. Bispyribac was incorporated to a large extent into plant components. Of the extractable residues, unchanged parent bispyribac-sodium was always the largest component and was thus defined

as the relevant residue for risk assessment and MRL setting purposes. Metabolism studies and residue trials results indicate that under practical conditions, residues of bispyribac-sodium are not expected to exceed the LOQ of 0.02 mg/kg in rice grain. In a confined rotational crop study total residues in the rotated wheat, radish, soybean did not exceed 0.01 mg/kg and thus no significant residues are expected in crops planted in soil previously treated with bispyribac-sodium. No significant residues occur in commodities to be processed or used in livestock diet, and therefore no further investigation in processing studies and livestock studies was required to support the representative use in rice.

In a chronic consumer exposure risk assessment it could be demonstrated that the maximum estimated dietary intake of residues of bispyribac-sodium is well below (<1%) the toxicological reference value ADI. As no ARfD was allocated an acute risk assessment is not necessary.

The route and rate of degradation of bispyribac-sodium in drained and flooded paddy rice soils was investigated under aerobic and anaerobic conditions at 20°C. Bispyribac-sodium was low to moderately persistent in aerobic drained paddy soils and moderately persistent in aerobic flooded paddy soils. It degraded to form the major metabolite M06 (DesMe-2023) that was further degraded to M05 (Na-BX-180; major metabolite only under drained conditions). Metabolite M06 (DesMe-2023) was low to moderately persistent and metabolite M05 (Na-BX-180) was moderately persistent in aerobic paddy soils both under drained or flooded conditions. Under anaerobic conditions, bispyribac-sodium is moderately to highly persistent in anaerobic flooded paddy soils. Metabolite M06 (DesMe-2023) and an additional metabolite M04 (MeBA) were identified as major metabolites under anaerobic conditions.

During the peer review some concerns were expressed regarding the lack of information in the DAR on the multi-compartmental model assumed on the fitting of data to calculate kinetic parameters for metabolites. The RMS has made available to EFSA a new addendum in March 2008 (dated July 2007).

No soil photolysis study is available based on the use in paddy rice just before flooding.

Dissipation of bispyribac-sodium in soil was also investigated in four rice field sites replicating the proposed intended use. Bispyribac-sodium was low persistent in these field trials ($DissT_{50}$ = 2.1 – 9.1 d). Metabolites M03 (Me2BA: max. <1µg /kg soil; < 13.9 %), M05 (NaBX-180: max. 1.88 µg /Kg soil; 21.8 % parent equivalents).M06 (DesMe-2023: max. 5.44 µg /Kg ; 45.3 % parent equivalents) and M10 (Na-DesMe-180: max.0.3µg /L < 7.74 % parent equivalents) were found in these trials.

PEC soil of bispyribac-sodium and its major soil metabolites M06 (DesMe-2023) and M05 (Na-BX-180) were calculated with MED-Rice tools (European Commission, 2003).

According to the available studies, bispyribac-sodium and metabolite M05 (Na-BX-180) are expected to exhibit medium mobility in soil whereas metabolite M06 (DesMe-2023) may be considered highly mobile.

Bispyribac-sodium is slowly hydrolysed at pH 5 and may be considered stable at pH 7 and 9. Bispyribac-sodium was found to be stable to direct aqueous photolysis. Bispyribac-sodium is considered not to be readily biodegradable.

In water sediment systems, bispyribac-sodium was converted to a number of metabolites through demethylation and breakage of ether bridges ($DT_{50\ whole\ system}$ = 10.7 – 59.9 d). The only major metabolite found in the water phase of one of the systems was M06 (DesMe-2023). In the sediment layer M10 (Na-DesMe-180) occurred as a major metabolite in one of the systems. The MED-Rice scheme was used to calculate PEC_{SW} and PEC_{SED} for bispyribac-sodium and its metabolites. The aerobic flooded soil study and the aerobic water sediment study were used to calculate geometric mean $DissT_{50\ water}$ (16.2 d) and geometric mean $DT_{50\ whole\ system}$ (22.1 d) used in the calculations. The application rate was reduced assuming a DT_{50} = 8.7 d for the drained soil period. PEC_{SW} and PEC_{SED} for metabolites were calculated according to the MED-Rice scheme. DT_{50} from the whole aerobic flooded soil experiments were used for M05 (Na-BX-180; $DissT_{50}$ = 25.9 d) and M06 (DesMe-2023;

$DissT_{50}$ = 28.3 d) were used to represent dissipation in both the sediment and the water phase. Maximum amounts of M05 (Na-BX-180; 21.8 % parent equivalents) and M06 (DesMe-2023; max. 45.3 % parent equivalents) observed in the field dissipation study were used to simulate a pseudo application of the metabolite.

Potential ground water contamination by bispyribac-sodium and its soil metabolites was assessed by calculating PEC_{GW} with the MED-Rice scheme.

Predicted environmental concentrations for the two rice scenarios were calculated to be < 0.001 µg / L for bispyribac-sodium and metabolite M05 (Na-BX-180) and 0.08 µg / L for M06 (DesMe-2023) in the sandy scenario. However, the presumed minor non transient metabolites M04 and M10 and major metabolite M03 in field studies need to be addressed for potential ground water contamination.

Due to the low potential of volatilization and the estimated rapid photochemical transformation, the environmental concentrations in air and the transport through air are considered negligible for bispyribac-sodium.

The first-tier TER values for insectivorous and herbivorous birds and mammals were above the Annex VI trigger values indicating a low risk. The risk from contaminated drinking water was considered low for both birds and mammals. Secondary poisoning was considered to be of no concern, given the hydrophilic properties of bispyribac-sodium.

Bispyribac-sodium was very toxic to aquatic organisms and should be classified as R50. Annex VI trigger values were met for all aquatic organisms in an "off-crop" risk assessment for both the active substance and all the metabolites, based on PEC_{pw} values derived in accordance with the MED-Rice guidance document. Following the MED-Rice guidance document the "in-crop" aquatic risk assessment focused on aquatic animals. Annex VI triggers were met for bispyribac-sodium and all metabolites, indicating a low risk to aquatic animals "in-field". Bioconcentration was not considered an issue as bispyribac-sodium is hydrophilic.

The risk to bees and not-target arthropods and biological methods of sewage treatment was assessed as low. Additionally the risk to soil dwelling organisms, i.e. earthworms, *Folsomia* and micro-organisms was assessed as low, both for the active substance and the major soil metabolites M06 DesMe-2023 and M05 Na-Bx-180. The tier 1 risk assessment to non-target plants indicated a need for risk mitigation, e.g. non-spray buffer zones of 30 m.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

Only use in rice has been assessed as representative EU use. A substantial number of data gaps would need to be identified, required and assessed to be able to complete the risk assessment for the environment of any other use.

Based on available data the first tier risk assessment to non-target plants indicated a need for mitigation, e.g. no-spray buffer zones of 30 m. (refer to point 5.8)

ISSUES THAT COULD NOT BE FINALIZED

The potential minor non transient metabolite found in field studies M04 and M10 and the major soil metabolite M03 need to be addressed for potential ground water contamination.

CRITICAL AREAS OF CONCERN

Contamination of groundwater by potentially relevant metabolites M03 and M10 above regulatory limits cannot be excluded.

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United Kingdom, MAFF, 1986/1992, Scientific Subcommittee on Pesticides and British Agrochemicals Joint Medical Panel., Estimation of Exposure and Absorption of Pesticides by Spray Operators (UK MAFF, 1986) and the Predictive Operator Exposure Model (POEM) (UK MAFF, 1992).

GUIDANCE DOCUMENTS[7]:

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FOCUS (2001). "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.

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FOCUS, 2008. "Pesticides in Air: Considerations for Exposure Assessment". Report of the FOCUS Working Group on Pesticides in Air, EC Document Reference SANCO/10553/2006 Rev 2 June 2008.

[7] For further guidance documents see http://ec.europa.eu/food/plant/protection/resources/publications_en.htm#council (EC) or http://www.oecd.org/document/59/0,3343,en_2649_34383_1916347_1_1_1_1,00.html (OECD)

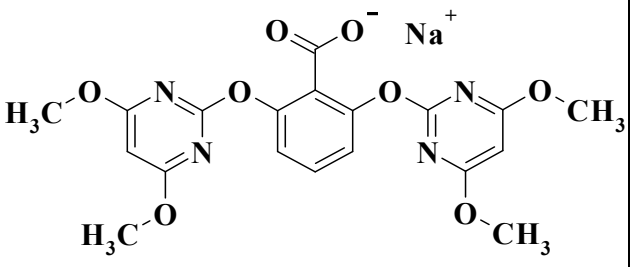
APPENDICES

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

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	bispyribac (unless otherwise stated, the following data relate to the variant bispyribac-sodium)
Function (*e.g.* fungicide)	Herbicide
Rapporteur Member State	Italy

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	sodium 2,6-bis(4,6-dimethoxypyrimidin-2-yloxy)benzoic acid
Chemical name (CA) ‡	benzoic acid, 2,6-bis [(4,6-dimethoxypyrimidin-2-yl)oxy]-,sodium salt
CIPAC No ‡	748.011
CAS No ‡	125401-92-5
EEC No (EINECS or ELINCS) ‡	not allocated
FAO Specification (including year of publication)‡	not available
Minimum purity of the active substance as manufactured (g/kg) ‡	≥930 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	C19 H17 N4 Na O8
Molecular mass ‡	452.36 g/mol
Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	T = 223 - 224 °C Purity = 99.9%
Boiling point (state purity) ‡	Not measurable due to thermal decomposition
Temperature of decomposition	T = 223 °C. Purity = 99.9%
Appearance (state purity) ‡	- Active substance Physical state: powder. Colour: white Odour: odurless Purity = 99.9% - Technical active substance Physical state: solid granular powder. Colour: white Purity: 99.2% Odour: odurless Purity = 95.0%
Realative density (state purity) ‡	1.47 at 20°C **density measured not relative density** (Purity = 99.9%)
Surface tension	69.79 mN/m at 20°C **(measured at 1g/L)** (Purity = 99.7%)
Vapour pressure (in Pa, state temperature) ‡	5.05 x 10^{-9} Pa at 25 °C (Purity = 98.6%) 3.79 x 10^{-11} mmHg at 25 °C (Purity = 98.6%)
Henry's law constant (Pa m^3 mol^{-1}) ‡	3 x 10^{-11} Pa m^3/mol at 25 °C (Purity = 98.6%)
Solubility in water (g/l or mg/l, state temperature) ‡	Unbuffered water: 68.7 g/L at 20°C
	pH_9_____:63.9 g/L at 20°C (Purity = 99.7%)
	pH_7_____:64.0 g/L at 20°C (Purity = 99.7%)
	pH_4_____: not feasible (Purity = 99.7%). The a.i. is not stable under acidic conditions. The determination of the water solubility in acidic aqueous solutions is not feasible.
Solubility in organic solvents (in g/l or mg/l, state temperature) ‡	methanol 25 g/L (at 20 °C)
	acetone 1.4 x 10^{-3} g/L (at 25 °C)
	methylene chloride 1.3 x 10^{-3} g/L (at 25 °C)
	ethyl acetate 6.1 x 10^{-5} g/L (at 25 °C)
	n-hexane 8.3 x 10^{-6} g/L (at 25 °C)
	toluene < 1 x 10^{-4} g/L (at 25 °C)
	n-octanoll 2.1 x 10^{-2} g/L (at 25 °C) Purity = 99.2 %
Partition co-efficient (log P_{OW}) (state pH and temperature) ‡	Unbuffered water/octanol: log P_{OW} = -1.03 at 23 °C (pH = 6.18). The test was performed with water saturated with n-octanol (pH 6.18) No effect of pH (between 4 and 10) is to be expected Purity = 98.6%
Hydrolytic stability (DT_{50}) (state pH and temperature) ‡	pH 5: DT50 = 88 days; acetate buffer at 25°C Purity = 97.0%
	pH 7: DT50 = 807 days; HEPES-buffer at 25°C pH 7: DT50 = 476 days; TRIS buffer at 25°C Purity = 97.0%
	pH 9: DT50 = 482 days; borate buffer at 25°C Purity = 97.0%
Dissociation constant ‡	pKa of the conjugated acid: 3.35 ± 0.09 at 20 °C Purity = 98.8%

UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) ‡	The highest absorption value in water is < 290 nm, therefore the molar extinction is not reported
Photostability (DT_{50}) (aqueous, sunlight, state pH)‡	pH = 7 TRIS buffer (light) DT50 = 466 days pH = 7 TRIS buffer (no light) DT50 = 1470 days Purity = 97.0%
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Φ = 0.0064 Environmental direct photolysis half-lives = 15 – 140 days Purity = 99.7%
Flammability ‡	Not highly flammable
Explosive properties ‡	Not explosive

Summary of representative uses evaluated (Bispyribac sodium)*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
	1.				Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Rice	**EU South**	**Nominee 400 SC**	**F**	**Weeds**	**SC**	**408 g/L**	**Overall spray**	**POST up to GS BBCH 25**	**1**	**n.a.**	**0.004 – 0.015**	**200 - 500**	**0.004 – 0.0306**	**n.a.**	**1**

Remarks:
(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 plants - 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) The minimum and maximum number of application possible under practical conditions of use must be provided
PHI - minimum pre-harvest interval
(l) Remarks may include: Extent of use/economic importance/restrictions
(m)

1 Groundwater assessment not finalized for metabolites M04, M10 and M03

* Uses for which the risk assessment can not be concluded are marked grey.

Methods of Analysis

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

Technical as (principle of method)	1) The sample was diluted with NaOH 4 mM and the content of a.i. was determined with HPLC/UV. Detection: 246 nm
Impurities in technical as (principle of method)	HPLC (external standard)
Plant protection product (principle of method)	1) No CIPAC method. 2) HLPC/UV determination. Detection: 230 nm

Analytical methods for residues (Annex IIA, point 4.2)

Residue definition for monitoring purposes:

Food of plant origin		Bispyribac and its salts, expressed as bispyribac-sodium
Food of animal origin		Not required for the applied for use
Soil		Bispyribac and its salts, expressed as bispyribac-sodium
Water	surface	Bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05.
	drinking/ground	Bispyribac and its salts, expressed as bispyribac-sodium
Air		Bispyribac and its salts, expressed as bispyribac-sodium

Monitoring/Enforcement methods (see EPCO Manual page 13):

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	1) R.Sur, 2001, GLP. Extraction with acetonitrile/water mixture. The extract was acidified with formic acid. Clean-up on ChemElut™ column eluted with dichloromethane. The eluate was concentrated and the residue was dissolved in acetonitrile/water (8:2, v/v). Determination: HPLC-MS/MS: electrospray interface (positive ion mode) Ions: m/z = 431 → m/z = 275, the daughter ion is used for quantification. LOD = Green material: 0.002 mg/Kg; Grain: 0.0003 mg/Kg; Straw: 0.0001 mg/Kg. LOQ = 0.02 mg/kg corresponding to the lowest fortification level. 2) Th Anspach, 2001, GLP. Independent Laboratory Validation. Extraction with an acetonitrile/water mixture. The extract was acidified with formic acid. Clean-up on ChemElut™ column eluted with dichloromethane. The eluate was concentrated and the residue was dissolved in acetonitrile/water (8:2, v/v). Determination: LC-MS/MS: electrospray interface (positive ion mode) Ions: m/z = 431.5 → m/z = 275.0 (for quantitation);

	m/z = 431.5 → m/z = 243.1 (for qualitative confirmation) LOD = Rice (grain): 0.002 mg/Kg. LOQ = 0.02 mg/kg corresponding to the lowest fortification level
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	A method for the determination of Bispyribac-sodium in/on animal matrices was not developed, since r**esidues of the parent compound in/on animal feed were below 0.02 mg/kg.**
Soil (principle of method and LOQ)	1) Schramel O., 2001, GLP. KIH2023, DesMe-2023, BX-180, DesMe-180: extraction via microwave (250 W) for three minutes with water/acetonitrile/formic acid/oxalic acid. Me_2BA, MeBA: extraction via microwave (250 W) for three minutes with water/acetonitrile/ammonium acetate. Determination: HPLC/MS-MS (turbo-ionspray interface) Soil types: - Heavy loamy sand (DIN), Sandy loam (USDA); - Weak clay loam (DIN), loam (USDA); - Weak clay loam (DIN), clay loam (USDA); - Clay loam (DIN), clay loam (USDA). LOD: 0.3 µg/Kg LOQ: 1.0 µg/Kg 2) Schramel O., 2001, GLP. Validation of the method. Extraction via microwave (250 W) for three minutes with water/acetonitrile/formic acid/oxalic acid. Determination: HPLC/MS-MS (turbo-ionspray interface) LOD: 0.3 µg/Kg LOQ: 1.0 µg/Kg
Water (principle of method and LOQ)	1) Sommer H., 2001, GLP. The water samples was directly injected into the HPLC-MS/MS instrument. Determination: HPLC-MS/MS. - Detector: triple quadrupole, in electrospray in positive mode. Ions: 431.2 parent ion; 275.1 product ion. • Surface water from the river Rhine sampled in Leverkusen-Hitdorf. • TOC = 17 mg/L • DOC = 4 mg/L • Conductivity at 25°C 428 □S/cm • pH = 7.5 • Water hardeness 8.3°dH • Dry residue after filtration (Mud content) 314 mg/L. LOD = not available LOQ = 0.05 µg/l. Open for surface water.

Air (principle of method and LOQ)	1) Hellpointner E., 2001, GLP. Adsorbtion of KIH2023 on Tenax tubes at rate of 2 L/min during a period of six hours. Extraction of KIH 2023 with acetonitrile. Determination: HPLC/DAD, DAD detector 246 nm • Climate conditions: • Temp. [°C] = 35; Rel. Air humidity % = 80 LOD = <0.17 µg/m^3 LOQ = 0.003 mg/m^3
Body fluids and tissues (principle of method and LOQ)	The submission of an analytical method for the determination of residues in body fluids and tissues is not necessary, because the active substance is not classified as toxic or highly toxic.

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	soil metabolism (values are given for day 119): range: 24.7 to 52.1%; median 38.4% (n = 2) (pyrimidine-label) range: 5.4 to 29.4%; median 17.4% (n = 2) (phenyl-label) paddy soil metabolism: (values are given for day 120): range: 34.8 to 48.7%; median 41.8% (n = 2) (pyrimidine-label) range: 9.7 to 25.4%; median 17.6% (n = 2) (phenyl-label)
Non-extractable residues after 100 days ‡	soil metabolism (values are given for day 119): range: 39.1 to 47.4%; median 43.3% (n = 2) (pyrimidine-label) range: 55.7 to 62.7%; median 59.2% (n = 2) (phenyl-label) paddy soil metabolism: (values are given for day 120): range: 35.9 to 51.0%; median 43.5% (n = 2) (pyrimidine-label) range: 62.6 to 82.8%; median 72.7% (n = 2) (phenyl-label)

Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	**Na-BX-180 *(M05)***
	and/or the corresponding acid BX-180 *(M02)*:
	
	soil metabolism:
	range at day 119: 1.3 to 14.7% (n = 4) (both labels);
	max.: 7.5% (pyrimidine-label, day 57), 15.0% (phenyl-label, day 15)
	
	field study (drained soil)
	max.: 1.88 µg / kg soil (21.8 % parent equivalents)
	
	DesMe-2023 *(M06)*
	and/or the corresponding acid DesMe-5750 *(M01)*:
	
	soil metabolism:
	range at day 119: n.d. to 2.1% (n = 4) (both labels);
	max.: 12.8% (pyrimidine-label, day 3), 14.4% (phenyl-label, day 3)
	
	field study (drained soil)
	max.: 5.44 µg / kg soil (45.3 % parent equivalents)
	
	paddy soil metabolism (flooded):
	soil: range at day 120: 0.1 to 0.4% (n = 4) (both labels), max.: 9.1% (pyrimidine-label, day 30)
	water layer: range at day 120: < 0.1 to 0.7% (n = 4) (both labels), max.: 19.1% (pyrimidine-label, day 14), 22.6% (phenyl-label, day 30)
	
	Me2BA *(M03)*
	field study (drained soil)
	max.: < 1.0 µg / kg soil (LOQ; < 13.9 % parent equivalents)

	Na-DesMe-180 *(M10)* field study (drained soil) max.: < 1.0 µg / kg soil (LOD; < 7.5 % parent equivalents) **MeBA *(M04)*** field study (drained soil) max.: < 0.3 µg / kg soil (LOD; < 7.7 % parent equivalents)

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

Anaerobic degradation ‡	**paddy soil metabolism:** Mineralisation at 20°C (values are given for day 120): range: 0.1 to 1.7%; median: 0.9% (n = 2) (pyrimidine-label) range: < 0.1 to 0.7%; median: 0.35% (n = 2) (phenyl-label) Non-extractable residues at 20°C (values are given for day 120): range: 23.4 to 60.8%; median: 42.1% (n = 2) (pyrimidine-label) range: 25.7 to 78.3%; median: 52.0% (n = 2) (phenyl-label) Major metabolites at 20°C: MeBA *(M04)*: soil: range at day 120: 1.5 to 6.4% (n = 2) (pyrimidine-label), max.: 6.4% (day 120, pyrimidine-label) water layer: range at day 120: 3.6 to 9.4% (n = 2) (pyrimidine-label), max.: 9.4% (day 120, pyrimidine-label) Entire system: max. 15.8 % DesMe-2023 *(M06)*: and/or the corresponding acid DesMe-5750 *(M01)*: soil: range at day 120: 0.9 to 10.2% (n = 4) (both labels), max.: 10.2% (day 120, pyrimidine-label) water layer: range: 10.6 to 14.7% (n = 4) (both labels), max.: 14.7% (day 120, pyrimidine-label) 13.7% (day 120, phenyl-label)
Soil photolysis ‡	No data available

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

Method of calculation	Calculation according to the evaluation program ®ModelManager (Environmental Kinetics), Version 1.1, Cherwell Scientific Ltd. Oxford, UK, 1999
Laboratory studies (range or median, with n value, with r^2 value) ‡	Parent: DT_{50lab} (20°C, soil aerobic): 6 - 19.6 d (n = 2, r^2 = 0.989 - 0.993) $DT50_{lab}$ (20°C, paddy soil aerobic (flooded), entire system): 18.9 - 19.5 days (n = 2, r^2 = 0.986 - 0.994) Na-BX-180 *(M05)*: DT_{50lab} (20°C, soil aerobic): 39.6 d (n = 1, r^2 = 0.9957). Associated formation fraction (f.f.) = 14 % $DissT_{50lab}$ (20°C, soil aerobic. Dissipation observed from the maximum): 33.5 d (n = 1, SFO, r^2 = 0.832) $DT50_{lab}$ (20°C, paddy soil aerobic (flooded), entire system): 14.4 – 27.6 d (n = 2, r^2 = 0.9593 - 0.9736). Associated formation fraction (f.f.) = 15 - 21 % $DissT50_{lab}$ (20°C, paddy soil aerobic (flooded), entire system. Dissipation observed from the maximum): 25.5 – 25.9 d (n = 2, r^2 = 0.90 - 0.93) DesMe-2023 *(M06)*: DT_{50lab} (20°C, soil aerobic): 1.9 – 15.4 d (n = 2, r^2 = 0.9957 - 0.9981). Associated formation fraction (f.f.) = 37 -86 % $DissT_{50lab}$ (20°C, soil aerobic. Dissipation observed from the maximum): 9.4 – 41.1 d (n = 2, SFO, r^2 = 0.83 - 0.85) $DT50_{lab}$ (20°C, paddy soil aerobic (flooded), entire system): 7.4 - 13.5 d (n = 2, r^2 = 0.9593 - 0.9736). Associated formation fraction (f.f.) = 79 - 85 % $DT50_{lab}$ (20°C, paddy soil aerobic (flooded), entire system. Dissipation observed from the maximum): 17.7 – 28.3 d (n = 2, r^2 = 0.88 - 0.99).
	$DT90_{lab}$ (20°C, soil aerobic): range: 19.9 - 65.3 d (n = 2), r^2 = 0.989 - 0.993 $DT90_{lab}$ (20°C, paddy soil aerobic (flooded), entire system): range: 62.7 - 64.7 d (n = 2), r^2 = 0.986 - 0.996
	$DT50_{lab}$ (10°C, aerobic): based on the above-mentioned results and assuming that a decrease in temperature of 10°C will multiply the half-lives with a factor of 2.2 (based on a Q10-factor of 2.2), it can be assumed that the resulting half-lives at 10°C would be still below 90 days.
	$DT50_{lab}$ (20°C, paddy soil anaerobic, entire system): range: 32.9 to 110 d (n = 2), r^2 = : 0.944 - 0.979

	degradation in the saturated zone: no data submitted and no data required
Field studies (state location, range or median with n value) ‡	DT_{50f}: ‡ (based on the whole study duration, including flooded phase) Italy, cropped, 2.1, 9.1 d (n = 2, r^2 = 0.999, 0.973), 1st order Spain, cropped, 7.6, 6.2 d (n = 2, r^2 = 0.913, 0.951), 1st order **For the drained phase DT_{50}'s were recalculated in Schaefer 2001a. However, this report is missing in the dossier and therefore it has not been peer reviewed; a data requirement has been identified. However since the values derived in this report are used in the modelling they are reported here:** DT_{50f}: ‡ (based on the drained, including flooded phase) Italy, cropped, 2.1, 8.6 d (n = 2, r^2 = 0.999, 0.973), 1st order Spain, cropped, 24.8, 8.1 d (n = 2, r^2 = 0.913, 0.951), 1st order
	DT_{90f}: ‡ Italy, cropped, 6.9, 30.2 d (n = 2, r^2 = 0.999, 0.973), 1st order Spain, cropped, 25.1, 20.5 d (n = 2, r^2 = 0.913, 0.951), 1st order
Soil accumulation and plateau concentration ‡	Not applicable

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence (yes / no) (if yes type of dependence) ‡	**Koc:** Parent: 143 – 604 mL/g (mean: 302 mL/g, 1/n = 0.9346 - 0.9901, 5 soils) Na-BX-180 *(M05)*: 131 – 601 mL/g (mean: 320 mL/g, 1/n = 0.88 - 0.94, 3 soils) DesMe-2023 *(M06)*: 60 – 106 mL/g (mean: 75 mL/g, 1/n = 0.9173 - 1.0322, 3 soils) **K_d:** Parent: 0.604 – 2.01 mL/g (mean: 1.156 mL/g, 5 soils) Na-BX-180 *(M05)*: 1.55 – 7.82 mL/g (mean: 3.96 mL/g, 3 soils) DesMe-2023 *(M06)*: 0.72 – 1.14 mL/g (mean: 0.878 mL/g, 3 soils) **pH dependence:** no dependence for parent and metabolites was observed in the available data **For GW modelling (MED-Rice calculations):** Parent:

	arith. mean: 302 mL/g, 1/n = 0.958 Na-BX-180 *(M05)*: arith. mean: 320 mL/g, 1/n = 0.90 DesMe-2023 *(M06)*: arith. mean: 75 mL/g, 1/n = 0.989

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

Column leaching ‡	No data available. Not required.
Aged residues leaching ‡	No data available. Not required.
Lysimeter/ field leaching studies ‡	No data available. Not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	MED-Rice, 2003 DT_{50} drained field: 8.7 d (geometric mean from drained aerobic soil studies and field dissipation studies) DT_{50} flooded field (total system): 22.1 d geometric mean form flooded aerobic soil study and water sediment study DT_{50} flooded field (water phase): 16.2 d geometric mean form flooded aerobic soil study and water sediment study DT_{50} sediment/water system: 22.1 d geometric mean form flooded aerobic soil study and water sediment study DT_{50} sediment: 22.1 d geometric mean form flooded aerobic soil study and water sediment study Kinetic: 1st order, field and lab data K_{oc}: 302 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: 30 g a.s./ha[a)] a) = The soil residue of KIH 2023 three days after application (at the time of flooding) was calculated from the maximum application rate and the aerobic soil DT^{50} of 8.7 days, yielding 23.6 g a.s./ha. That residue was used as effective application rate of KIH 2023 for the purpose of PEC calculations according to MED-Rice.

$PEC_{(s)}$ (mg/kg)		Clay scenario		Sand scenario	
		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial		0.0253	-	0.0211	-
Short term	24h	0.0245	0.0249	0.0205	0.0208
	2d	0.0237	0.0245	0.0198	0.0205
	4d	0.0223	0.0238	0.0186	0.0198
Long term	7d	0.0203	0.0227	0.0170	0.0190
	28d	0.0105	0.0168	0.0088	0.0141
	50d	0.0053	0.0128	0.0044	0.0107
	100d	0.0011	0.0077	0.0009	0.0064

Metabolite Na-BX-180 *(M05)*:

Method of calculation	MED-Rice, 2003 DT_{50lab} flooded aerobic soil study (total system): 25.9 d $DissT_{50}$ flooded aerobic soil study (water phase): 25.9 d DT_{50} sediment/water system: 25.9 d DT_{50} sediment: 25.9 d Kinetic: 1st order, lab data K_{oc}: 320 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: 4.5 g /ha

$PEC_{(s)}$ (mg/kg)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial	4.87	-	4.10	-

Metabolite DesMe-2023 *(M06)*:

Method of calculation	MED-Rice, 2003 DT_{50} max. in flooded aerobic soil study (total system): 28.3 d DT_{50} max. in flooded aerobic soil study (water phase): 28.3 d DT_{50} sediment/water system: 28.3 d DT_{50} sediment: 28.3 d Kinetic: 1st order, lab data K_{oc}: 75 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: 13.2 g /ha

$PEC_{(s)}$ (mg/kg)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial	8.85	-	5.91	-

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature) ‡	pH 5: Parent: DT_{50} at 25°C: 88 d Me2BA *(M03)*: DT_{50} at 20°C: 1663 d
	pH 7: DT_{50} at 25°C: pH 7 (HEPES): 807 d pH 7: (TRIS): 476 d
	pH 9: DT_{50} at 25°C: 482 d
Photolytic degradation of active substance and relevant metabolites ‡	DT50 at pH 7: 466 days (Xenon arc lamp)
Readily biodegradable (yes/no) ‡	No study available: classified as not readily biodegradable in the absence of data
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	water: $DissT_{50}$: 7.7 - 56.4 d $DissT_{90}$: 25.5 - 187 d (Simple first order [SFO], r^2 = 0.973 - 0.985, n = 2) Whole system: DT_{50}: 10.7 - 59.9 d DT_{90}: 35.6 - 199 d (SFO, r^2 = 0.991 - 0.994, n = 2)
Mineralization	9.9 - 26.6% AR (at day 120 = study end, 2 labels, 2 systems)
Non-extractable residues	13.1 – 78.8% AR (at day 120 = study end and day 28, 2 labels, 2 systems)
Distribution in water / sediment systems (active substance) ‡	maximum of 13.1% AR (day 3, phenyl-label) to 17.6% AR (2 hours, pyrimidine-label) in sediment (2 labels, 2 systems)
Distribution in water / sediment systems (metabolites) ‡	**Water:** DesMe-2023 *(M06)*: maximum of 6.4% AR (day 16, phenyl-label) to 22.6% AR (day 90, pyrimidine-label) (2 labels, 2 systems) Na-DesMe-180 *(M10)*: maximum of n.d. to 2.1% AR (day 56, phenyl-label) (2 labels, 2 systems) **Sediment:** DesMe-2023 *(M06)*: maximum of 2.1% AR (day 16, pyrimidine-label) to 4.1% AR (day 16, pyrimidine-label) (2 labels, 2 systems) Na-DesMe-180 *(M10)*: maximum of 1.3% AR (day 56, pyrimidine-label) to 13.4% AR (day 90, phenyl-label) (2 labels, 2 systems)

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

Parent

Method of calculation	MED-Rice, 2003 DT_{50} drained field: 8.7 d (geometric mean from drained aerobic soil studies and field dissipation studies) DT_{50} flooded field (total system): 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} flooded field (water phase): 16.2 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} sediment/water system: 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} sediment: 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) Kinetic: 1st order, field and lab data K_{oc}: 302 mL/g
Application rate	Crop: rice Numbers of application: 1 Interval: - Application rate: 30 g a.s./ha[a)] Depth of sediment: 0.05 m water level: 0.1 m a) = The soil residue of KIH 2023 three days after application (at the time of flooding) was calculated from the maximum application rate and the aerobic soil DT^{50} of 8.7 days, yielding 23.6 g a.s./ha. That residue was used as effective application rate of KIH 2023 for the purpose of PEC calculations according to MED-Rice.
Main routes of entry	Outflow from paddy (based on calculation according to MED-Rice Step 1)

$PEC_{(sw)}$ (µg / l)		Clay scenario		Sand scenario	
		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial		0.3764	-	0.6053	-
Short term	24h	0.3606	0.3685	0.5800	0.5926
	2d	0.3455	0.3608	0.5557	0.5801
	4d	0.3172	0.3460	0.5101	0.5564
Long term	7d	0.2790	0.3253	0.4487	0.5231
	14d	0.2068	0.2832	0.3325	0.4554
	21d	0.1533	0.2484	0.2465	0.3994
	28d	0.1136	0.2194	0.1827	0.3528
	42d	0.0624	0.1747	0.1004	0.2810

Metabolite Na-BX-180 *(M05)*:

Method of calculation	MED-Rice, 2003 DT_{50} flooded field (total system): 25.9 d DT_{50} flooded field (water phase): 25.9 d DT_{50} sediment/water system: 25.9 d DT_{50} sediment: 25.9 d Kinetic: 1st order, lab data K_{oc}: 320 mL/g
Application rate	Crop: rice Numbers of application: 1 Interval: - Application rate: 4.5 g /ha
Main routes of entry	Outflow from paddy (based on calculation according to

	MED-Rice Step 1)

PEC$_{(sw)}$ (µg / l)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Max	0.074	-	0.12	-

Metabolite DesMe-2023 *(M06)*:

Method of calculation	MED-Rice, 2003 DT_{50} flooded field (total system): 28.3 d DT_{50} flooded field (water phase): 28.3 d DT_{50} sediment/water system: 28.3 d DT_{50} sediment: 28.3 d Kinetic: 1st order, lab data K_{oc}: 75 mL/g
Application rate	Crop: rice Numbers of application: 1 Interval: - Application rate: 13.2 g /ha
Main routes of entry	Outflow from paddy (based on calculation according to MED-Rice Step 1)

PEC$_{(sw)}$ (µg / l)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Max	0.55	-	0.73	-

PEC (sediment)

Parent

Method of calculation	MED-Rice, 2003 DT_{50} drained field: 8.7 d (geometric mean from drained aerobic soil studies and field dissipation studies) DT_{50} flooded field (total system): 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} flooded field (water phase): 16.2 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} sediment/water system: 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} sediment: 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) Kinetic: 1st order, field and lab data K_{oc}: 302 mL/g
Application rate	Crop: rice Numbers of application: 1 Interval: - Application rate: 30 g a.s./ ha[a)] a) = The soil residue of KIH 2023 three days after application (at the time of flooding) was calculated from the maximum application rate and the aerobic soil DT^{50} of 8.7 days, yielding 23.6 g a.s./ha. That residue was used as effective application rate of KIH 2023 for the purpose of PEC calculations according to MED-Rice.

$PEC_{(sed)}$ (µg / kg)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial	peak: 1.5293 at day 0	-	peak: 2.4224 at day 0	-
Short term	1.4821 at day 1	peak: 1.5056 at day 1	2.3476 at day 1	peak: 2.3848 at day 1
Long term	study end: 0.0664 at day 100	study end: 0.4664 at day 100	study end: 0.1052 at day 100	study end: 0.7388 at day 100

Metabolite Na-BX-180 *(M05)*:

Method of calculation	MED-Rice, 2003 DT_{50} flooded field (total system): 25.9 d DT_{50} flooded field (water phase): 25.9 d DT_{50} sediment/water system: 25.9 d DT_{50} sediment: 25.9 d Kinetic: 1st order, lab data K_{oc}: 320 mL/g
Application rate	Crop: rice Numbers of application: 1 Interval: - Application rate: 4.5 g /ha

PEC$_{(sed)}$ (µg / kg)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Max	0.31	-	0.50	-

Metabolite DesMe-2023 *(M06)*:

Method of calculation	MED-Rice, 2003 DT_{50} flooded field (total system): 28.3 d DT_{50} flooded field (water phase): 28.3 d DT_{50} sediment/water system: 28.3 d DT_{50} sediment: 28.3 d Kinetic: 1st order, lab data K_{oc}: 75 mL/g
Application rate	Crop: rice Numbers of application: 1 Interval: - Application rate: 13.2 g /ha

PEC$_{(sed)}$ (µg / kg)	Clay scenario		Sand scenario	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Max	0.67	-	0.89	-

PEC_{pw} (paddy water):

Parent:

Method of calculation	MED-Rice, 2003 DT_{50} drained field: 8.7 d (geometric mean from drained aerobic soil studies and field dissipation studies) DT_{50} flooded field (total system): 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} flooded field (water phase): 16.2 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} sediment/water system: 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) DT_{50} sediment: 22.1 d (geometric mean from flooded aerobic soil study and water sediment study) Kinetic: 1st order, field and lab data K_{oc}: 302 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: 30 g a.s./ ha[a)] a) = The soil residue of KIH 2023 three days after application (at the time of flooding) was calculated from the maximum application rate and the aerobic soil DT^{50} of 8.7 days, yielding 23.6 g a.s./ha. That residue was used as effective application rate of KIH 2023 for the purpose of PEC calculations according to MED-Rice.

PEC_{pw} initial (maximum) (µg/L)	Clay scenario	Sand scenario
	4.648	7.767

Metabolite Na-BX-180 *(M05)*:

Method of calculation	MED-Rice, 2003 DT_{50} flooded field (total system): 25.9 d DT_{50} flooded field (water phase): 25.9 d DT_{50} sediment/water system: 25.9 d DT_{50} sediment: 25.9 d Kinetic: 1st order, lab data K_{oc}: 320 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: 4.5 g a.s./ ha

PEC_{pw} initial (maximum) (µg/L)	Clay scenario	Sand scenario
	0.85	1.42

Metabolite DesMe-2023 *(M06)*:

Method of calculation	MED-Rice, 2003 DT_{50} flooded field (total system): 25.9 d DT_{50} flooded field (water phase): 25.9 d DT_{50} sediment/water system: 25.9 d DT_{50} sediment: 25.9 d Kinetic: 1st order, lab data K_{oc}: 75 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: 13.2 g a.s./ ha

PEC_{pw} initial (maximum) (µg/L)	Clay scenario	Sand scenario
	6.55	8.76

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	MED-Rice, 2003 <u>Parent compound:</u> DT_{50} drained field: 8.7 d DT_{50} flooded field (total system): 22.1 d DT_{50} flooded field (water phase): 16.2 d DT_{50} sediment/water system: 22.1 d DT_{50} sediment: 22.1 d Kinetic: 1st order, field and lab data K_{oc}: 302 mL/g <u>Na-BX-180 *(M05)*:</u> DT_{50} flooded field (total system): 25.9 d DT_{50} flooded field (water phase): 25.9 d DT_{50} sediment/water system: 25.9 d DT_{50} sediment: 25.9 d Kinetic: 1st order, lab data K_{oc}: 320 mL/g <u>DesMe-2023 *(M06)*:</u> DT_{50} flooded field (total system): 28.3 d DT_{50} flooded field (water phase): 28.3 d DT_{50} sediment/water system: 28.3 d DT_{50} sediment: 28.3 d Kinetic: 1st order, lab data K_{oc}: 75 mL/g
Application rate	Crop: rice no crop interception Numbers of application: 1 Interval: - Application rate: parent 30 g a.s./ ha[a)] a) = The soil residue of KIH 2023 three days after application (at the time of flooding) was calculated from the maximum application rate and the aerobic soil DT^{50} of 8.7 days, yielding 23.6 g a.s./ha. That residue was used as effective application rate of KIH 2023 for the purpose of PEC calculations according to MED-Rice. M05: 4.5 g/ha

	M06: 13.2 g/ha
$PEC_{(gw)}$	
Maximum concentration	see detailed results in table below
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	see detailed results in table below

PEC(gw) - FOCUS modelling results (based on MED-Rice calculations!)

Model /Crop	Scenario	Parent (µg/l)	Metabolite (µg/l)		
			M05	M06	-
	Rice, clay scenario	< 0.001	< 0.001	< 0.001	-
	Rice, sand scenario	<0.001	<0.001	0.0893	

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

Direct photolysis in air ‡	Not studied – no data requested
Quantum yield of direct phototransformation	parent: Φ = 0.0064
Photochemical oxidative degradation in air ‡	Half-life: 0.8 hours Chemical lifetime: 1.2 hours derived by the Atkinson method of calculation.* *The basis for the assessment was 12-hrs day concentration of 1.5 E6 OH radicals /cm³
Volatilization ‡	from plant surfaces: ‡ Guideline not yet available
	from soil: ‡ Guideline not yet available

PEC (air)

Method of calculation	Guideline not yet available (Vapour pressure: 5.05 x 10^{-9} Pa (at 25°C) Henry Law Constant: 3 x 10^{-11} pa x m³/mol (at 25°C))

$PEC_{(a)}$

Maximum concentration	Guideline not yet available

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**Soil** Definition for risk assessment: bispyribac and their salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05, M03 (from field studies) and M04 (only under anaerobic conditions). Definition for monitoring: Bispyribac and its salts expressed as bispyribac-sodium **Water** **Ground water** Definition for exposure assessment: bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05, M03, M10 and M04. Definition for monitoring: Pending the finalization of the assessment. **Surface water** Definition for risk assessment: bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06. Definition for monitoring: Bispyribac and its salts expressed as bispyribac-sodium, M01 and its salts expressed as M06, M02 and its salts expressed as M05. **Air** Definition for risk assessment: bispyribac and its salts expressed as bispyribac-sodium Definition for monitoring: Bispyribac and its salts expressed as bispyribac-sodium

M05 = NA-BX-180 or the corresponding carbonic acid BX-180 *(M02)*
M06 = DesMe-2023 or the corresponding carbonic acid DesMe-5750 *(M01)*
M10 = Na-DesMe-180 or the corresponding carbonic acid DesMe-180 *(M09)*

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

Soil (indicate location and type of study)	Not applicable (new substance)
Surface water (indicate location and type of study)	Not applicable (new substance)
Ground water (indicate location and type of study)	Not applicable (new substance)
Air (indicate location and type of study)	Not applicable (new substance)

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	N, R 53

Effects on Non-target Species

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

Acute toxicity to mammals	(rat) LD_{50} 2635 mg a.s./kg bw
Acute toxicity to birds (a.s.)	(quail) LD_{50} > 2250 mg/kg bw
Acute toxicity to birds (SC 400)	(quail) LD_{50} > 2000 product/kg bw equivalent to > 727mg a.s.//kg bw
Dietary toxicity to birds	(quail) LC_{50} > 5620 mg a.s./kg diet equivalent to >2081 mg a.s./kg bw
Dietary toxicity to birds	(duck) LC_{50} > 5620 mg as/kg diet equivalent to > 2057 mg a.s./kg bw
Reproductive toxicity to birds	(quail) NOEC 1000 mg as/kg diet equivalent to 116 mg a.s./kg bw
Reproductive toxicity to mammals	(rat, 2-generation) NOAEC 1000 mg a.s./kg diet equivalent to 50 mg a.s./kg bw

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.03	rice	Large herbivorous bird	acute	> 1067	10
			short-term	> 2057	10
			long-term	217	5
0.03	rice	Large insectivorous bird	acute	> 1233	10
			short-term	> 2273	10
			long-term	128	5
0.03	rice	Small herbivorous mammal	acute	445	10
			long-term	29.8	5
0.03	rice	Insectivorous mammal	acute	10135	10
			long-term	521	5

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests				
Rainbow trout (*Oncorhynchus mykiss*)	Bispyribac-sodium	96 h (acute)	LC_{50}	> 95 [a]
Rainbow trout (*Oncorhynchus mykiss*)	Bispyribac-sodium SC 400	96 h (acute)	LC_{50}	> 35.6 [a] (> 100mg prod:/L)
Bluegill sunfish (*Lepomis macrochirus)*	Bispyribac-sodium	96 h (acute)	LC_{50}	> 95 [a]
Fathead minnow *(Pimephales promelas)*	Bispyribac-sodium	32 d (chronic)	NOEC	≥10 [a]
Daphnia magna	Bispyribac-sodium	48 h (acute)	EC_{50}	> 95 [a]
Daphnia magna	Bispyribac-sodium SC 400	48 h (acute)	EC_{50}	> 35.6 [a] (> 100mg prod:/L)
Daphnia magna	Bispyribac-sodium	21 d (chronic)	NOEC	110 [b]
Lymnaea stagnalis	Bispyribac-sodium	41 d (chronic)	NOEC	≥10 [a]
Chironomus riparius	Bispyribac-sodium	28 d (chronic)	EC_{50}	> 105 [a]
Freshwater algae *(Pseudokirchneriella spp.)*	Bispyribac-sodium	72 h (chronic)	E_rC_{50} [f] E_bC_{50}	2.08 [a] 0.83 [a]
Freshwater algae *(Selenastrum spp.)*	Bispyribac-sodium SC 400	72 h (chronic)	E_rC_{50} [f] E_bC_{50}	3.82 [a] (11.2mg prod./L) 1.5 [a] (4.4 mg prod./L)
Freshwater blue- green algae *(Anabaena spp.)*	Bispyribac-sodium 80 S	120 h (chronic)	E_rC_{50}	> 1.0 [b]
Freshwater diatom *(Naviculla pelliculosa)*	Bispyribac-sodium 80 S	120 h (chronic)	E_rC_{50}	> 1.0 [b]
Marine diatom *(Skeletonema costatum)*	Bispyribac-sodium 80 S	120 h (chronic)	E_rC_{50}	> 1.1 [b]
Aquatic Plant (*Lemna gibba)*	Bispyribac-sodium	7 d (chronic)	E_rC_{50} E_bC_{50}	0.0127 [a] 0.0204 [a]
Aquatic Plant (*Lemna gibba)*	Bispyribac-sodium SC 400	7 d (chronic)	E_rC_{50} [d] E_bC_{50} [e]	0.0167 [b] (0.0566 mg prod./L) 0.0112 [b] (>0.036 mg prod./L)

a: endpoint related to nominal concentrations
b: endpoint related to mean measured concentrations
d: based on frond number
e: based on dry weights
f: value used for risk assessment as exponential growth fullfilled (OECD Guideline 201, draft 2002)
g: value used for risk assessment as exponential growth fullfilled (OECD Guideline 221, draft 2002)

Metabolites

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Aquatic Plant	DesMe-2023 (M06)	7 d (chronic)	E_rC_{50}	0.098 [b, d]

(Lemna gibba)			E_bC_{50}	0.23 [b, d]
Aquatic Plant (Lemna gibba)	Na-BX-180 (M05)	7 d (chronic)	E_rC_{50} [c] E_bC_{50}	0.0126 [b, e] 0.0089 [b, e]
Aquatic Plant (Lemna gibba)	MeBA (M04)	7 d (chronic)	E_rC_{50} [c] E_bC_{50}	17.2 [a] 7.66 [a]
Aquatic Plant (Lemna gibba)	DesMe-180 (M09)	7 d (chronic)	E_rC_{50} E_bC_{50}	3.1 [b, d] 5.0 [b, d]
Chironomus riparius	DesMe-180 (M09)	28 d (chronic)	EC_{50}	> 100 [a]
Microcosm or mesocosm tests				
Not applicable				

a: endpoint related to nominal concentrations
b: endpoint related to mean measured concentrations
c: value used for risk assessment as exponential growth fullfilled (OECD Guideline 221, draft 2002)
d: the metabolite resulted highly instable under test conditions
e: the metabolite resulted slightly instable under test conditions

Toxicity/exposure ratios for aquatic species

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

Application rate (kg as/ha)	Crop/ formulation	Organism	Time-scale	Initial PECsw (µg as / L)	TER*	Annex VI Trigger
0.03	Rice, a.s.	*Oncorhynchus mykiss*	96 h (acute)	0.61	> 155738	100
0.03	Rice, SC400	*Oncorhynchus mykiss*	96 h (acute)	0.61	> 58361	100
0.03	Rice, a.s.	*Pimephales promeleas*	32 d (chronic)	0.61	16393	10
0.03	Rice, a.s.	*Daphnia magna*	48 h (acute)	0.61	> 155738	100
0.03	Rice, SC400	*Daphnia magna*	48 h (acute)	0.61	> 58361	100
0.03	Rice, a.s.	*Daphnia magna*	21 d (chronic)	0.61	180328	10
0.03	Rice, a.s.	*Lymnaea stagnalis*	41 d (chronic)	0.61	16393	10
0.03	Rice, a.s.	*Chironomus riparius*	28 d (chronic)	0.61	> 172131	10
0.03	Rice, a.s.	*Pseudokirchneriella subcapitata*	72 h (chronic) EbC50	0.61	1360	10
0.03	Rice, SC400	*Selenastrum capricornutum*	72 h (chronic) EbC50	0.61	2459	10
0.03	Rice, a.s.	*Anabaena flos-aquae*	120 h (chronic)	0.61	> 1639	10
0.03	Rice, a.s.	*Lemna gibba*	7 d (chronic)	0.61	20.82	10
0.03	Rice, SC400	*Lemna gibba*	7 d (chronic)	0.61	18.4	10

* Worst-case scenario assuming the initial PECsw of the parent compound resulting from rice paddy field outflow + drift 1m.

Toxicity/exposure ratios for the most sensitive aquatic organisms in surface water – potential ecotoxicologically relevant aquatic metabolites (indicator species Lemna gibba as most sensitive aquatic organism) (Annex IIIA, point 10.2)

Name	Crop	Organism	Time-scale	Initial PECsw (µg as / L)	TER [a]	Annex VI Trigger
DesMe-2023 (M06)	rice	*Lemna gibba*	7 d (chronic)	0. 73 [c]	134	10
MeBA (M04)	rice	*Lemna gibba*	7 d (chronic)	0.61 [b]	12557	10
DesMe-180 (M09)	rice	*Lemna gibba*	7 d (chronic)	0.61 [b]	5082	10
Na-BX-180 (M05)	rice	*Lemna gibba*	7 d (chronic)	0.12 [c]	74	10

[a] E_rC_{50} values used for TERcalculation;
[b] Worst-case scenario assuming the initial PECsw of the parent compound resulting from rice paddy field outflow as being representative for the initial PECsw of the metabolites.
[c] $PECs_w$ for M05 and M06 recalculated in March 2009

Toxicity/exposure ratios in surface water – potential ecotoxicologically relevant sediment metabolites

Name	Crop	Organism	Time-scale	Initial PECsw (µg as / L)	TER*	Annex VI Trigger
DesMe-180	rice	*Chironomus riparius*	28 d (chronic)	0.61	> 163934	10

* Worst-case scenario assuming the initial PECsw of the parent compound resulting from rice paddy field outflow as being representative for the initial PECsw of the metabolites.

Toxicity/exposure ratios for the most sensitive aquatic organisms in paddy water (pw) (Annex IIIA, point 10.2)*

Application rate (kg as/ha)	Crop	Organism	Time-scale	Initial PECpw (µg as / L)	TER*	Annex VI Trigger
0.03	rice	*Oncorhynchus mykiss*	96 h (acute)	7.77	> 12226	100
0.03	Rice, SC400	*Oncorhynchus mykiss*	96 h (acute)	7.77	> 4582	100
0.03	rice	*Pimephales promeleas*	32 d (chronic)	7.77	1287	10
0.03	rice	*Daphnia magna*	48 h (acute)	7.77	> 12226	100

0.03	Rice, SC400	*Daphnia magna*	48 h (acute)	7.77	> 4582	100
0.03	rice	*Daphnia magna*	21 d (chronic)	7.77	14157	10
0.03	rice	*Chironomus riparius*	28 d (chronic)	7.77	> 13513	10

* The risk to plants (algae and higher plants) were not considered as bispyribac-sodium is a herbicide

Toxicity/exposure ratios for the most sensitive aquatic organisms in paddy water (pw) – potential ecotoxicologically relevant aquatic metabolites*

Name	Crop	Organisme	Time-scale	Initial PECpw (µg / L)	TER [a]	Annex VI Trigger
DesMe-2023 (M06)	Rice	*Oncorhynchus mykiss*	96 h (acute)	8.76 [c]	1223	10
		Daphnia magna	48 h (acute)	8.76 [c]	1223	
MeBA (M04)	Rice	*Oncorhynchus mykiss*	96 h (acute)	7.77 [b]	1223	10
		Daphnia magna	48 h (acute)	7.77 [b]	1223	
DesMe-180 (M09)	Rice	*Oncorhynchus mykiss*	96 h (acute)	7.77 [b]	1223	10
		Daphnia magna	48 h (acute)	7.77 [b]	1223	
Na-BX-180 (M05)	Rice	*Oncorhynchus mykiss*	96 h (acute)	1.42 [c]	6690	10
		Daphnia magna	48 h (acute)	1.42 [c]	6690	10

* EFSA revised the risk assessment for metabolites in paddy water after the peer review, to be in line with the in-field risk assessment of the parent substance, i.e. risk to plants (algae and higher plants) were not considered as bispyribac-sodium is a herbicide.
a: Assuming a 10-fold higher toxicity for the metabolite than for the parent
b: Worst-case scenario assuming the initial PECpw (PEC paddy water) of the parent compound as being representative for the initial PECpw of the metabolites.
c: PEC_{pw} for M05 and M06 was recalculated in March 2009 (after finalizing the peer review).

Toxicity/exposure in paddy water – potential ecotoxicologically relevant sediment metabolite

Name	Crop	Organism	Time-scale	Initial PECpw (µg as / L)	TER	Annex VI Trigger
DesMe-180 (M09)	rice	*Chironomus riparius*	28 d (chronic)	7.77 [a]	> 12870	10

[a] Worst-case scenario assuming the initial PEC_{pw} of the parent compound resulting from rice paddy field outflow as being representative for the initial PEC_{pw} of the metabolites.

Bioconcentration

Bioconcentration factor (BCF)	not relevant as log Pow for bispyribac-sodium and all ecotoxicological relevant metabolites is < 3.
Annex VI Trigger for the bioconcentration factor	not relevant
Clearance time (CT_{50}) (CT_{90})	not relevant
Level of residues (%) in organisms after the 14 day depuration phase	not relevant

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

Acute oral toxicity (48 h)	LD50: > 140.67 µg a.s./bee
Acute oral toxicity (SC 400) (48 h)	LD50: > 106.72 µg a.s./bee
Acute contact toxicity (48 h)	LD50: > 200 µg a.s./bee
Acute contact toxicity (SC 400 (48 h)	LD50: > 200 µg a.s./bee

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.03	rice	oral	< 0.28	50
0.03	rice	contact	< 0.15	50

Field or semi-field tests
Not required

Effects on other arthropod species in laboratory tests (IIA, 8.3.2 and IIIA, 10.5.1)

Species	Stage	Test substance	Appl. rate in test (g as/ha)	Corrected mortality M %	Reproductive performance after 7 days R %	Reduction of beneficial effect E (%)	Classification IOBC
Aphidius rhopalosiphi	Adults	Bispyribac-sodium SC 400	0.3	12.2	75.1	34.06	Harmless
			3.0	0	45.1[(b)]	54.9	
			30.0	4.1	93.6	10.24	
Typhlodromus pyri	Adults	Bispyribac-sodium SC 400	0.3	1	78	22.78	Harmless
			3.0	6	83[(a)]	21.98	
			30.0	5	95	9.75	
Chrysoperla carnea	Larvae	Bispyribac-sodium SC 400	0.3	2.1	72.19	29.33	Harmless
			3.0	4.2	84.44	19.11	
			30.0	18.8[(b)]	92.38	24.99	
Pardosa ssp.	Adults	Bispyribac-sodium SC 400	30	0	-		Harmless

(a) calculated after 5 days

(b) statistically significant compared to the control

Field or semi-field tests Not required

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

Acute toxicity (a.s.)	LC_{50} >957 mg a.s./kg d.wt.s.
Acute toxicity (400SC)	LC_{50} >340 mg a.s./kg d.wt.s.

Metabolites: (Earthworm):

Acute toxicity metabolite DesMe-2023 (M06)	LC_{50} > 855 mg p.m./kg d.wt.s.
Acute toxicity metabolite Na-BX-180 (M05)	LC_{50} > 890 mg p.m./kg d.wt.s.

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

Application rate (kg as/ha)	Crop / formulation	Time-scale	Initial PECs related to 5 cm soil depth (mg /kg dw)	TERa	Annex VI Trigger
0.03	Rice (a.s.)	acute	0.0251	>38127	10
0.03	Rice (SC 400)	acute	0.0251	>13545	10
Metabolites: (Earthworm): **DesMe-2023 (M06)**					
0.03	rice	acute	0.0062	>137903	10
Metabolites: (Earthworm): **Na-BX-180 (M05)**					
0.03	rice	acute	0.0015	>593333	10

Effects on Folsomia candida (Annex IIA, point 8.6)

Chronic toxicity 28d (DesMe-2023)	NOEC 85.5 mg p.m./kg d.wt.s.
Chronic toxicity 28d (Na-BX-180)	**NOEC 3.08 mg p.m./kg d.wt.s.**

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

Appl. rate (kg a.s./ha)	Test subst	NOEC (mg /Kg dw)	Initial PECs related to 5 cm soil depth (mg /kg dw)	TERlt	Annex VI Trigger
0.03	DesMe-2023	85.5	0.0062	13790	10
0.03	Na-BX-180	3.08	0.0015	2053	10

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

Nitrogen mineralization (a.s.)	No effects up to 0.15 kg a.s./ha (= 5 x field rate)
DesMe-2023 (M06)	No effects up to 0.15 kg p.m./ha (= 5 x field rate)
Na-BX-180 (M05)	No effects up to 0.1 kg p.m./ha (= 3 x field rate)
Carbon mineralization (a.s.)	No effects up to 0.15 kg a.s./ha (= 5 x field rate)

Effects on non-target terrestrial plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

(most sensitive species and most sensitive parameters)

Test	Most sensitive species	Test-substance	End-point (plant dry weight) g a.s/ha
Seedling emergence	Lettuce	Bispyribac-sodium SC 400	EbC50 1.9
Seedling emergence	Lettuce	Bispyribac-sodium WP 80	EbC50 3.58
Vegetative vigor	Radish	Bispyribac-sodium SC 400	EbC50 0.18
Vegetative vigor	Radish	Bispyribac-sodium WP 80	EbC50 1.57

Toxiciy exposure ratios of Bispyribac-sodium for non-target terrestrial plants (according to Guidance Document on terrestrial ecotoxicology SANCO/10329/Oct.2002 and EPPO Environmental risk assessment scheme Chap. 12, Non target terrestrial higher plants, Draft Sept. 2002)

Tier 1 risk assessment

TER values based on worst toxicity value of the most sensitive species from the studies with the two formulated products

Application rate (g as/ha)	**Most sensitive species**	**Distance from treated area** (m)	**PEC_{drift}** (g a.s./ha)	**E_bC_{50}** (g a.s./ha)	**TER**	**Trigger**
Vegetative vigour						
30	Radish	1	0.831	0.18	**0.2**	5
30	Radish	10	0.087	0.18	**2.1**	5
30	Radish	20	0.045	0.18	**4.0**	5
30	Radish	30	0.03	0.18	6.0	5
Seedling emergence						
30	Lettuce	1	0.831	1.9	**2.3**	5
30	Lettuce	5	0.171	1.9	11.1	5

- **Ecotoxicologically relevant compounds** (see EPCO Manual page 112)**:**

Compartment	
soil	Bispyribac and its salt, expressed as bispyribac-sodium
water	Bispyribac and its salt, expressed as bispyribac-sodium
sediment	Bispyribac and its salt, expressed as bispyribac-sodium
groundwater	Bispyribac and its salt, expressed as bispyribac-sodium

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10)

Active substance	**N, R 50/53**
Preparation	**N, R50*/53**

* EFSA proposes classification of R50 for Nominee based on the Lemna formulation toxicity study.

Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Absorption complete and rapid (peak plasma levels within 15 min to 1h after dosing), some saturation of absorptive processes evident (30 mg/kg bw)
Distribution ‡	primarily to liver, lung (and plasma); considerable radioactivity in GIT at sacrifice
Potential for accumulation‡	none
Rate and extent of excretion ‡	rapid, extensive (>90%); primary route: faecal, mainly by biliary excretion (~80% in males and 50% in females) secondary route: urinary (10% in males, 30% in females)
Metabolism in animals ‡	Limited metabolism: bispyribac-sodium is the major component in all media except male mice urine. Six metabolites formed, none of them major. Demethylation is the primary metabolic pathway, leading to the primary metabolite DesMe-2023/DesMe-5750 (*M06/M01*); M06 was the primary component in male mouse urine
Toxicologically relevant compounds (animals and plants) ‡	Bispyribac (and bispyribac-sodium)
Toxicologically relevant compounds (environment)	Bispyribac and its salt, expressed as bispyribac-sodium

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	2635 mg/kg bw
Rat LD_{50} dermal ‡	> 2000 mg/kg bw
Rat LC_{50} inhalation ‡	> 4.48 mg/l/4 h (whole body, dust exposure)
Skin irritation ‡	Non-irritant
Eye irritation ‡	Non-irritant
Skin sensitization (test method used and result) ‡	Sensitiser (Magnusson & Kligman Test); R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver/ bile duct proliferation (rat, mouse and dog) Red blood cells (rat)
Relevant oral NOAEL ‡	7.2 mg/kg bw/d (90-d rat) 10 mg/kg bw/d (52-wk dog) 6.8 mg/kg bw/d (90-d mouse)
Relevant dermal NOAEL ‡	1000 mg/kg bw/d (21-d rat, highest dose tested)
Relevant inhalation NOAEL ‡	No data – not required

Genotoxicity (Annex IIA, point 5.4) ‡	No genotoxic potential

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

Target/critical effect ‡	Liver, red blood cells (rats and mice)
Relevant NOAEL ‡	1.1 mg/kg bw/d (2-yr rat) 14.1 mg/kg bw/d (104-wk mouse)
Carcinogenicity ‡	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	No reproductive toxicity. Liver and bile ducts in

	parents. Reduced body weights in pups.
Relevant parental NOAEL	1 mg/kg bw/d
Relevant reproductive NOAEL	>500 mg/kg bw/d (highest dose tested)
Relevant offspring NOAEL	50 mg/kg bw/d
Developmental toxicity	
Developmental target / critical effect	No developmental toxicity or teratogenicity. Reduction in maternal body weight gain.
Relevant maternal NOAEL	Rat: 300 mg/kg bw/d Rabbit: 100 mg/kg bw/d
Relevant developmental NOAEL	Rat: 1000 mg/kg bw/d (highest dose tested) Rabbit: 300 mg/kg bw/d (highest dose tested)

Neurotoxicity (Annex IIA, point 5.7) ‡

Testing not necessary. No indications of neurotoxicity.

Other toxicological studies (Annex IIA, point 5.8) ‡

Metabolites	Low acute oral toxicity of metabolites M2, M3, M4, M6, M8 and M9 (LD_{50}>4000 mg/kg bw) All were negative in genotoxicity studies (Ames test)
Mechanistic studies	Measurements of bile acids in serum, studies of gall bladder and bile duct changes: limited value.

Medical data (Annex IIA, point 5.9) ‡

No adverse effects on human health in manufacturing personnel

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/d	rat, 2-yr and 2-generat° studies	100
AOEL ‡	0.072 mg/kg bw/d	rat, 90-d study	100
ARfD ‡	Not allocated – not necessary		

Dermal absorption (Annex IIIA, point 7.3) ‡

No data; a default dermal absorption value of 100% was used for the calculations

Acceptable exposure scenarios (including method of calculation)

Operator	With German model: exposure is 54% of the AOEL without PPE, 7% with PPE With UK POEM model: exposure is 530% of the AOEL without PPE, 43% with PPE
Workers	Exposure not expected in the period following ttmt
Bystanders	0.4% of the AOEL (Ganzelmeier, 1995)

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Xi; R 43; May cause sensitisation by skin contact

Residues

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

Plant groups covered	Rice
Rotational crops	Wheat, radish and soybean
Plant residue definition for monitoring	bispyribac and its salt expressed as bispyribac-sodium
Plant residue definition for risk assessment	bispyribac and its salt expressed as bispyribac-sodium
Conversion factor (monitoring to risk assessment)	n/a

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

Animals covered	Ruminants: lactating goat Poultry: laying hen
Animal residue definition for monitoring	no residue definition required as intake by livestock is below 0.1mg/kg diet
Animal residue definition for risk assessment	no residue definition required as intake by livestock is below 0.1mg/kg diet
Conversion factor (monitoring to risk assessment)	n/a
Metabolism in rat and ruminant similar (yes/no)	Yes. Since metabolic pattern in the lactating goat is very similar to that in the rat, a pig metabolism study is not required.
Fat soluble residue: (yes/no)	no

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

.....	Wheat, radish and soybean. Uptake of radioactive substances from treated soil (2.25 x proposed maximum field rate) after 30-day re-plant of rotational crops leads to maximum residues (TRR) in all tested crops/matrices below 0.01 mg/kg. 120-day samples were not analyzed, and the originally-scheduled planting 360 days after treatment was not carried out, as none of these activities were triggered. No residues above 0.01 mg/kg expected in rotational crops.

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

.....	Stable 1 year (green plant materials) 8 months (grain and straw)

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

	Ruminant: yes/no	Poultry: yes/no	Pig: yes/no
Intakes by livestock ≥ 0.1 mg/kg diet/day:	no	no	no

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Rice	Mediterr. EU	8 x <0.02 mg/kg in grain 8 x <0.02 mg/kg in straw		0.02 mg/kg	0.02 mg/kg

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

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

ADI	0.01 mg/kg bw/day
TMDI (European Diet) (% ADI)	<1% (WHO / 60 kg person); <1% in all populations (PSD / 70.1 kg adult, 43.6 kg child, 8.7 kg toddler / 97.5th percentile diet)
NEDI (% ADI)	n/a
Factors included in NEDI	n/a
ARfD	Not allocated, not necessary
Acute exposure (% ARfD)	n/a

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
not applicable; no study conducted	n/a	n/a	n/a

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

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

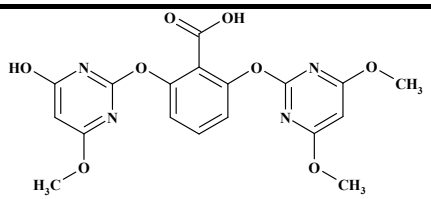
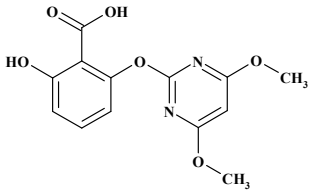
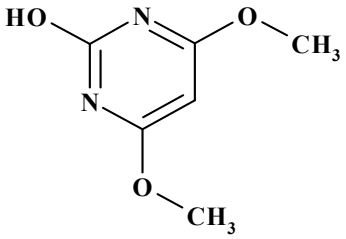
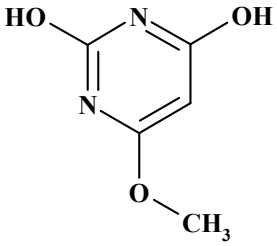
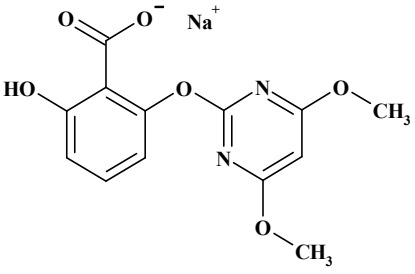
Rice grain	0.02 mg/kg (LOQ)

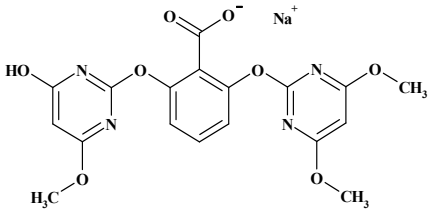
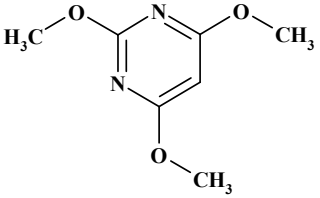
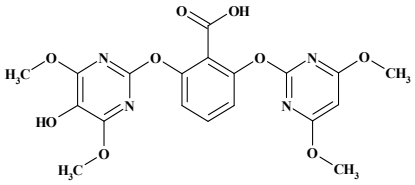
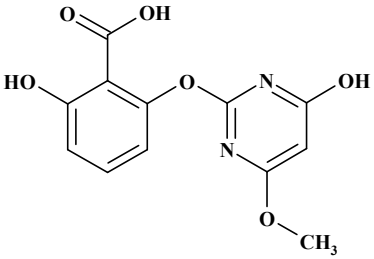
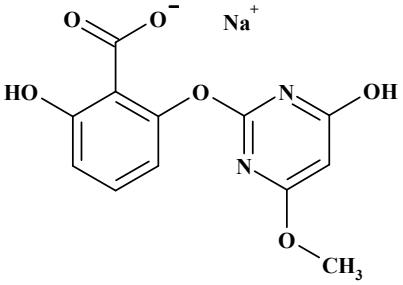
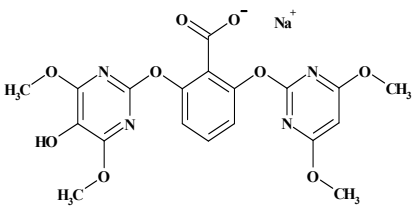
APPENDIX B – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

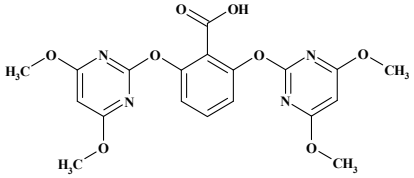
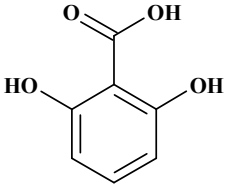
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstragct
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
EU	European Union
F_2	filial generation, second
FAO	Food and Agriculture Organisation of the United Nations
FIA	fluorescence immuno assay
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
Ha	Hectare
HC5	Hazardous Concentration 5%
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-DAD	high performance liquid chromatography with diode array detection
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
	lethal concentration, median
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
kg	kilogram
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
HPLC-DAD	high performance liquid chromatography with diode array detection
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mg	milligram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry

n/a	not applicable
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
Ppp	plant protection product
QSAR	quantitative structure activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name (CAS)	Structural formula
M01, DesMe5750, KIH-2023-M-1	2-(4,6-dimethoxypyrimidin-2-yl)oxy-6-(4-hydroxy-6-methoxypyrimidin-2-yl)oxybenzoic acid	
M02 BX-180 KIH-2023-M-2 PHU 1240	2-(4,6-dimethoxypyrimidin-2-yl)oxy-6-hydroxy benzoic acid	
M03 Me2BA KIH-2023-M3 FHW 0111H M15876 PHU 1305	2-hydroxy-4,6-dimethoxypyrimidine	
M04 MeBA FHW 0111I KIH-2023-M-4 M15877	2,4-dihydroxy-6-methoxypyrimidine	
M05 Na-BX-180 BX-180-Na FHW 0111G KIH-2023-M-2-Na M2-Na M18558	benzoic acid, 2-[(4,6-dimethoxy-2-pyrimidinyl)oxy]-6-hydroxy, sodium salt	

Code/Trivial name	Chemical name (CAS)	Structural formula
M06 DesMe-2023 KIB-8651 FHW 0111F KIH-2023-M-1-Na M01-Na M18558	benzoic acid, 2-[(4,6-dimethoxy-2-pyrimidinyl)oxy]-6-[(4-hydroxy-6-methoxy-2-pyrimidinyl)oxy], sodium salt	
M07 Me3BA FHW 0112A KIH-2023-M-7	2,4,6-trimethoxypyrimidine	
M08 5-OH-5750 KIH-2023-M-8	2-(4,6-dimethoxy-5-hydroxypyrimidin-2-yl)oxy-6-(4,6-dimethoxypyrimidin-2-yl)oxybenzoic acid	
M09 DesMe-180 FHW 0112B KIH-2023-M-9 M18537	2-hydroxy-6-[(4-hydroxy-6-methoxypyrimidin-2-yl)oxy] benzoic acid	
M10 Na-DesMe-180 M-9-Na	sodium 2-hydroxy-6-(4-hydroxy-6-methoxypyrimidin-2-yl)oxybenzoate	
M11 5-OH-2023 M-8-Na	sodium 2-(4,6-dimethoxy-5-hydroxypyrimidin-2-yl)oxy-6-(4,6-dimethoxypyrimidin-2-yl)oxybenzoate	

Code/Trivial name	Chemical name (CAS)	Structural formula
M12 KIA-5750 KIH2023-free acid M12433	benzoic acid, 2,6-bis[(4,6-dimethoxypyrimidin-2-yl)oxy]	
M13 2,6-DBA γ-resorcyclic acid FHW 0110H	2,6-dihydroxybenzoic acid	
M17 Glu-DesMe-5750 KIH-2023-M-17	2-(4,6-dimethoxypyrimidin-2-yl)oxy-6-(4-ß-D-glucopyranosyl-oxy-6-methoxypyrimidin-2-yl)oxy benzoic acid