PEER REVIEW REPORT ON **PYRIPROXYFEN** 12 02 2009

TABLE OF CONTENTS

Comments on the Draft Assessment Report on pyriproxyfen (EAS)

RMS NL

End of commenting period: 06 October 2006 (MS, NOT)

Date	Supplier	File
29.09.2006	Notifier	01 pyriproxyfen comments NOT 2006-09-29.doc
29.09.2006	Notifier	02 pyriproxyfen comments NOT 2006-09-29.doc
06.10.2006	The United Kingdom	03 pyriproxyfen comments UK 2006-10-06.doc
09.10.2006	Austria	04 pyriproxyfen comments AT 2006-10-09.doc
11.10.2006	Germany	05 pyriproxyfen comments DE 2006-10-11.doc
20.03.2007	EFSA	06 pyriproxyfen comments EFSA 2007-03-20.doc

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

1. Identity (B.1)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, Level 4, 4.1 Identity of the active substance (page 145)	Notifier: 'See 4.5' should read 'Sufficient information is submitted'.	

2. Physical/Chemical Properties (B.2)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, Level 2, 2.1.2 Physical and chemical properties (page 13)	Notifier: The new GLP studies for relative density, spectra (IR, ^{1}H-NMR and Mass), water solubility at pHs 5, 7 and 9, and partition coefficient at pHs 5, 7 and 9 were submitted to the RMS in January 2006.	These studies were initiated following the completeness check.
(2)	Vol. 1, Level 2, Appendix 3, List of endpoints, relative density (page 94) Vol. 3, Table B.2.1, B.2.1.4 relative density	Notifier: A new GLP study (NNP-0102) was submitted to the RMS in January 2006. The relative density was measured using the air comparison pycnometer method (OECD 109). The result is as follows; D_4^{20} = 1143 kg/m^3	This study was initiated following the completeness check.

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No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Vol. 3, Table B.2.1, B.2.1.10 spectra	Notifier: A new GLP study (NNP-0104) was submitted to the RMS in January 2006. The study includes IR, ^{1}H-NMR and Mass spectra to confirm the spectroscopic properties of pyriproxyfen.	This study was initiated following the completeness check.
(4)	Vol. 1, Level 2, Appendix 3, List of endpoints, solubility in water (page 95) Vol. 3, Table B.2.1, B.2.1.11 solubility in water	Notifier: A new GLP study (NNP-0105) was submitted to the RMS in January 2006. The water solubility was measured at different pHs using the column elution method (OECD 105). The results are as follows; Water solubility at 20±0.5°C = 0.058 mg/L at pH5 0.101 mg/L at pH 7 0.119 mg/L at pH 9 These data indicate that the water solubility is independent of pH in the environmental range.	This study was initiated following the completeness check.

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(5)	Vol. 1, Level 2, Appendix 3, List of endpoints, partition co-efficient (page 95) Vol. 3, Table B.2.1, B.2.1.13 partition coefficient	Notifier: A new GLP study (NNP-0103) was submitted to the RMS in January 2006. The *n*-octanol/water partition coefficient was measured at different pHs using the HPLC method (OECD 117). The results are as follows; Log Pow = 4.85 at pH5 4.86 at pH 7 4.87 at pH 9 These data indicate that the partition coefficient is independent of pH in the environmental range.	This study was initiated following the completeness check.
(6)	Vol. 2, A.2 Physical and chemical properties Vol. 3, B.2.3 References relied on	Notifier: The following four new studies submitted to the RMS in January 2006 should be added in the reference lists; - Report No. NNP-0102 (Relative Density) - Report No. NNP-0104 (Spectroscopic Properties (IR, NMR, MS)) - Report No. NNP-0105 (Water Solubility) - Report No. NNP-0103 (n-Octanol/Water Partition Coefficient)	

3. Data on application and further information (B.3)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations

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section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.3.2.7 Number and timing of applications and duration of protection afforded (Annex IIIA 3.7), Remark (page 20)	Notifier: In document M-III, Notifier mentioned 7 - 15 days between the two applications, taking account that in practice, farmers would judge the efficacy of the first application and they might not perform the second application until they see that the pest population is recovering. However, considering the consistencies with the interval 10 days as in the GAP, Notifier does not object to replacing the interval of 7 to 15 days, as mentioned in document M-III, with 10 days.	

4. Proposal for classification and labelling (B.4)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.1, Level 3, cover page (page 141)	Notifier: 'Safety phrase: S60, S61' should not appear on page 141. The document should be re-formatted such that the safety phrases appear on the previous page (page 140).	

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5. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.1, Level 2, 2.3.1.1 Toxicokinetics, Absorption Vol. 1, Level 2, Appendix 3, Rate and extent of absorption Vol. 3, B.6.1 Absorption, distribution, excretion and metabolism (Absorption rate)	Notifier: Pages 17, and 102 (Vol.1) and pages 57, 70, 144, and 155 (Vol.3): Notifier considers that the oral absorption rate of 63% proposed in the dossier is already a worst case estimate. The value of 40% is not consistent with the data and is unnecessarily conservative. As unchanged pyriproxyfen was not eliminated in bile the pyriproxyfen in faeces is the unabsorbed dose and this can be used to calculate absorption. This is a more scientific approach as it avoids mixing data from different experiments.	The basis for the calculation of the amount of the low and high dose absorbed should be made more clear in the DAR. In particular, the problem which arises from the lack of a determination of radioactivity in the residual carcass at the end of the bile fistula experiment should be stated. On page 57 the absorption of 39-49% is said to be based on radioactivity recovered from urine, bile and tissues whereas on page 70 and page 144 the same range is quoted based on urine, CO_2, tissues, cage wash, residual carcass and bile. The values used to calculate absorption and the experiments from which they are taken need to be explained in more detail. For highly lipophilic compounds, lower oral absorption can be observed with bile-duct cannulated rats compared with normal rats because of a shortage of bile acid or slow gastrointestinal motility caused by physical restraint of rats. As unchanged pyriproxyfen was not eliminated in bile the pyriproxfen in faeces has not been absorbed whereas the metabolites in faeces of normal rats have been absorbed. This can be used as the basis of a more scientific approach for estimating absorption as it avoids mixing data from different experiments. Absorption rate (%) = dose (100%) - unabsorbed compound in normal rats (% of the dose) = dose (100%) - pyriproxyfen detected in faeces with normal rats (% of the dose) The amount of pyriproxyfen in faeces of rats was 21%-37.2% after single (2 or 1000 mg/kg) administration of [phenoxyphenyl-^{14}C]pyriproxyfen or [pyridyl-2,6-^{14}C]pyriproxyfen, and it was decreased to 6.5%-11.4% after repeated (2 mg/kg) administration.

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No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			Therefore, the absorption rate was 63%-79% after single administration and 89-93% after repeated administration to normal rats. Notifier considers that the oral absorption rate of 63% proposed in the dossier is already a worst case estimate. The proposed value of 40% is not consistent with the data and is unnecessarily conservative. Page 17 4th paragraph 1st sentence (Vol.1), page 102 (Vol.1), page 57 3rd paragraph 2nd sentence (Vol.3), page 70 1st paragraph 1st sentence (Vol.3) and page 144 2nd paragraph 1st sentence (Vol.3): Notifier considers that absorption was ca. 63% of the applied dose, based on the metabolites excreted in the urine, faeces, expired CO_2, tissues, cage wash and residual carcass. Page 18 1st paragraph (Vol.1), page 70 3rd paragraph (Vol.3) and page 144 4th paragraph (Vol.3): Notifier considers that for risk assessment purposes, 63% oral absorption is taken as a worst-case estimate. Therefore, the section of absorption in page 17 (Vol.1), page 70 (Vol.3) and page144 (Vol.3) should be changed as follows: As unchanged pyriproxyfen was not eliminated in bile in biliary excretion study, it was considered that the pyriproxfen in faeces of normal rats is unabsorbed compounds whereas the metabolites in faeces of normal rats are absorbed compounds. Based on this finding, the absorption was determined to be ca. 63% of the applied dose after single (2 or 1000 mg/kg) administration of [phenoxyphenyl-^{14}C] pyriproxyfen or [pyridyl-2,6-^{14}C] pyriproxyfen to rats, since 21-37.2% of the applied dose in faeces was unabsorbed pyriproxyfen. After repeated (2 mg/kg) oral administration of [phenoxyphenyl-^{14}C]

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			pyriproxyfen, absorption was ca. 89% at minimum since faecal pyriproxyfen was 6.5 - 11.4%. In mice absorption after a single dose of 2 or 1000 mg/kg was ca. 75% AR at minimum since faecal pyriproxyfen was 12 - 25%. For risk assessment purposes, 63% oral absorption is taken as a worst-case estimate.
(2)	Vol. 3, B.6.1 Absorption, distribution, excretion and metabolism and B.6.1.4 Summary and conclusions	Notifier: Page 17 4th paragraph (Vol.1), page 57 3rd paragraph (Vol.3), page 70 1st paragraph (Vol.3) and page 144 2nd paragraph (Vol.3): Notifier does not believe there is any evidence for a first pass effect and suggests this should be changed.	Notifier questions the conclusion concerning first pass metabolism. First pass metabolism is normally determined by measuring bioavailability following oral and intravenous administration, it is not clear how a conclusion concerning first pass metabolism has been determined from the data supplied. The use of the term first pass metabolism in this DAR may be inconsistent with the generally accepted definition of the term.
(3)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Short-term and semi-chronic toxicity Vol. 3, B.6.3.3 Subacute inhalation studies, STUDY 1 Vol. 3, B.6.3.5 Summary	Notifier: Page 21 4th paragraph (Vol.1), page 90, page 105 the last paragraph (Vol.3): Notifier considers that increased LDH and slight changes of some organs weights in male at 1000 mg/m^3 should be of little toxicological significance as described in the dossier (Document M-II) and the original report (Report No. NNT-80-0031). Therefore, Notifier thinks the description related to increased LDH, and changes of liver, spleen and lung weights in male at 1000 mg/m^3 should be deleted.	Notifier strongly believes that increased LDH and slight changes of some organs weights in male at 1000 mg/m^3 should be considered of little toxicological significance. These differences were marginal, showed no dose-dependency, were within physiological changes, and there were no related histopathological changes or no statistically significant changes.

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(4)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Short-term and semi-chronic toxicity Vol. 3, B.6.3.4 Semichronic oral studies, STUDY 4 Vol. 3, B.6.3.5 Summary	Notifier: Page 23 1st paragraph (Vol.1), pages 103 1st paragraph, page 107 2nd paragraph (Vol.3): Notifier suggests that the sentence of "Based on higher cholesterol levels and higher liver weights the NOAEL is set at <30 mg/kg bw/d for males and 30 mg/kg bw/d for females" should be changed as follows, "Based on slightly higher cholesterol levels and slightly higher liver weights the NOAEL is set at <30 mg/kg bw/d for males and 30 mg/kg bw/d for females".	Notifier considered that the changes of cholesterol levels and liver weights were slight or marginal in male at 30 mg/kg bw/d as described in the dossier (Document M-II) and the original report (Report No. NNT-11-0081).
(5)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity, STUDY 1	Notifier: Page 116 1st paragraph, page 119 1st paragraph (Vol.3): Notifier considers that this finding, "At post-mortem necropsy, an increased incidence of dark areas in the liver was noted in females at 3000 mg/kg food", was not treatment-related as described in the dossier (Document M-II) and the original report (Report No. NNT-11-0085 and NNT-41-0112). Therefore, Notifier thinks this sentence and the incidence of this finding in the table 6.5.1.1 should be deleted.	An increased incidence of dark area in the liver was noted in only females at 3000 mg/kg food and no histopathological changes related to this change were observed. Therefore, Notifier considers that this finding was not treatment-related.

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity, STUDY 1	Notifier: Page 116 2nd paragraph (Vol.3), page 119 1st paragraph: "Treatment-related histopathological changes were noted in the liver at 3000 mg/kg food. A slightly increased incidence of liver necrosis was noted in males at 3000 mg/kg that died during the study. Liver necrosis was only noted in one surviving animal at 600 mg/kg food." Notifier considers the sentences should be deleted, and the incidence of this finding in Table 6.5.1.1 should be also deleted.	It was generally secondary to some other cause of death and not treatment-related since no incidence of liver necrosis was noted in the rats sacrificed at week 53 and week 105 as described in the dossier (Document M-II) or the original report (Report No. NNT-11-0085 and NNT-41-0112). Moreover, percent of the incidence of liver necrosis is 13% for males and 8% for females. These are within the range of historical data (0.0-24.0% for males, 0.0-18.0% for females).
(7)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity, STUDY 1	Notifier: Page 116 3rd paragraph (Vol.3): Notifier suggests that the sentences of "Based on the decreased body weight gain the NOEL is set at 120 mg/kg food (equal to 5.4 mg/kg bw/day in males and 7.0 mg/kg bw/day in females). The NOAEL is set at 600 mg/kg food (equal to 27.2 mg/kg bw/day in males and 34.4 mg/kg bw/day in females)" should be changed to "Based on the decreased body weight gain the NOEL is set at 600 mg/kg food for males (27.31 mg/kg/day) and 120 mg/kg/day for females (7.04 mg/kg/day)".	As recorded in Table 6.5.1.1 the decreased body weight gain was not observed in males given 600 mg/kg food.

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(8)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Long-term toxicity Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity, STUDY 1 Vol. 3, B.6.5.2 Summary	Notifier: Page 23 4th paragraph (Vol.1), page 116 3rd paragraph, page 119 2nd paragraph (Vol.3): The histopathological changes were not considered to be treatment-related as mentioned in the comments provided under point No 6. Incidence of necrosis in the liver. Therefore, "and histopathological changes in the liver" should be deleted.	
(9)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity, STUDY 2	Notifier: Page 118 1st paragraph lines 5-6 (Vol.3): The slightly reduced body weight gain was not statistically significant and is not described in the dossier (Document M-II) or the original report (Report No. NNT-11-0084).	Notifier considers that the effect was marginal and not necessarily treatment-related, therefore, this sentence, "A slightly reduced body weight gain was noted in females over the study period (0-76 weeks, 89% of control)", should be deleted.

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(10)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Long-term toxicity Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity, STUDY 2 Vol. 3, B.6.5.2 Summary	Notifier: Page 24 5th paragraph (Vol.1), page 118 the last paragraph, page 120 the last paragraph (Vol.3): Notifier considers that the NOAEL for females should be 600 mg/kg food as described in the dossier (Document M-II) and the original report (Report No. NNT-11-0085). "The NOAEL is set at 120 mg/kg food" should be changed to "the NOAEL is set at 120 mg/kg food for males (16.4 mg/kg bw/day) and 600 mg/kg food for females (107.3 mg/kg bw/day)".	There was no significant effect on either survival, liver weights or the incidence of histopathology changes in the kidney in female mice given 600 mg/kg (table 6.5.1.2). There is also no evidence of a significant increase in the incidence of amyloidosis in any tissue of female mice at this dose level.
(11)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Long-term toxicity Vol. 3, B.6.5.2 Summary	Notifier: Page 24 3rd paragraph (Vol.1), page 119 2nd paragraph (Vol.3): The sentences of "At post-mortem necropsy, an increased incidence of dark areas in the liver was noted in females at 3000 mg/kg food. Treatment-related liver necrosis was noted in males at 3000 mg/kg food" should be deleted. Notifier considers that this finding was not treatment-related as described in the dossier (Document M-II) and the original report (Report No. NNT-11-0085 and NNT-41-0112).	An increased incidence of dark areas in the liver was only noted in the main study but no histopathological changes related to this finding were observed. An increased incidence of liver necrosis was only noted in the animals that died before the end of the dosing period. It was generally secondary to some other cause of death and not treatment-related since no incidence of liver necrosis was noted at the scheduled sacrifice at week 53 and week 105 as described in the dossier (Document M-II) or the original report (Report No. NNT-11-0085 and NNT-41-0112).

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(12)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Reproduction and developmental toxicity Vol. 1, Level 2, 2.3.2 Table 2.3.2.1 Vol. 3, B.6.6.1 Reproductive toxicity, STUDY 1 Vol. 3, B.6.6.3 Summary and Table 6.6.3.1	Notifier: Page 25 2nd paragraph, page 27 Table 2.3.2.1(Vol.1), page 124 2nd paragraph, page 139 Table 6.6.3.1, page 140 2nd paragraph (Vol.3): Notifier considers the NOAEL for parental toxicity was 1000 mg/kg food. The "Parental NOAEL=13.3; LOAEL=66.7" for 2-Generation, oral, rat in Vol. 1 (Level 4) should be changed to "Parental and developmental NOAEL=76.4 mg/kg ; LOAEL=386 mg/kg"	A JMPR evaluation decided that the increase in relative liver weights in F1 males at 1000 mg/kg food was not adverse. The effects were marginal, there was no absolute organ weight change and no histopathological change that was consistent with the weight change. Therefore, the NOAEL for parental toxicity was 1000 mg/kg food. Our recommendation for achieved doses are as follows: 200 mg/kg food = 15.5 mg/kg bw/day 1000 mg/kg food = 76.4 mg/kg bw/day 5000 mg/kg food = 386 mg/kg bw/day Each value was calculated during the pre-mating period in each generation and by sex and group; the lowest values among them were selected.
(13)	Vol. 3, B.6.6.1 Reproductive toxicity, STUDY 2	Notifier: Page 124 Characteristics (Vol.3): "Teratogenic effects: ≥ 1000 mg/kg bw/day" should be changed to "Teratogenic effects: Not teratogenic", because no teratogenicity was observed even in the highest dose level.	

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(14)	Vol. 3, B.6.6.1 Reproductive toxicity, STUDY 2, Table 6.6.1.2, Food consumption, Macroscopy	Notifier: Page 125 Table 6.6.1.2 (Vol.3): At food consumption, "ic"s for 300, 500, 1000 (mg/kg food) of male should be removed, and "dc" for 1000 (mg/kg food) of male should be added. The key to the pathology findings is confusing. We propose to add footnote "j" (j: observed in dead animals) to the three findings for females and amend "f" to show that male data are for animals killed after 12 weeks.	There are differences between the values/marks in Table 6.6.1.2 and the data in the study report. Food consumption was decreased during the early part of the treatment period but increased during the later stages of the study. This is not adequately represented in Table 6.6.1.2. It would be better to include information on doses at which food consumption was reduced in Table 6.6.1.2 as increased food consumption is not of toxicological importance. The macroscopic findings for females (liver enlarged, liver congestion and adrenal enlarged) are for dead animals only and the findings for males are for animals killed after 12 weeks.
(15)	Vol. 3, B.6.6.1 Reproductive toxicity, STUDY 2, Conclusions	Notifier: Page 127 2nd paragraph 3rd & 5th sentences (Vol.3): Notifier considers that salivation was toxicologically meaningless, because the finding was transient, and that the increased food consumption noted in males at 300 and 1000 mg/kg bw/day and in females at 1000 mg/kg bw/day was not toxicologically important for pyriproxyfen.	Notifier proposes to add a sentence of "Salivation was transient and thought to be toxicologically meaningless" after the 3rd sentence and a sentence of ", however it was not toxicologically important" after the 5th sentence.
(16)	Vol. 1, Level 2, 2.3.1.2 Toxicodynamics, Reproduction and developmental toxicity Vol. 3, B.6.6.1 Reproductive toxicity, STUDY 2, Table 6.6.1.2	Notifier: Page 25 3rd paragraph (Vol.1), page 126 Table 6.6.1.2, page 127 3rd paragraph 1st sentence &5th paragraph 3rd sentence, page 139 Table 6.6.3.1, page 140 3rd paragraph 2nd-3rd sentences (Vol.3): Notifier considers that decreased numbers of corpora lutea and live foetuses, and increased placenta weights were not treatment related in the combined teratology and reproductive toxicity study (Reproductive	Corpora lutea and live fetuses: Notifier considers that the reduced numbers of corpora lutea and of live foetuses observed at 1000 mg/kg bw/day were not treatment related, because the differences were marginal and within the range of historical controls. This is noted in Appendix111 of the study report. Therefore, Notifier suggests that the words, "and decreased numbers of corpora lutea." in Vol.1&Vol.3 (Summary) and "(the number of) corpora lutea and" in Vol.3 (both Study 3, Summary table - Critical effects) should be deleted. Placental weights:

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section 2 - Mammalian toxicology (B.6)

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	and Conclusions Vol. 3, B.6.6.3 Summary and Table 6.6.3.1, Teratogenicity and reproductive toxicity study	toxicity STUDY 2). The NOAEL for developmental toxicity should therefore be 1000 mg/kg bw/day, the highest dose tested.	An increase in placental weight was observed at 1000 mg/kg bw/day, but the effect was slight and no adverse effect was noted in foetuses. In the teratogenicity study in rats, no change was observed in placental weights even at 1000 mg/kg bw/day. Therefore, it was not considered to be toxicologically significant, so that the concerning words, "and based on a decreased number of live foetuses and increased placenta weights." in Vol.1&Vol.3 (Summary), and "but the number of corpora lutea and live foetuses were significantly lower and placental weights were significantly higher in dams at 1000 mg/kg bw/day." in Vol.3, should be deleted.
(17)	Vol. 3, B.6.6.2 Teratogenicity studies, STUDY 1, Characteristics	Notifier: Page 128 Characteristics (Vol.3): "Teratogenic effects: ≥ 1000 mg/kg bw/day" should be changed to "Teratogenic effects: Not teratogenic", because no teratogenicity was observed even at the highest dose level.	
(18)	Vol. 3, B.6.6.2 Teratogenicity studies, STUDY 1, Table 6.6.2.1, Post implantation loss	Notifier: Page 130, Table 6.6.2.1 Post implantation loss (Vol.3): Early post implantation losses in the groups given 0 and 100 mg/kg bw/day should be 4.4 and 6.7 respectively and not 4.0 and 7.0 respectively. The early post implantation rate was not statistically different and Notifier considers that values should be changed to "No treatment-related findings".	

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section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(19)	Vol. 3, B.6.6.2 Teratogenicity studies, STUDY 1, Conclusions	Notifier: Page 131, the last paragraph 2nd sentence (Vol.3): In the rat teratogenicity study, the litter size and the early post implantation rate were not statistically different and Notifier considers that the sentences should be removed.	
(20)	Vol. 3, B.6.6.2 Teratogenicity studies, STUDY 2, Characteristics	Notifier: Page 132 Characteristics (Vol.3): "Teratogenic effects: 300 mg/kg bw/day" should be changed to "Teratogenic effects: Not teratogenic", because no teratogenicity was observed even at the highest dose level.	
(21)	Vol. 3, B.6.6.2 Teratogenicity studies, STUDY 2, Table 6.6.2.2	Notifier: Page 133 (Vol. 3): The number of Non-pregnant females and Excluded females appear twice in the table, the second set of data could be deleted.	
(22)	Vol. 3, B.6.6.3 Summary and Table 6.6.3.1	Notifier: Page 139 Table 6.6.3.1, page 140 2nd paragraph (Vol.3): Notifier considers that no effect on developmental toxicity was observed even at 1000 mg/kg bw/day in the rat teratogenicity and reproductive toxicity study and the NOAEL was 1000 mg/kg bw/day (See the comment point No.17 and requests the RMS to reconsider the evaluation of this study in the DAR.	

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section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(23)	Vol. 3, B.6.6.2 Teratogenicity studies, STUDY 3, Conclusions Vol. 3, B.6.6.3 Summary and Table 6.6.3.1, Peri-post natal study	Notifier: Page 138 5th paragraph, 1st sentence, page 139 Table 6.6.3.1, Peri-post natal study & page 141 1st paragraph, page 152 1st paragraph (Vol.3): Notifier considers that the findings (increased incidences of renal pelvis dilatation and hyperaemia and/or inflammatory cell infiltration in the propria of the urinary bladder) observed in a peri- and postnatal toxicity study should be removed from lists of critical effects in the above sections.	At necropsy of the offspring after 3 weeks postpartum, increased incidences of dilatation of the renal pelvis, and hyperemia and/or inflammatory cell infiltration in the propria of the urinary bladder were noted in the 500 and 300 mg/kg bw/day dose groups, but no such effects were seen in offspring examined at 8 weeks postpartum. Moreover, no renal pelvis dilatation was observed in foetuses in the rat teratogenicity study. Therefore, the findings were thought to be growth retardation, but not visceral anomalies.
(24)	Vol. 3, B.6.6.3 Summary and Table 6.6.3.1	Notifier: Page 139 Table 6.6.3.1, page 140 1st, 2nd, 3rd and 4th paragraphs (Vol.3): The NOAELs for reproduction and for teratogenicity in the 2-generation study, the teratogenicity and reproductive toxicity study and the rat teratogenicity studies should be >the values quoted and not ≥ the values quoted to be consistent with the summaries on the following pages. Also, the NOAEL for teratogenicity in the rabbit study should be >300 mg/kg in both the table and in paragraph 4 as no developmental effects were found even at 1000 mg/kg.	
(25)	Vol. 1, Level 2, 2.3.3 ARfD (acute reference dose)	Notifier: Pages 27-29, page 103, page 142 (Vol.1) and pages 153–155 (Vol.3): Since the only alert for the establishment of the ARfD is the observed mortality and clinical signs in the acute oral toxicity study in mice and there are no	The RMS also proposes to discuss this further in the expert meeting. The EU document 'Guidance for setting an acute reference dose' (7199/VI/99 rev 5) states that one of the criteria for not setting an ARfD is that the pesticide is of very low acute oral toxicity (e.g. no adverse clinical signs and deaths have been observed at the limit dose for LD_{50} testing) (Chapter

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
	Vol. 1, Level 2, Appendix 3, ARfD (acute reference dose) Vol. 1, Level 3, 3.1 Background to the proposed decision Vol. 3, B.6.10.4 ARfD (acute reference dose)	further alerts, Notifier believes that it is not necessary to set an ARfD taking into account the EU document 'Guidance for setting an acute reference dose' (7199/VI/99 rev 5) and the daily consumption of residues.	4.4). However, this does not mean that an ARfD must be set if there are adverse clinical signs or deaths at the limit dose in an individual study. Although the RMS considers that deaths in the mouse study at a dose of 2000 mg/kg mean that it is necessary to set an ARfD, notifier does not consider this is a correct interpretation of the guidance. The above guidance only means that an ARfD is not needed if there are no adverse clinical signs or deaths at 2000 mg/kg, the limit dose recommended by the EU testing guidelines. There is no strict requirement to set an ARfD when deaths or clinical signs occur at the limit dose. The only alert is observed in male mice at 2000 mg/kg of the limit dose and there are no further alerts. On the basis of low acute toxicity data of pyriproxyfen, Notifier considers that it is not necessary to allocate an ARfD. The relationship between the ARfD and the consumption of residues also needs to be considered when deciding whether an ARfD is required. There is no result in residues in food that will exceed the value proposed by the RMS. The calculations for the NESTI and IESTI intake using the proposed ARfD confirm that NESTI and IESTI are negligible, and do not exceed 0.07% by Dutch and UK models and 0% by FAO/WHO models for both adults and children (See details in Volume 3, Annex B, B.7.15.3 and B.7.15.4). The EU guidance states that under the above circumstances an ARfD is not necessary. The JMPR (FAO/WHO, 2004) also states that the numerical cut-off for setting ARfDs was about 5 mg/kg bw; i.e. if calculations indicated that an ARfD would be greater than this value (RMS proposes an ARfD of 10 mg/kg bw), then it would not be necessary on practical grounds to set an ARfD. As acute effects only occur at high doses that are considerably greater than the daily consumption of residues, an ARfD is not needed to ensure safe use

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			of pyriproxyfen. In addition, based on the same toxicological data, The JMPR (FAO/WHO, 1999) concluded that it was not necessary to establish an ARfD. Notifier believes without a doubt that it is not necessary to set up an ARfD.
(26)	Vol. 1, Level 2, 2.3.4 AOEL Vol. 1, Level 2, Appendix 3, AOEL Vol. 1, Level 3, 3.1 Background to the proposed decision Vol. 3, B.6.10.5 AOEL	Notifier: Page 29, page 103 (Vol.1), pages 155-156 (Vol.3): Notifier suggests that the AOEL should be based on the NOAEL from the short-term toxicity study, 23.5 mg/kg bw/day in the 13-weeks oral toxicity study in rats. It is not appropriate to select the NOEL of 10 mg/kg bw/day, from the 1-year study in dogs for pyriproxyfen, even if chronic exposure occurs by the re-entry activities.	For tomato and eggplant, the RMS considers that it cannot be excluded that the exposure duration of re-entry activities will exceed 3 months. However, based on Notifier's experience of the actual use for tomato and eggplant in a glasshouse, a maximum of two applications per growing season are claimed (two crop cycles per year making four applications per year) which leads to a max 80 days of exposure (20 hectare treated 4 times per year, 2 treatments per crop cycle with 2 cycles per year, makes 80 hectares treated in one year. Worst case is a hand held sprayer or knapsack sprayer on the back with a maximum of 1 hectare treated per day. This makes a maximum 80 days exposure to the product during application in this extreme worst case.). Even if chronic exposure occurs by the re-entry activities, it is not appropriate to select the NOEL of 10 mg/kg bw/day, from the 1-year study in dogs. The RMS considered that the NOAELs from the 13-weeks and 6-months studies (23.5 and 24.0 mg/kg bw/day, respectively) in rats were too close to the LOAEL of 30 mg/kg bw/day from the 1-year oral toxicity study in dogs. However, the effects at the LOAEL of 30 mg/kg bw/day were very slight. The NOAEL for females was 30 mg/kg bw. As for male dogs, there were minimal effects on cholesterol levels and liver weights (caused by only one male dog out of 4 dogs), but no histopathological changes in the liver were observed at the LOAEL of 30 mg/kg bw/day. (See details in Volume 3, Annex B, B.6.3.4 Semichronic oral studies, STUDY 4, and the comment No.4). Therefore, it can be assumed that the real NOAEL in this study is just slightly lower than 30 mg/kg bw/day. As for NOAEL of 13.3 mg/kg bw/day, which the RMS considers the next lower NOAEL, Notifier

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
			considers that the dose of 76.4 mg/kg bw/day should be selected as the NOAEL for 2-generation study in rats (See the comment No. 12). Therefore, the overall NOAEL of 23.5 mg/kg bw/day in the 13-weeks oral toxicity study in rats is the most appropriate selection for the derivation of the AOEL.
(27)	Vol. 1, Level 2, 2.3.4 AOEL Vol. 1, Level 3, 3.1 Background to the proposed decision Vol. 3, B.6.10.5 AOEL	Notifier: Page 29, page 142 (Vol.1) and page 155 (Vol.3): Notifier suggests that a systemic AOEL of 0.148 mg/kg bw/day should be set	Notifier considers that the absorption of 63% propsed in the dossier is already a worst case estinate and that the AOEL should be based on the NOAEL from the short-term toxicity study, 23.5 mg/kg bw/day. See the comments in both No. 1 and No. 26. Therefore, A systemic AOEL of 0.148 mg/kg bw/day should be set.

6. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.1.1 Primary crops, STUDY 2	Notifier: Page 184 4th paragraph (Vol.3): A typographical error of "2'-OH-PYR" should be changed to "2-OH-PY".	
(2)	Vol. 3, B.7.2.1 Ruminants, STUDY 1 and STUDY 2	Notifier: Page 204 4th paragraph 1st sentence (Vol.3) and page 216 2nd paragraph 1st sentence (Vol.3): A typographical error of "eggs" should be changed to "milk".	
(3)	Vol. 3, B.7.2.1 Ruminants, STUDY 1 and STUDY 2	Notifier: Page 204 4th paragraph 2nd sentence (Vol.3) and page 216 2nd paragraph 2nd sentence (Vol.3): A typographical error of "hen samples" should be changed to "goat samples".	
(4)	Vol. 3, B.7.2.1 Ruminants, STUDY 1 and STUDY 2 Poultry, STUDY 1 and STUDY 2	Notifier: Pages 207-212 Table B.7.2.1-2 to -9 (Vol.3), pages 220-223 Table B.7.2.1-13 to -19 (Vol.3), pages 231-232 Table B.7.2.1-23 to -25 (Vol.3) and pages 239-240 Table B.7.2.1-30 to -31 (Vol.3): Total of 35 typographical errors of "sulphate" should be changed to "sulfate".	
(5)	Vol. 3, B.7.2.1 Ruminants, STUDY 1	Notifier: Page 209 Table B.7.2.1-4 (Vol.3): A typographical error of "14C" should be changed to "^{14}C".	

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section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 3, B.7.2.1 Ruminants, STUDY 2	Notifier: Page 215 3rd paragraph 1st and 2nd sentence (Vol.3): Two typographical errors of "study 3" should be changed to "study 1".	
(7)	Vol. 3, B.7.2.1 Ruminants, STUDY 2	Notifier: Page 223 Table B.7.2.1-19 (Vol.3): A typographical error of "Identification()"should be changed to "Identification(A)".	
(8)	Vol. 3, B.7.2.2 Poultry, STUDY 1	Notifier: Page 228 3rd paragraph 1st sentence (Vol.3): A typographical error of "and thigh" should be deleted because the same descriptions repeated in the next paragraph.	
(9)	Vol. 3, B.7.2.2 Poultry, STUDY 1	Notifier: Page 233 3rd paragraph 1st sentence (Vol.3): A typographical error of "0.004-0.0049 mg eq /kg" should be changed to "0.004-0.049 mg eq /kg".	
(10)	Vol. 3, B.7.2.1 Poultry, STUDY 2	Notifier: Pages 235-236 (Vol.3): Total 8 typographical errors of "2-OH-pyridine" should be changed to "2-OH-PY".	
(11)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 238 Table B.7.2.1-28 (Vol.3): A typographical error of "2-OH-PYR" should be changed to "2-OH-PY".	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(12)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 238 Table B.7.2.1-29 (Vol.3): A typographical error of "2-OH-pPYR" should be changed to "2-OH-PY".	
(13)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 239 Table B.7.2.1-30 (Vol.3): A typographical error of "2-OH-PYR" should be changed to "2-OH-PY".	
(14)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 240 Table B.7.2.1-31 (Vol.3): A typographical error of "2-OH-PYR" should be changed to "2-OH-PY".	
(15)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 240 Table B.7.2.1-32 (Vol.3): A typographical error of "2-OH-PYR" should be changed to "2-OH-PY".	
(16)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 240 Table B.7.2.1-32 (Vol.3): PYPA of 5.7%TRR and 0.012 mg eq/kg (skin with fat) should be replaced to PYPAC of 5.7%TRR and 0.012 mg eq/kg (skin with fat).	
(17)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 241 Table B.7.2.1-33 (Vol.3): Symbols of (C) should be added to Extractable of Day 3 excreta of both values, 92 and 7.2, and symbols of (D) should be added to Extractable of Day 7 excreta of both values, 94 and 7.4, respectively.	

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section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(18)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 241 Table B.7.2.1-33 (Vol.3): A typographical error of "2-OH-PYR" should be changed to "2-OH-PY".	
(19)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 241 4th paragraph 2nd sentence (Vol.3): A typographical error of "2-OH-pyridine" should be changed to "2-OH-PY".	
(20)	Vol. 3, B.7.2.2 Poultry, STUDY 2	Notifier: Page 242 the 1st paragraph 2nd sentence (Vol.3): A typographical error of "2-OH-PYR" should be changed to "2-OH-PY".	
(21)	Vol. 3, B.7.2.4 List of identified compounds	Notifier: Page 244-245 Table (Vol.3): Crop/Commodity of PYPA, "Hen (skin with fat)", should be changed to " Hen (gizzard)".	
(22)	Vol.3 B.7.7.2 Effects on residue levels	Notifier: Page 264 Guidelines and limitations point 2 (Vol.3): Pyriproxyfen residues in cotton seed are expected to be <0.01 mg/kg and not <0.1 mg/kg.	
(23)	Vol.3 B.7.7.3 Summary of processing studies	Notifier: Page 264 1st paragraph 2nd sentence (Vol.3): Pyriproxyfen residues in cotton seed are expected to be <0.01 mg/kg and not <0.1 mg/kg.	
(24)	Vol.3 B.7.12.3 Summary of proposed MRLs	Notifier: Page 267 Table (Vol.3): The STMR and HR for cotton seed should be "<0.01" mg/kg instead "0.01*". In addition, please add a footnote for "0.01*" in MRL column.	

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section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(25)	Vol.3 B.7.15.2 Intakes by humans	Notifier: Page 270 Table B.7.15.2-2 (Vol.3): Consumption for cotton seed should read $0.00010^{(2)}$.	

7. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, Level 2, 2.5.2, Fate and behaviour in soil Vol. 3, B.8.1.3, Summary route and rate of degradation in soil	Notifier: In Table 2.5.2-1, on page 38, and in Table B.8.1.3-1, on page 320, the DT_{90} (20°C, d) of PYPAC should be 123, 70 and 1.3 days, mean 65 days, rather than 118, 69 and 1.3 days, mean 63 days, to be consistent with the DT_{90} values reported in Table B.8.1.1.1-18, on page 302. Please consider revising these values accordingly.	
(2)	Vol. 1, Level 2, 2.5.2, Fate and behaviour in soil	Notifier: In Table 2.5.2-2, on page 40, the maximum soil DT_{50} for PYPAC used in the PEC_s calculations should be 37 rather than 36 days, to be consistent with the calculations reported in Vol. 3 of the DAR. Please consider revising this value accordingly.	
(3)	Vol. 1, Level 2, 2.5.3, Fate and behaviour in water	Notifier: On page 45, it is stated that the water-sediment study with metabolites 4'-OH-Pyr and PYPAC is not acceptable because anaerobic conditions were not established in the sediment layer. We understand that the RMS has accepted this study and considers that the lack of anaerobic conditions in the sediment layer does not influence the metabolic pathway or the degradation rates. Please consider deleting this statement.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(4)	Vol. 1, Level 2, 2.5.3, Fate and behaviour in water Vol. 3, B.8.4.4, Fate and behaviour in water, Summary and assessment	Notifier: In Table 2.5.3-1, on page 46, Vol. 1, and in Table B.8.4.4-1, on page 375, Vol. 3, it is stated that the DT_{50} and DT_{90} values are provisional because anaerobic conditions were not established in the sediment layer of the water-sediment studies during incubation. We understand that the RMS has accepted these studies and considers that the lack of anaerobic conditions does not influence the metabolic pathway or the degradation rates. Please consider updating these tables accordingly.	
(5)	Vol. 1, Level 2, 2.5.4, Fate and behaviour in air Vol. 1, Level 2, Appendix 3, List of endpoints Vol. 3, B.8.8, Predicted environmental concentrations in air (PECa)	Notifier: The estimated Henry's Law Constant of pyriproxyfen at 22-25°C should be $<1.16 \times 10^{-2}$, rather than $<1.16 \times 10^{-5}$ Pa m^3 mol^{-1}. Please consider revising the DAR accordingly.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 1, Level 2, 2.5.4, Fate and behaviour in air Vol. 3, B.8.8, Predicted environmental concentrations in air	Notifier: The reported DT_{50} for pyriproxyfen in air calculated using the Atkinson method (0.26 hrs) is inconsistent with the value reported by the RMS in the Physchem section (3.8 hrs). Please check this and consider revising the DAR accordingly.	
(7)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 111, 'PYPAC DT_{50lab} (20°C, aerobic): 1.3 - 123 d' should read 'PYPAC DT_{90lab} (20°C, aerobic): 1.3 - 123 d'. Please consider revising this.	
(8)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 112, the DT_{50f} for the Washington soil should be 5.9 d, r^2 0.93, rather than 9.8 d, r^2 0.72 and the DT_{90f} should be 20 d, rather than 33 d, to be consistent with the information reported in the DAR. Please consider revising this in the list of endpoints.	
(9)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On pages 113, 114-115 and 115-116, the crop interception factor for cotton used in the PEC_s calculations for pyriproxyfen and its metabolites 4'-OH-Pyr and PYPAC, should be 75%, rather than 40%, to be consistent with the calculations reported in the DAR. Please consider revising this and updating the PEC_s values in the list of endpoints accordingly.	The recommended FOCUS crop interception value for cotton at boll opening (BBCH 40-89) is 75%.

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(10)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 115, the DT_{50} for PYPAC used in the PEC_s calculations should be 37 rather than 36 days, to be consistent with the calculations reported in the DAR. Please consider revising this.	
(11)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On pages 119 and 127, the FOCUS Step 3 PEC_{sw} and PEC_{sed} values for cotton (actual and TWA) for pyriproxyfen are inconsistent with those reported in the DAR. Please check this and consider revising these values accordingly.	
(12)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 120, please consider revising the water solubility of 4'-OH-Pyr used in the PEC_{sw} calculations to 1.4 mg/L and removing '(set to value parent)', to be consistent with the information reported in the DAR.	The RMS recalculated PEC_{sw} / PEC_{sed} values for 4'-OH-Pyr using a laboratory determined water solubility value for this metabolite of 1.4 mg/L. This study was submitted by Notifier in April 2005.
(13)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 121, the FOCUS Step 1 24 h actual PEC_{sw} value for 4'-OH-Pyr should read as 0.3785 µg/L. Please consider revising this value in the list of endpoints.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(14)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 123, several of the FOCUS Step 1 actual PEC_{sw} values for cotton for DPH-Pyr are inconsistent with those reported in the DAR. The Step 1 14-day TWA PEC_{sw} value should also be 0.0144, rather than 0.00144 µg/L. Please check this and consider revising these values accordingly.	
(15)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On pages 123 & 124 and 131 & 132, the DT_{50} soil for PYPAC used in the PEC_{sw}/PEC_{sed} calculations should be 37 rather than 36 days, to be consistent with the calculations reported in the DAR. Please consider revising this.	
(16)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 125, several of the FOCUS Step 2 PEC_{sw} values for cotton (actual and TWA) for PYPAC are inconsistent with those reported in the DAR. Please check this and consider revising these values accordingly.	
(17)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 131, the FOCUS Step 2 7-day actual PEC_{sed} value for cotton for DPH-Pyr should be 0.1281, rather than 0.2181 µg/kg, to be consistent with the value reported in the DAR. Please consider revising this.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(18)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 133, several of the FOCUS Step 2 PEC_{sed} values for cotton (actual and TWA) for PYPAC are inconsistent with those reported in the DAR. Please check this and consider revising the values accordingly.	
(19)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 133, the crop interception factor for cotton used in the PEC_{gw} calculations for pyriproxyfen and its metabolites 4'-OH-Pyr and PYPAC, should be 75%, rather than 40%, to be consistent with the calculations reported in the DAR. Please consider revising this in the list of endpoints.	The recommended FOCUS crop interception value for cotton at boll opening (BBCH 40-89) is 75%.
(20)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 134, the DT_{50} for pyriproxyfen in air, calculated using the Atkinson method (0.26 days) is inconsistent with the value reported by the RMS in the Physchem section (3.8 hrs). Please check this and consider revising the value in the list of endpoints accordingly.	
(21)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: On page 134, the estimated Henry's Law Constant for PYPAC should be 2.00×10^{-4} Pa m^3 mol^{-1}, rather than 1.97×10^{-9} Pa m^3 mol^{-1}, to be consistent with the value reported in the DAR. Please consider revising this.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(22)	Vol. 2, Annex A.8 Environmental fate and behaviour Vol. 3, B.8.10, References relied on	Notifier: For Annex Point IIIA 9.2.3/04, (Report No. NNP-0068), the study title should be 'PYPAC - Water solubility', rather than '4'-OH-Pyriproxyfen - Water solubility'. Please consider revising this in the reference lists. Study Report No. NNP-0067, '4'-OH-Pyriproxyfen - Water solubility' has not been included in the reference lists, but is referred to in the DAR. Please consider adding this study to the reference lists.	
(23)	Vol. 3, B.8.6.1, Predicted concentrations in surface water	Notifier: In the substance specific input data used for the surface water modelling calculations, DT_{50} water and DT_{50} sediment values are listed for pyriproxyfen and its metabolites. However, as it was not possible to calculate separate degradation rates for water and sediment based on the data from the water-sediment studies, we understand that mean DT_{50} values for the total water-sediment system were used by the RMS for water and sediment, rather than separate values, in accordance with FOCUS guidance. Please consider revising the list of input parameters accordingly to reflect this.	

section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(24)	Vol. 3, B.8.6.3, Predicted concentrations in groundwater	Notifier: In Table B.8.6.3-1, on page 386, the crop interception factor for cotton used in the PEC_{gw} calculations for pyriproxyfen and its metabolites should be 75%, rather than 40%, to be consistent with the calculations reported in the DAR. Please consider revising the crop interception factors and corrected dose values in this table.	The recommended FOCUS crop interception value for cotton at boll opening (BBCH 40-89) is 75%.

8. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, Level 2, 2.6.1, Effects on terrestrial vertebrates (page 54); Vol. 1, Level 2, Appendix 3, List of endpoints; Vol. 3, B.9.1.3 (page 403 and 404)	Notifier: Regarding the Daily doses for the reproductive toxicity studies, they are calculated for each sex in the DAR. However, the Daily doses separated sex-by-sex are not considered meaningful, because birds were housed with one male and one female per pen throughout the studies and hence the feed consumptions were only the mean values for pairs (i.e. not specific values for each sex). Thus, the Daily doses for mallard and bobwhite reproductive toxicity studies should be 73.8 and 83.8 mg a.s./kg bw/day, respectively.	The Guidance document SANCO/4145/2000 also does not require such separation of the Daily dose on the basis of sex.
(2)	Vol. 1, Level 2, 2.6.2, Effects on aquatic species, Table 2.6.2-10; Vol. 3, B.9.2.3.1.2, Tables B.9.25 (page 443) and B. 9.25 (page 444)	Notifier: For the calculation of refined long-term TERs for pyriproxyfen, a FOCUS Step 3 surface water PEC value of 0.393 µg a.s./L has been used (resulting from 1.6% drift over 1.3 m). This drift value is inconsistent with the previous tables, where the standard default drift distance for field crops of 1 m has been used (2.77% drift). The PEC value is also inconsistent with that calculated in the Fate and Behaviour section i.e. 0.381 µg a.s./L (Table 2.5.3-14). Note also that the table on page 444 (Vol. 3, B.9.2.3.1.2) should be renumbered to B.9.26.	

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section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Vol. 1, Level 2, 2.6.2, Effects on aquatic species, Risk assessment: Vol. 1, Level 2, Appendix 3, List of endpoints; Vol. 3, B.9.2.2.1.4 (page 436); Vol. 3, B.9.2.3.1.2 (page 443)	Notifier: By considering the results of the microcosm study such as NOECpopulation, NOECcommunity and recovery potential of the affected community and populations, the study design and natural ecology, it is proposed to set NOEAEC of 20 μg a.s./L.	In the microcosm study, *Daphnia* group *galeata*, the most sensitive taxa, was clearly recovered from the direct effect within 8 weeks (exactly 5 weeks after the treatment) even at 20 μg a.s./L. Concerning rotifers, the indirect effect was observed at 20 μg a.s./L, however, most rotifer populations, as well as total rotifer abundance, were back to normal levels within 8 weeks. In the case of one minor species only, abundance levels were higher until the end of the study. Accordingly, considering the function and composition of the natural ecosystem, it can be considered that the NOEAEC is 20 μg a.s./L. Also, as mentioned in the SANCO guidance (SANCO/3268/2001), indirect effects observed in indoor microcosm studies (i.e. relatively small scale) may be overestimated. It also should be noted that fate conditions in the microcosm study were reasonably worst-case e.g. no macrophytes, static water system and lighting levels lower than those that would be experienced in the outdoor environment. Taking this into account and the large resilience of real aquatic communities, it is considered that significant indirect effect is unlikely to be occurred in the field.

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(4)	Vol. 1, Level 2, 2.6.2, Effects on aquatic species, Risk assessment: Vol. 3, B.9.2.3.1.2 (page 444)	Notifier: On page 64, when discussing the refined long-term risk assessment for pyriproxyfen, it is stated that the long-term TER based on the EAC from the microcosm study is above the Annex VI trigger of 10. However, this trigger value applies to the long-term TER values obtained with single species laboratory chronic toxicity studies (fish and *Daphnia*). The HARAP guidance document (1999) indicates that microcosms should be assessed on a case by case basis, with the possibility of using the EAC directly in the risk assessment without an uncertainty factor. This is indicated in Vol. 3, B.9.2.3.1.2, page 444.	
(5)	Vol. 1, Level 2, 2.6.3, Effects on bees and other arthropod species (page 68); Vol 3, B.9.4.2.3 (page 459)	Notifier: The rate of 124 g a.s./ha in 95 L water is equivalent to 1305 mg a.s./L. This means that the concentration of test solution is significantly higher than those of application solutions for tomato/eggplant in southern Europe greenhouse (i.e. 50-75 mg a.s./L). This should be noted.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 1, Level 2, 2.6.3, Effects on bees and other arthropod species (page 68); Vol. 1, Level 3, 3.1 Background to the proposed decision (page143); Vol. 1, Level 4, Demand for further information, 4.9 Ecotoxicology; Vol 3, B.9.4.2.3 (page 459)	Notifier: The bee brood risk assessment indicates that the rate used in the field study (75 g a.s./ha) was too low to address the risk due to exposure on tomato and egg plant in Southern Europe (1-2 X 112.5 g a.s./ha). This is a protected (glasshouse) use where the main risk is to bumble bees used for commercial glasshouse pollination. Exposure to honey bees will be extremely low and bumble bees are currently not addressed at Annex I. It is not appropriate for this to be included as an Annex I data requirement, rather it should be addressed at Member State level as indicated in the DAR.	The use on tomato and egg plant in Southern Europe occurs only in glasshouses (i.e. a protected use) and so exposure of honey bees from outside of the greenhouse will be extremely low. This is consistent with Commission Directive 96/12/EC, which recognises that use in glasshouses on non-bee pollinated crops is indicative of low risk. In the case of glasshouse tomatoes and egg plants, these may be bee pollinated and so there is the possibility of exposure. However, in the case of commercial glasshouse crops, pollination is carried out by bumble bees and these are currently not addressed under Annex I. Also, because of the controlled nature of this pollination, if necessary risk management measures can be implemented through the use of appropriate label phrases. Accordingly, these should be considered at a national level to take into account local circumstances.
(7)	Vol. 1, Level 2, 2.6.3.2, Other arthropod species, Table 2.6.3.2-1; Vol. 1, Level 2, Appendix 3, List of endpoints; Vol. 3, Table B.9.40	Notifier: Concerning the ER50 value for *Aphidius rhopalosiphi*, the regression analysis should be conducted with careful data handling. In this study, since the lowest dose (31.25 g a.s./ha) is lower than the NOER (62.5 g a.s./ha) and then out of dose-effect relationship range (62.5-125 g a.s./ha), this rate should not be included in the regression analysis for ER50 evaluation. Based on this, an ER50 value of 92 g a.s./ha seems to be more appropriate.	

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section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(8)	Vol. 1, Level 2, 2.6.3, Effects on bees and other arthropod species, Table 2.6.3.2-2; Vol. 3, Table B.9.42	Notifier: In Table 2.6.3.2-2, the sublethal HQ values of 0.93, 3E-4, <0.17 and 5E-5 should not be in bold (as in Table B.9.42). The off crop HQ values (1 m) for *Aphidius rhopalosiphi* and *Orius laevigatus* need to be corrected in both tables (the calculation has divided by the uncertainty factor of 10 rather than multiplied).	
(9)	Vol.1, Level 2, Appendix 3, List of endpoints: Vol. 1, Level 4, Demand for further information, 4.9 Ecotoxicology; Vol. 3, B.9.8 (page 470)	Notifier: A new GLP study (NNW-0178) to assess the effects of technical pyriproxyfen on soil respiration and nitrification according to OECD 216 and 217 guidelines has been conducted and was submitted with the DAR response in January 2006. No adverse effects were detected on soil microbial respiration and nitrification at 1.5 mg a.s./kg soil, the highest concentration tested.	The worst case initial soil PEC of pyriproxyfen is 0.060 mg a.s./kg for cotton use according to the DAR. Therefore, the NOEC 1.5 mg a.s./kg is 25 times higher than the PEC. Moreover, the effects of metabolite to soil micro-organisms are assessed to be covered by study with parent pyriproxyfen, as mentioned in the DAR. Therefore the risk of pyriproxyfen as well as its metabolites for soil microflora is acceptable.
(10)	Vol. 2, A.9, Ecotoxicology Vol. 3, B.9.11, References relied on	Notifier: A new study (Report No. NNW-0178) submitted in January 2006 should be added in the reference lists.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(11)	Vol. 1, Level 4, Demand for further information, 4.9 Ecotoxicology; Vol. 3, B.9.4.1.1 (page 449) and B.9.4.2.1 (page 458)	Notifier: Additional information is required to accept the study data obtained in the honey bee acute toxicity study by Hoberg J.R. (2001). According to the 5 batch analysis and the specification defined in the dossier (Document J Specification No. 01), the tested sample is in a range of technical grade of pyriproxyfen and study should be valid. It is made clear that this is not required for Annex 1 inclusion. In addition, in Volume 3, Annex B.9.4.4.1 it states that further studies are not needed since acceptable data for the toxicity of the formulation to honey bees are available.	In the Vol. 1, Level 2, Appendix 3, List of endpoints, the data has already been included as valid.
(12)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: It is not clear why two NOEC values have been given for the reproductive toxicity to birds endpoints (for the two species tested, mallard duck and bobwhite quail). In the case of the dietary toxicity to birds, the single worst-case endpoint has been given for the two species tested.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(13)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: In the table of toxicity/exposure ratios for aquatic organisms no values have been given for fish algae and *Lemna* (although it is stated that the TERs given are for the most sensitive aquatic organisms i.e. aquatic invertebrates). In the case of the long-term TER values (cotton) a timescale of 21 d has been given (i.e. for the *Daphnia* chronic toxicity study) but the endpoint used is actually from the microcosm study (56 d duration). The Annex VI trigger (10) given for the long-term TER value (cotton) is based on the use of the *Daphnia* chronic toxicity endpoint but as it is actually based on a higher tier microcosm study the trigger should be lower. In the DAR it is set at 1 i.e. the NOEAEC and EAC are the same, allowing direct comparison with the PEC. The comparison of the surface water PEC values for the tomato/eggplant use with the cotton use should point out that the former is FOCUS Step 2 and the latter FOCUS Step 3 i.e. the comparable difference will be larger resulting in an even bigger safety margin for tomato/eggplant. A long-term TER value of 130 could be calculated for the tomato/eggplant use using the microcosm EAC (5.0 µg a.s./L).	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(14)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: In the bioconcentration table, the level of residues (%) in organisms after the 14 day depuration period should be ≤10.4% (or rounded to 10%) rather than ≤11%.	
(15)	Vol. 1, Level 2, Appendix 3, List of endpoints	Notifier: In the table for other non-target organisms, the conclusion for the plant screening data that pyriproxyfen shows no herbicidal activity, should be added (as for insecticidal and fungicidal activity).	
(16)	Vol. 3, B.9.1.5.2 (page 411)	Notifier: Concerning DPH-Pyriproxyfen, the value of “hen: 4.1% AR” cannot be traced. It is estimated the value as “hen: 3.5% AR” (i.e. 3.5% = (2.2% + 5.8%) / 2 x (84% + 89.5%) / 2)).	
(17)	Vol. 3, B.9.2.2.2.3 (page 437)	Notifier: In the *Chironomus* study with pyriproxyfen, 4’-OH-Pyr and PYPAC were observed in the test media and so the risk assessment based on the results obtained also applies to these metabolites.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(18)	Vol. 3, B.9.2.2.3.1.2 (page 442)	Notifier: In the aquatic invertebrate risk assessment for pyriproxyfen, it is considered that TWA-PECs may be applicable for the risk assessment based on the recovery potential demonstrated in the recovery test with *Daphnia pulex* and limitation of acute effect (only at the highest level, 20 ppb) in the microcosm study. Therefore, Notifier would suggest that the section dealing with the use of time-weighted-average concentrations in the 2nd paragraph, i.e. "Refinement using 21-day TWA……..exposure occurring early on in the exposure period" could be reviewed.	In the recovery test with *Daphnia pulex*, it is demonstrated that the chronic reproductive effects are clearly reversible with rapid recovery when the survivors were transferred to clean water. Furthermore, in the microcosm study, a reduction of *Daphnia* group *galeata* was observed only at the highest test level (20 µg a.s./L). The strong acute effect on *D.* group *galeata* observed at significantly higher levels than those relevant to surface water exposure following recommended use of pyriproxyfen, should not be relevant to the judgement of TWA-PEC applicability for the chronic endpoint risk assessment.
(19)	Vol. 3, B.9.4.1.2.1 (page 454)	Notifier: It is stated that in study 2 (a bumble bee brood test) the methods deviated from the current guideline (EPPO, 2002). However, this guideline is for honey bee brood and there is currently no validated test guideline for bumble bee brood.	
(20)	Vol. 3, B.9.4.1.3 (page 455)	Notifier: The guideline requirements referred to by the RMS in the residue study (EPPO, 2000) are for a laboratory acute toxicity test. It does not include requirements for a residual toxicity study.	

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Confidential section

9. Confidential Section (Annex C)

No.	Column 1 Reference to RMS draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 4, Annex C, C.1.5, Additional information required to be submitted by the notifier	Notifier: A new study (NNA-0097) was submitted to the RMS in January 2006 to confirm the identity of Impurity #2 in pyriproxyfen technical material responding to the question raised on the draft DAR from RMS.	This study was initiated following the draft DAR from the RMS and the identification of impurity #2 was confirmed in the study. No further questions were raised.
(2)	Vol. 4, Annex C, C.3, References relied on	Notifier: Please add the report of NNA-0097 newly submitted for confirmation of the identity of Impurity #2 in the reference list.	

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

10. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 4, C.1.2, detailed specification of the active substance	UK: We consider that the specification needs amending with [redacted]	
(2)	Vol 4, C.1.5, additional data required	UK: We agree with the data requirement for a confirmatory method (with accompanying validation data) for the method of analysis for the determination of [redacted] in technical material	
(3)	Vol 3 , B.2.1.4 relative density and B.2.1.10, spectra	UK: Data requirements for relative density and spectra (1 and 2 in vol 1 4.2) seem a bit harsh as only reason for rejection is they were not carried out to GLP.	
(4)	Vol 3, B.2.1.11, solubility in water and B.2.1.13, partition coefficient	UK: With regards to these sections (3 and 4 in vol 1 4.2) we would agree with a data requirement being set.	
(5)	Vol 3, B.4.2, classification and labelling of preparations, physical chemical properties	UK: the statement at B.4.2 is incorrect, surface tension data indicate the need for a R65 (as stated in the Tox section) and S62 risk phrases.	

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section 2 - Mammalian toxicology (B.6)

11. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.6.14.2.1, Internal exposure and risk assessment	UK: In Tables 6.14.2.1 – 6.14.2.3, only route specific exposure values (dermal and respiratory) have been compared individually to the systemic AOEL. It is more appropriate to base the 'risk-index' on a comparison of total systemic exposure values with the AOEL.	
(2)	Vol. 3, B.6.14.2.1, Internal exposure and risk assessment	UK: In Tables 6.14.2.2 and 6.14.2.3, a body weight assumption of 70 kg has been used in the risk assessment for bystanders and harvest workers. As these groups are likely to include females and young people, a body weight assumption of 60 kg may be more appropriate.	
(3)	Vol. 3, Appendix 3, Section 2.4 Dutch Glasshouse Model	UK: No details have been provided for the Dutch Model calculations other than the usage information and the calculated exposure values. For transparency, further details of the calculation should be provided.	
(4)	Vol. 3, B.6.14.3, Conclusions	UK: Although the Dutch Model estimates indicate that the Southern European use of 'Pyriproxyfen 10EC' on glasshouse crops will result in a level of operator exposure without the use of PPE which exceeds the AOEL, the DAR concludes that this use is acceptable in view of the worst case assumptions made in the model. It would be useful for this conclusion to be supported with alternative estimates using EUROPOEM data for glasshouse applications.	

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section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(5)	Vol. 3, Appendix 3, Section 4 Worker Exposure	UK: As 'Pyriproxyfen 10EC' is applied up to 2 times on glasshouse crops, the exposure estimates (currently based on a single application/crop) should consider the likelihood of a build up of foliar residues from repeated applications.	
(6)	Vol. 3, Appendix 3, Section 4 Worker Exposure	UK: No details have been provided for the Dutch Model calculations for re-entry exposure in glasshouses other than the usage information and the calculated exposure values. For transparency, further details of the calculation should be provided.	
(7)	Vol. 3, Appendix 3, Section 4 Worker Exposure	UK: As harvest workers may not be aware of which products have been applied to the crop in which they are working or of the precautions to be taken as a result, it may not be appropriate to assume that these workers will wear PPE other than that used habitually when carrying out harvesting operations.	

section 3 - Residues (B.7)

12. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 3, B.7.3.1, definition of residue in plants	UK: We agree with the residues definition in plants as parent pyriproxyfen only, as this is the major component in plants, with none of the metabolites being present at significant amounts in the plants at harvest.	
(2)	Vol 3, B.7.3.2, definition of residue in animal products	UK: we agreed that a residue definition in animal products is not required as the crops are not usually fed to animals.	
(3)	Vol 3, 7.12.1, proposed MRLs	UK: We agree with the proposed EU MRLs although we note that some other member states may ask for further cotton residue trials data	

section 4 - Environmental fate and behaviour (B.8)

13. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.6.1 PECsurface water	UK: While we support the use of the Dutch national model for calculation of PECsw from glasshouse uses, for illustrative purposes to identify a safe use, it should be noted that a different approach has been used here (i.e. for FOCUS Step 2 calculations after assuming a s surface water loading of 0.1% the results were divided by a factor accounting for the default drift value of 2.38%). We suggest the following statement should be added "However, MS.s may wish to consider the potential for surface water contamination in their own localities arising from glasshouse use"	
(2)	Vol. 3, B.8.6.3, Table B.8.6.3-1 PECgroundwater	UK: Table 8.6.3-1 states 40% crop interception but text above it states 75% interception. Please clarify	

section 5 - Ecotoxicology (B.9)

14. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 3, B.9.2.1., acute toxicity to aquatic life	UK: Helpful summary tables of the studies, very clear and all that is necessary for acute studies done to guideline and GLP.	
(2)	B.9.5.3: Risk assessment for non-target arthropods	UK: Whilst the principle of the risk calculations proposed by the RMS is understood, it is noted that the standard ESCORT 2 HQ procedure and triggers were only validated for Tier 1 glass slide tests on *A. rhopalosiphi* and *T. pyri* and only using 'typical' contact toxins. We feel that, given the mode of action and route of uptake of pyriproxyfen, there should be some further discussion over the relevance of the standard suite of studies in terms of species used, life stages, route of uptake, duration - and whether they are indeed fully able to address the exposure and risks from such an IGR	

15. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.2.2.5 oxidising properties	AT: The result given under 2.9.1 “physical compatibility with other products” (reactions with granular zinc and KMnO4) does not address this Annex point. A test according to EEC/A17 is required.	
(2)	Vol. 3, 2.9.1 physical compatibility	AT: The statement given does not cover physical compatibility.	
(3)	Vol. 3, B.5.2 anal. methods in plants	AT: More information concerning linearity is requested as it seems that linearity data are not in accordance with guidance document SANCO 825/00 (one point calibration) and the determined recoveries therefore in doubt.	
(4)	Vol. 4, C.1.1.2 starting materials	AT: The commercial availability of the starting materials (especially number 1) should be reported.	
(5)	Vol. 4, C.1.5 confirmation of one impurity by MS	AT: Is the study completed yet?	

section 2 - Mammalian toxicology (B.6)

16. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier>>: <<comment>>	

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section 3 - Residues (B.7)

17. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier>>: <<comment>>	

section 4 - Environmental fate and behaviour (B.8)

18. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier>>: <<comment>>	

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section 5 - Ecotoxicology (B.9)

19. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. #, <<data point>>, <<description>>	<<MS/notifier>>: <<comment>>	

* When mentioning page numbers of the DAR in your comments, **the page numbers should refer to the pdf-version** (not the WORD-version) of the DAR to ensure consistency among the Member States.

20. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, List of endpoints	DE: Remark: "The Definition of the Residue: (Annex IIA, point 7.3) Relevant to the environment" on page 134 differs from Vol. 1, 2.5.1. Please add a note in List of endpoints that metabolites are not relevant for monitoring. On the other hand, if for monitoring metabolites have to be included, please change chapter 2.5.1. In the last case, methods for metabolites are missing.	
(2)	Vol. 1, 2.2 and Vol. 3, B.5.2	DE: Remark: A clear conclusion on the suitability of additional MS traces to confirm positive findings is missing.	The summary in Vol. 1, 2.2 seems to restrict the MS detection on one fragment ion (m/z 136). The original studies are not available in DE.
(3)	Vol. 1, 2.2 and Vol. 3, B.5.3	DE: Remark: Except from the method for residues in air a clear conclusion on the suitability of additional MS traces to confirm positive findings is missing.	For air only, confirmation is mentioned.

21. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, Chapter B.6.10.4 (ARfD)	DE: Proposal: We propose to use the developmental study in rats (Saegusa 1988c) instead of the acute oral toxicity studies to derive the ARfD. 12/42 dams out of the high dose group died between day 4 and day 9 of dosing. Bodyweight decrease was observed in this group following the first dosage. Incidence of skeletal variation were increased in high and mid dose group pups. Using the developmental NOAEL of this study (100 mg/kg bw/d) and a safety factor of 100 results in the ARfD of 1 mg/kg bw/d.	
(2)	Vol. 1, Chapter 2.3 (List of endpoints)	DE: Remark: There is a typing error for the AOEL value (0.1 instead of 0.04 mg/kg bw/d). Comparing following values with the summary in Table 6.6.3.1, reproductive NOAEL should probably read 333 instead of 443 mg/kg bw/d and the developmental NOAEL should probably read 100 instead of 1000 mg/kg bw/d.	

22. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.2.3.1.2, Long-term risk (of the as for aquatic organisms)	DE: Although there is a factor of more than 300 between the laboratory endpoint (NOEC = 0.015 µg as/L) and the result of the microcosm study (NOEAEC = 5.0 µg as/L), the conclusions of the RMS can generally be supported. However, the RMS is kindly asked to provide a justification for a) equalizing the $NOEAEC_{MICRO}$ with an EAC and b) setting the trigger value to 1 without any safety margins.	The microcosms were run as an indoor study over a relatively short period of 8 weeks. The study design is not believed to cover effects on the whole aquatic community. Therefore, a safety factor should still be applied on the $NOEAEC_{MICRO}$.

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

23. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 1, LOEP	EFSA: there is a new 2006 FAO specification and the end points should be amended accordingly and in line with EPCO manual E4.	
(2)	Vol 3, B..2.1.4, relative density	EFSA: We agree that a new density method is required.	
(3)	Vol 3, B.2.1.5, vapour pressure	EFSA: It is not understood why the vapour pressure has been accepted without a purity. Also it is not clear what is meant by the statement in the comments column. This should be explained	
(4)	Vol 3, B.2.1.6,Henry's law	EFSA: A new calculation will be required when the new water solubility study is provided.	
(5)	Vol 3, B.2.1.10, spectra	EFSA: We agree that new spectra are required.	
(6)	Vol 3, B.2.1.11, solubility in water	EFSA: We agree that a new study on solubility in water is required.	
(7)	Vol 3, B.1.12, solubility in organic solvents	EFSA: Further details of the test method should be provided.	
(8)	Vol 3, B.2.1.13	EFSA: We agree that a new study for partition coefficient is required to investigate the effect of pH.	
(9)	Vol 3, B.2.1.16, photochemical degradation	EFSA: It is not clear why this study has been accepted given that it used pyrex glass.	
(10)	Vol 3, B.2.1.19, stability in air Atkinson calculation.	EFSA: Why is the value calculated by the RMS and not by the company. If it has been calculated by the RMS what are the references for.	

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section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(11)	Vol 3, B.2.1.22 and 23 explosive and oxidising properties.	EFSA: Some further information on the structural case that was presented by the applicant would be helpful.	
(12)	Vol 3, B.2.2, general	EFSA: In the methods and results column it appears that a lot of the text in the original template used to make this document has been left in by mistake. This makes the table unclear and it should be amended.	
(13)	Vol 3, B.2.2.5, oxidising properties	EFSA: Some further details of the case that was made by the applicant would be helpful.	
(14)	Vol 3, B.2.2.15, shelf life	EFSA: The container material should be given.	
(15)	Vol 3, B.2.9.1, compatibility with other products.	EFSA: It is not clear what EPA 63-14 is for when in the box below it states that mixing with other products is not required.	
(16)	Vol 3, B.5.2, plant methods	EFSA: At the most only two acceptable ions above 100 have been monitored therefore confirmatory methods are required. In addition to this as more than one crop is covered by the representative uses then all of the matrix groups should be validated.	
(17)	Vol 3, B.5.3, soil and water methods.	EFSA: The validation for the GC-MS confirmatory methods should be given.	
(18)	Vol 4, C.1..1.2, starting materials	EFSA: Is the starting material [redacted] commercially available. If not then a specification and method of manufacture should be provided.	
(19)	Vol 4, C.1.2.2, isomers	EFSA: From the statement it is not clear if there is any data to demonstrate the biological activity of the isomers.Thsis should be addressed.	

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section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(20)	Vol 4, C.1.2.3, specification	EFSA: From the 5 batch data the proposed specification for [redacted] is not justified.	
(21)	List of studies relied on version 1 November 2005.	EFSA: The list should be amended as it is currently not reliable for example Kimura, M. 2000a,b,c could not be found in the DAR.	

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section 2 - Mammalian toxicology (B.6)

24. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol.3, B.6, General comment	EFSA: Tables with figures instead of statements (increased, decreased, …) would be more helpful for the interpretation of the results.	
(2)	B.6.6.2, Teratogenicity studies, p.128 Vol.1, p.103, LoEP	EFSA: The statistically increased and dose-related incidence of skeletal variation (opening of the foramen transversarium of the 7th cervical vertebra) to be discussed in relation with the determination of the developmental NOAEL. The list of end points should be amended with the lowest developmental NOAEL related to this effect.	
(3)	B.6.12, Dermal absorption, p.163	EFSA: It should be clarified that the two doses are representative for the undiluted product and the spray dilution (to the minimum recommended use concentration for field application).	
(4)	Vol.4, C.1.4.1, p.17	EFSA : RMS to confirm that the levels of the impurities in the final technical specification are acceptable in comparison to what has been tested in the toxicological batches.	

section 3 - Residues (B.7)

25. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.1.1, Tomato metabolism	EFSA: The conclusion that residues of the free and conjugated PYPA metabolite would not bee relevant in tomatoes harvested at PHI 3 because the PHI in the metabolism study (7 days) in longer than the one defined in the GAP (3 days) lacks the consideration that a) PHI 3 days is a minimum waiting period, not obliging the farmer to harvest after exactly 3 days and no later, and b) the metabolic activities in the fruits continue after harvest.	
(2)	Vol. 3, B.7.1.2, Succeeding crops	EFSA: Some clarification should be given on the rotational crops issue. 4-OH-PYR is a relevant metabolite in soil compartment and also more persistent than parent as DT90 is up to 234 days. RMS could have elaborated on this. Only 30 days plant back interval was investigated, if metabolites are taken up, higher residues may occur at a later plant back interval. Apart from solvents partition, were any attempts made to identify the residues in wheat grain and straw? What does mean “when a correction is made for direct treatment … residue levels are not expected to exceed the trigger.	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	B.7.15.1. Intakes by domestic animals and B.7.3.2 Definition of the residue in animal products	EFSA: According to the current European Feed Composition Table only cotton seed would be a relevant commodity. However, cotton gin trash is known as a feed item relevant for cattle and relevant residue levels of pyriproxifen might be expected in gin trash (according to the metabolism study at 2N rate, which has been considered applicable to the proposed GAP by RMS) It should be mentioned that a scenario where gin trash is fed to cattle has not been evaluated.	
(4)	Vol. 3, B.7.6.2, Cotton residue trials	EFSA: Given the fat solubility of parent and the results of the metabolism study (even though growth stage at application not indicated) it might be discussed whether 2 residue trials in cotton are indeed sufficient to exclude that occasionally residues >0.01 mg/kg in cotton seed may arise.	

section 4 - Environmental fate and behaviour (B.8)

26. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.2.3, Summary of adsorption desorption and mobility in soil	EFSA: On page 335 of Volume 3 it is stated that no pH dependency of adsorption at environmental relevant pH range is expected based on RMS estimated pKa values. A calculated pKa value is available for pyriproxyfen (phys chem. list of endpoints, 6.87) but not for the metabolites. Please provide the pKa values estimated and the estimation method used (Software version number etc.) for the two metabolites. As the metabolites are a phenol and a carboxylic acid, pH dependant adsorption might be expected. For pyriproxifen in acidic soils (not investigated) stronger adsorption might be expected. EFSA cannot accept the current statement regarding lack of pH dependant adsorption based on the information currently presented in the DAR.	
	Vol 1 List of endpoints, soil adsorption/desorption pH dependence.	LoEP Vol 1 p 112. The statement No pH dependency is expected may need to be reconsidered.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(2)	Vol. 3, B.8.3, Predicted environmental concentrations in soil.	EFSA: On pages 338-339 of Volume 3 accumulated concentrations are presented for Northern and Southern Europe for the use on tomato / eggplant for metabolite 4-OH Pyr. As the SFO DT90 for this metabolite is 235 days (i.e. less than 365 days), when it is assumed one crop is grown per year accumulation would not be expected. Accumulated concentrations are however calculated, so presumably it was assumed more than 1 crop would be planted per year which would probably be the case for glasshouse production? However it is currently not stated that it was assumed several crops were grown per year. In fact it is stated yearly applications were assumed in calculations, though the application rate used as the yearly application is not stated? Clarification is needed regarding the calculations?	
	Vol 1 List of endpoints, PECsoil and Soil accumulation and plateau concetration	LoEP Vol 1 p 112. The calculation for cotton can be deleted (there is no accumulation the level is the same as for a single application). For tomato / egg plant the endpoints need changing in line with the comment above on Vol. 3. LoEP Vol 1 p 113-116. For the cotton PEC (pyriproxifen and metabolites) calculations are presented assuming 40% crop interception. In the DAR 75% crop interception is appropriately assumed base on the growth stages in the intended uses table. The endpoints should be consistent with the calculation presented in the DAR.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Vol. 3, B.8.6.1/2, Predicted environmental concentrations in surface water and sediment. Vol 1 List of endpoints, PECsurface water & PECsediment.	EFSA: On pages 377-378 of Volume 3 it is stated that DT50 in soil , maximum observed soil formation fractions and 50% crop interception were used to calculate PEC at step 2 of FOCUS for the glasshouse use patterns. These values were not used. When No runoff / drainage is selected (as was the case here) the PEC calculated do not use any of this soil information in the calculation. LoEP Vol 1 p 117-133. In line with this comment regarding Vol 3 the input values that are not used in the calculations for the protected uses should be deleted from the method of calculation and main routes of entry boxes. (Step 1 and 2 calculations for glasshouse use).	
(4)	Vol. 3, B.8.6.3, Predicted environmental concentrations in groundwater Vol 1 List of endpoints, PECgroundwater	EFSA: On pages 385-387 groundwater exposure assessments for pyriproxyfen or its metabolites 4-OH-Pyr and PYPAC are not presented for the applied for uses in glasshouses. An assessment is required as more than one protected crop can be grown per season and the application rate to the protected crops can be higher than for cotton. Therefore it is clear that the available cotton calculations alone are not sufficient to cover the protected uses that require assessment. LoEP Vol 1 p 133-134. In line with this comment regarding Vol 3 the endpoints need to include information regarding the glasshouse uses on eggplant and tomatoes.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(5)	Vol 1 List of endpoints, Route of degradation in soil supplemental studies, soil photolysis	EFSA: LoEP Vol 1 p 111. Please add the DT50 calculated in the irradiated experiment including the equated natural light energy input (i.e. ca. 10-19 days summer sunlight at 43°N)	
(6)	Vol 1 List of endpoints, Rate of degradation in soil, laboratory studies	EFSA: LoEP Vol 1 p 111. Please annotate the DT50 for 4-OH-Pyr to indicate that these values are rate of decline observed in a study dosed with the parent compound and are not true degradation rates for 4-OH-Pyr. For the 10°value for pyriproxyfen please add the range calculated (i.e. 6.2-55 days) and not just the mean value as currently presented.	
(7)	Vol 1 List of endpoints, soil adsorption / desorption	EFSA: LoEP Vol 1 p 112. Please add the units for Kf and Kfoc (presumably L/kg)	
(8)	Vol 1 List of endpoints, Route and rate of degradation in water, photolytic degradation	EFSA: LoEP Vol 1 p 116. Please quote the DT50 with its associated equivalent light intensity (xenon light isn't very helpful in putting the DT value in context). I.e. 8.5-14.5 days at 43°N summer sunlight is more useful.	
(10)	Vol 1 List of endpoints, Degradation in water / sediment DT50 / 90 values	EFSA: LoEP Vol 1 p 116. Please indicate with an annotation that the DT values for water and sediment presented are dissipation values as observed in the study and not kinetically derived degradation values.	

section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(11)	Vol 1 List of endpoints, Definition of the residue	EFSA: LoEP Vol 1 p 134. Please quote all the residues for which an assessment is triggered. In this context the definition for groundwater should include: pyriproxifen, 4-OHPyr and PYPAC. Following current guidance an assessment is only triggered in soil for parent pyriproxifen. For soil the references to the metabolites should therefore be deleted.	
(12)	Vol 3 B.8.10 References relied on and the separate list of information tests and studies relied on.	EFSA: Vol. 3 page 391 and the separate list of information tests and studies relied on: Please delete Fathulla 1995a (anaerobic aquatic metabolism). There is no data requirement for this study type and it is not relied on in the exposure / risk assessment.	
(13)	Vol 3 B.8.10 References relied on and the separate list of information tests and studies relied on.	EFSA: Vol. 3 pages 394-5 and the separate list of information tests and studies relied on: Please delete all the annex III references (References for the plant protection product) as none of these reports (calculations) are summarised in the DAR or referred in the DAR. Therefore they cannot have been relied on. The calculations in the DAR would appear to be those carried out by the RMS and not those provided by the applicant?	

section 5 - Ecotoxicology (B.9)

27. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9, background information	EFSA: The background information and the table with an overview of metabolites are very much appreciated.	
(2)	Vol. 3, B.9.1.5.1, Risk of active substance to birds	EFSA: We agree that the risk from intake of contaminated drinking water could be assessed based on PEC surface water for the glasshouse uses. However, for field use exposure from intake of diluted spray solution in leaf axils or from puddles should be considered.	It was agreed in the PRAPeR 08 expert meeting that for the time being, until further guidance is available, an assessment in accordance with the recommendations in the GD for birds and mammals should be done for the acute time frame using the allometric equation and a dilution factor of 5.
(3)	Vol.3, B.9.2.1.1, Acute toxicity of the active substance	EFSA: Since initial measured concentrations in the acute toxicity studies with aquatic organisms were <80% of nominal in all cases but one, toxicity values should be expressed as initial measured concentrations according to the recommendations in the GD on aquatic ecotoxicology.	
(4)	Vol. 3, B.9.2.2.1.4, Microcosm and mesocosm studies	EFSA: On p. 435, the last sentence, it is stated that recovery of Cladocerans was observed on day 28 while in Table B.9.19 a significant reduction is indicated also on day 28. Please clarify.	
(5)	Vol. 3, B.9.2.3.1.1, Acute risk to aquatic organisms	EFSA: It was noted that the acute risk to *Daphnia* was calculated with PEC_{sw} based on FOCUS Step 1 which includes also 10% drift and run-off input. The header to Table B.9.20 says PECs based on 2.77% spray drift which is confusing.	

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section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 3, B.9.2.3.1.2, Acute risk to aquatic organisms	EFSA: It was noted that it was proposed that no assessment factor is needed for the microcosm study. We do not agree to this and propose that this is discussed in an experts meeting.	
(/)	Vol. 3, B.9.4.2.3, Risk to bee brood	EFSA: We agree to the data requirement for the applicant to address the risk to bee brood for the use in tomato and egg plant in Southern EU.	
(8)	Vol.3, B.9.7	EFSA: We agree to the data requirement for a new study on effects on soil nitrogen turnover and respiration.	It was noted that the applicant has indicated that a study is available.
(9)	Vol. 3, B.9 General	EFSA: A full specification of the material used in all studies should be provided by the applicant and the compliance with the specification of the technical material should be assessed.	Directive 91/414, Annex IIA 8. Ecotoxicological studies Test substance (vi) A detailed description (specification) of the material used, as provided for under point 1.11 must be provided. Where testing is done using active substance the material used should be of that specification that will be used in the manufacture of preparations to be authorized except where radiolabelled material is used.
(10)	Vol. 1, List of endpoints, General	EFSA: Please use the EPCO No E 4, revision 4 (September 2005) template for the list of endpoints.	
(11)	Vol. 1, List of endpoints, TER for aquatic organisms	EFSA: It is not clear from the LoEP that the TER of 123 for *Daphnia* is calculated with a PEC_{sw} based on FOCUS Step 1.	

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section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(12)	Vol. 1, List of endpoints, TER for aquatic organisms	EFSA: Please report TER values for fish calculated with PEC from FOCUS steps and LC_{50}/NOEC from laboratory studies since fish is not covered by the microcosm study.	
(13)	Vol. 1, List of endpoints, Bioconcentration	The level of residues at 14 days was reported as 10.4% in the study (and not <11%).	
(14)	Vol. 1, List of endpoints, toxicity to bees	EFSA: LD_{50} values from non acceptable studies should not be included in the LoEP.	
(15)	Vol.3, B.9.11, List of references relied on	EFSA: Since the study by Hoberg (2001) on acute toxicity of pyriproxifen to bees was no accepted it should be deleted from the list of references relied on.	