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Comments on the Draft Assessment Report on spirodiclofen

End of commenting period: 20.08.2004 (MS, NOT)

Date	Supplier	File
19.07.2004	Slovenia	01 spirodiclofen comments SI.doc
28.07.2004	Belgium	02 spirodiclofen comments BE.doc
28.07.2004	United Kingdom	03 spirodiclofen comments UK.doc
11.08.2004	Poland	04 spirodiclofen comments PL.doc
16.08.2004	Sweden	05 spirodiclofen comments SE.doc
18.08.2004	Bayer CropScience	06 spirodiclofen comments NOT.doc
25.08.2004	Austria	07 spirodiclofen comments AT.doc
26.08.2004	Denmark	08 spirodiclofen comments DK.doc
22.09.2004	EFSA	09 spirodiclofen comments EFSA.doc
20.04.2009	German Professional beekeepers organisation	10 spirodiclofen comments German Professional beekeepers organisation 2009-04-20.doc
20.04.2009	European Professional beekeepers organisation	11 spirodiclofen comments European Professional beekeepers organisation 2009-04-20.doc

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

1. 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)	PEC groundwater and PECsoil. Vol.1 2.5.2 list of end points Vol.3 B.8.2.4 & B.8.3	SLO: The assumed interception is not consistent. The predicted concentrations in ground water are based on interception values of 65, 70 and 40% for apple, citrus and grape, respectively. The predicted concentrations in soils are based on an interception value of 50% for all three crops.	

section 5 - Ecotoxicology (B.9)

2. 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 2.6.1.1 Birds List of end points	SLO: See comments 7-9 on volume 3.	
(2)	Vol.1 2.6.1.2 Mammals	SLO: See comments 10-14 on volume 3.	
(3)	Vol.1 2.6.2 Effects on aquatic species – chronic risk of spirodiclofen List of end points	SLO: There is no clear position in the DAR on the chronic risks of spirodiclofen for aquatic organisms. Volume 3 states that chronic exposure to spirodiclofen is unlikely as there was a fast dissipation from the water column in the water-sediment study (DT50 0.3-1.1 days). If this is supported no further assessment is needed in volume 1 and the list of end points.	
(4)	Vol.1 2.6.3.2 Other arthropod species List of end points	SLO: See comments 16-17 on volume 3.	
(5)	Vol.1 2.6.4.2 Effects on other soil macro-organism	SLO: Reference should be made to 2.6.6 where the risks of metabolites for Collembola are assessed based on accepted studies.	
(6)	Vol.1 list of end points - Bioaccumulation	SLO: The BCF based on total radioactivity should also be reported.	See comments 9 and 13.
(7)	Vol.3 B.9.1.4 Risk assessment for birds - acute risk assessment	SLO: In the acute risk assessment the RUD values used are not mentioned. Using the standard 90th percentile value of 52 for small insects according to SANCO/4145/2000 leads to a higher PECfeed (7.5 mg/kg wwt for orchard and 5.0 mg/kg wwt for vine).	

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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.3 B.9.1.4 Risk assessment for birds - short-term risk assessment and long-term risk assessment	SLO: In the short-term risk assessment and the long-term risk assessment the RUD values used are not mentioned. Using the standard 50th percentile value of 29 for small insects according to SANCO/4145/2000 leads to a higher PECfeed (4.2 mg/kg wwt for orchard and 2.8 mg/kg wwt for vine).	
(9)	Vol.3 B.9.1.4 Risk assessment for birds - long-term risk assessment (bioaccumulation and food chain behaviour)	SLO: The BCF in fish of 491 L/kg based on total radioactivity should be used.	The risks of metabolites formed in the bioaccumulation study should be covered by the assessment of the risk of bioaccumulation for fish eating birds for the active substance as most of these metabolites are not assessed separately. Therefore it is more appropriate to use the BCF based on total radioactivity.
(10)	Vol.3 B.9.1.6 Risk assessment for mammals - acute risk assessment	SLO: In the acute risk assessment the RUD values used are not mentioned. Using the standard 90th percentile value of 85 for short grass according to SANCO/4145/2000 leads to a higher PECfeed. Several parameters are not in accordance with the final guidance of SANCO/4145/EC such as FIR/bw of 1.14 in stead of 1.39, interception of 0.5 in stead of 0.4.	

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.3 B.9.1.6 Risk assessment for mammals – long-term risk assessment	SLO: In the long-term risk assessment the RUD values used are not mentioned. Using the standard 90th percentile value of 46 for short grass according to SANCO/4145/2000 leads to a higher PECfeed. Several parameters are not in accordance with the final guidance of SANCO/4145/EC such as FIR/bw of 1.14 in stead of 1.39, interception of 0.5 in stead of 0.4. This proves to be crucial as also after the refinement the trigger of TERlt>5 is not met with the correct values.	
(12)	Vol.3 B.9.1.6 Risk assessment for mammals – long-term risk assessment	SLO: Refinement of the NOEC based on the assumption that continuous exposure does not occur is not acceptable. The decline in residue is accounted for at the exposure side and should not be refined on the toxicity side.	
(13)	Vol.3 B.9.1.6 Risk assessment for mammals - long-term risk assessment (bioaccumulation and food chain behaviour)	SLO: Several parameters are not in accordance with the final guidance of SANCO/4145/EC such as DFI for a earthworm-eating mammal of 1.1 in stead of 1.4 g fresh material/day and a DFI for a fish-eating mammal of 346 in stead of 390 g fresh material/day.	
(14)	Vol.3 B.9.1.4 Risk assessment for birds - long-term risk assessment (bioaccumulation and food chain behaviour)	SLO: The BCF in fish of 491 L/kg based on total radioactivity should be used.	The risks of metabolites formed in the bioaccumulation study should be covered by the assessment of the risk of bioaccumulation for fish eating birds for the active substance as most of these metabolites are not assessed separately. Therefore it is more appropriate to use the BCF based on total radioactivity.

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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
(15)	Vol.3 B.9.2.3.1.3 Bioaccumulation	SLO: See comment 9 and 13.	
(16)	Vol.3 B.9.5.3 Risk assessment – non-target arthropods	SLO: It is mentioned that the maximum recommended dose for foliage dwelling species is 40% of the field dose as recommended in SETAC guidance (1994), whereas in the actual risk assessment 50% of the field dose is used. This is not consistent.	
(17)	Vol.3 B.9.5.3 Risk assessment – table B.9.40	SLO: Table B.9.40 reports the interception factor of 50% as in-crop vegetation distribution factor which is confusing.	
(18)	Vol.9.7 Effects on soil non-target macro-organisms	SLO: Reference should be made to B.9.3.3 where the risks of metabolites for Collembola are assessed based on accepted studies.	

section 2 – Mammalian toxicology (B.6)

3. 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.6.1.6 Absorption, excretion and distribution studies	Be: from the toxicokinetic studies it appears that oral absorption of spirodiclofen reaches 60-76%. The use of a factor of 0.58 for oral absorption should be clarified	
(2)	Vol.3, B.6.6.1 reproductive toxicity	Be: agreement with NOAEL systemic toxicity<70 ppm (5.2 mg/kg bw/d) but we propose to take into account the decreased body weight observed in F2 pups at birth for fixing the NOAEL reprotoxicity. This gives a NOAEL repro= 70 ppm and not 350 ppm as proposed by the RMS.	
(3)	Vol.3, B.6.8 Mechanistic studies	Be: The notifier concluded that the metaboliteBAJ2510 interfere with steroid hormone synthesis at the level of general biochemical pathways (Krebs cycle and pyruvate/citrate shuttle) but has no specific effects on the steroid synthesis. - We think that different aspects suggest that cholesterol synthesis is inhibited and this could reduce hormonal synthesis. - Is malate dehydrogenase the unique mitochondrial source of NADPH ? What is the opinion of the RMS ?	

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4. 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, Section C.1.2.4., methods of analysis for impurities	UK: No details of the GC Headspace method of analysis for the impurity [redacted] appear to have been submitted.	

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. 3, B.6.1.1, Toxicokinetic studies	UK: The lack of repeat dose data for females is of concern, particularly as there are marked sex differences in metabolism and there is evidence this compound might act as an endocrine disrupter. We also note the high log Kow	
(2)	Vol. 3, B.6.1.1, Toxicokinetic studies	UK: Only limited data are presented for few tissues. In study1, tabulation of the radioactivity levels in tissues would allow an independent assessment. It would also make it clear which tissues have been evaluated. As presented in the DAR, only the liver, kidney, plasma, gastro-intestinal tract and skin are mentioned (other tissues tells us nothing). Did it reach the bone marrow (mutagenicity) or sex organs (testes and uterine tumours)?	
(3)	Vol. 3, B.6.1.1, Toxicokinetic studies	UK: it would have been preferable to have labelled the molecule in two positions rather than one	
(4)	Vol.3, B.6.3, short term toxicity	UK: Tables for 28 day oral studies are not sufficiently transparent to enable an independent assessment	28 day rat needs values and statistical significance to make an independent assessment. 28 day dog the males and females data has been presented together

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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, B.6.3.3 semichronic oral studies	UK: We would probably accept the LOEL for liver hypertrophy in rat and mouse as a NOAEL	14 week Wistar rat study we would sugget historical control data would help interpretation of the adrenal effects
(6)	Vol 3, B.6.3.4 summary short term and semichronic oral studies	UK: We agree that the dog is the most sensitive species tested in this way, but note that a NOAEL has not been determined for short-term exposure in the dog.	
(7)	Vol 3, B.6.4.3 Genotoxicity summary	UK: Equivocal results in HPRT assay and significant increases in chromosome abberations in the cytogenetics assay in the absence of historical control data, lead us to conclude further clarification and possibly a second *in vivo* study should be required.	Tumours are seen in two species, so it is important to be clear about possible genotoxicity
(8)	Vol 3, B.6.5.3, long term toxicity/carcinogenicity	UK: Increased organ weights and increased T3 (tri-iodothyroxine) levels in females suggest a treatment-relate effect at 20 ppm (the lowest dose used) but the lack of actual values in the table makes it difficult to interpret.	The RMS has proposed a NOAEL of 50 ppm for this study. But we sugest actual values and perhaps mechanistic data are required to dismiss possible effects at the lowest dose.
(9)	Vol 3, B.6.6.1, Reproductive toxicity	UK: RMS has determined a LOEL of 70 ppm (5.2 mg/kg bw/day), the lowest dose used. Again, there is insufficient information in the tables to make an independent assessment. The possible lack of evaluation of the spermatids/sperms at this dose is of particular concern.	

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 3, B6.8.1.2, mechanistic studies	UK: From a brief consideration of the DAR we could not find a proposal for clear mechanisms for the observed tumours, endocrine effects or immunotoxicity, however it does seem that spirodiclofen has more than one mechanism of toxicity	
(11)	Vol 3, B.6.10.3, Proposed ADI	UK: The RMS proposed an ADI of 0015 mg/kg bw/day. We cannot accept this value at present without further clarification	The proposed ADI is based on the NOAEL determined for the critical adrenal effects in the 12-month dog study and an assessment factor of 100. Adrenal effects were apparent at 25 ppm (4.1 mg/kg bw/day) in the chronic mouse study (i.e. the LOEL) and a NOAEL was not determined for females. The LOEL for adrenal effects in the 12 month dog study was (150 ppm 4.54 mg/kg bw/day). Based on the data, the mouse could be more sensitive than the dog and a NOAEL was not determined for the mouse study. This aspect might be addressed by incorporating an additional uncertainty factor to the assessment. In addition, the absence of NOAELs for the chronic mouse and rat multigeneration study give rise to concern when setting the ADI.
(12)	Vol 3, B.6.10.5, Proposed AOEL	UK: We suspect NOAELs could be set for at least 2 of the 3-month studies. (see comment at 5 above) If so this might affect the derivation of the AOEL.	
(13)	Vol 3, B.6.11, formulation toxicity	UK: we consider that two skin sensitisation studies supporting the same formulation is a misuse of animals. The active substance was positive for skin sensitisation and the fomulation should be classified based on the GPMT test	

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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
(14)	Vol 3, B.6.12, dermal penetration	UK: we consider the use of Rhesus monkeys for dermal penetration studies is an inappropriate use of primates.	UK has advised this company of this view when similar data were submitted on a different substance.
(15)	Vol 3, B.6.12, dermal penetration	UK : It is not clear if the radiolabelled active substance was applied in the formulation concentrate or a dilution. Values for the both concentrate and the dilution(s) are required.	
(16)	Vol 3, B.6.12, dermal penetration	UK: The application site was not given in the text (some sites are more amenable to absorption than others), and only male monkeys were considered.	
(17)	Vol 3, B.6.12, dermal penetration	UK: Approximately 8% of the radioactivity was not recovered and there was no necropsy. Therefore, it must be assumed that this 8% remains in the body.	
(18)	Vol 3, B.6.14.1, operator exposure	UK: For the UK POEM knapsack model the application parameters typically assumed are 1 ha or 400 litres of spray solution applied per day. A realistic worse case assessment for hand-held application would therefore be 0.4 ha (400 litres/1000 litres) rather than the 0.15 ha which has been modelled.	

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.6.14.1, operator exposure	UK: As there is currently no agreed model for the EUROPOEM database, details of which datasets have been used for the assessment should be given so that the assessment is transparent.	
(20)	Vol 3, B.6.14.4, risk assessment	UK: In Table 6.14.4 estimates of exposure for dermal exposure and inhalation exposure using the various predictive exposure models are compared individually to the proposed systemic AOEL of 0.008 mg/kg bw/day (0.56 mg/ 70 kg person/day). As route specific AOEL's have not been proposed for this substance, the assessment (operators and bystanders) should consider exposure on the basis of total systemic exposure, i.e. dermal and inhalation exposure should be combined. Recommendations should be based on these total systemic exposures.	All estimates of exposure will need to be revised if a dermal absorption value higher than the 2% proposed is agreed. (see comment 17 above)

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
(21)	Vol 3, B.6.14.3 Worker exposure	UK: This section concludes that worker exposure will probably be limited to a short period of re-entry tasks shortly after application. As it can be expected that pome fruit, stone fruit and grapes will be harvested by hand, this statement appears incorrect and the assessment for re-entry workers should consider hand-harvesting over a full working day.	
(22)	Vol 3, B.6.14.3 Worker exposure	UK: The use of protective clothing for re-entry workers to reduce levels of exposure to within acceptable levels may not be realistic, as these workers may not be aware of the compounds which have been used on the crops they are harvesting. Whilst it is expected that work clothing worn will offer some protection from dislodgeable foliar residues, the realistic worse case for these workers would be to consider exposure for an unprotected worker.	
(23)	Vol 3, 6.14.4, risk assessment	UK: Clearly exposures would need to be compared against any revised AOEL (see comment 12 above)	

section 3 - Residues (B.7)

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.7.12.2, Proposed MRLs	UK: An MRL has not been proposed for apples and pears in Southern Europe due to insufficient trials being performed to the proposed GAP. Comparing the data in Tables B.7.6.3.3a and B.7.6.3.3b, the data sets for both N and S Europe show very similar residue data. An extrapolation could therefore be valid from N to S Europe and therefore a full data set for S Europe may not be necessary.	
(2)	Vol 3, B.7.12.4, residue definition in animal products	UK: we agree with the RMS that the issues raised by a fat soluble parent and a metabolite which is not fat soluble should be discussed by appropriate experts to try and resolve this potential difficulty for monitoring.	

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

7. Environmental fate and behaviour (B.8)

No comments

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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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 3, B.9.1.4 Summary of avian toxicity data	UK: Given the concerns expressed in the mammalian toxicology section regarding the mechanisms of toxicity and possible endocrine effects of the a.s. and the -enol metabolite, we would liked to have seen some discussion here as to the suitability of the avian reproduction test and resulting end-point to address all the potential for reproductive effects in birds. It may well be a suitable test and end-point but some clarification would be welcome.	
(2)	Vol 3, B.9.1.5 Risk assessment for birds	UK: This does not substantially affect the levels of risk determined - but for clarification could the RMS please explain how the ETE figures for small insects were arrived at?	Our own calculations according to the Tier 1 principles outlined in the latest EC Guidance Document on Risk Assessment for Birds and Mammals (SANCO/4145/2000) arrive at respective ETE values for the acute assessment of 7.79 mg a.s./kg bw/day and for the short and long term assessments of 4.34 mg a.s./kg bw/day (orchard example only).
(3)	Vol 3, B.9.1.6 Risk assessment for mammals	UK: As above – we are not clear how the ETE for herbivorous mammals was calculated in accordance with SANCO/4145/2000.	Our figures for the acute and dietary risk assessments are 17.01 and 4.88 mg a.s./kg bw/day respectively (orchards only - not including crop interception).

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 3, B.9.1.6 Risk assessment for mammals	UK: In the long term risk assessment for mammals, there is discussion of some of the effects seen in the rat multigeneration study but it is still not clear why a NOEC of 70 ppm has been chosen over the reproductive NOAEL stated in B.6.6.1 of 350 ppm. We note that concerns relating to the mechanisms of toxicity have been expressed regarding the mammalian toxicity package and these may further influence the choice of end-point.	Please see also the comment (9) on the interpretation of the reproduction study in the mammtox section above as the resolution will also be relevant here.
(5)	Vol 3, B.9.2.3.1.2 Long term risk to aquatic life	UK: Further clarification is required of the reason for concluding there is a chronic risk requiring large buffer zones for mitigation as the DAR states that chronic exposure to spirodiclofen is unlikely to occur	Spirodiclofen is applied only once per season and dissipates rapidly from water (DT50 0.3-1.1 days) thus a chronic assessment would not normally be triggered. Despite this, a chronic risk assessment is conducted because the data are available and concludes a need for large buffer zones (compared with those required according to acute and sediment-dweller risk assessments). Since there is considered to be minimal chronic exposure we would question whether these large buffer zones are really needed (despite the availability of chronic data), unless there are other reasons why a chronic assessment is required (perhaps related to bioconcentration or uncertain reproductive effects).

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.9.4.2 Risk to bees	UK: Will bees be exposed through the recommended use of spirodiclofen? Section B.3.2.3 would suggest that there is no use during the flowering periods of crops attractive to bees. However there may be residual activity which needs to be considered as well as the potential for flowering weeds to be sprayed. It may be possible to sufficiently minimise any exposure through appropriate labelling. If there is still considered to be potentially adverse levels of exposure through recommended use, then we would agree with the need for further data on bee brood development. Given the residual activity of the compound and the slow realisation of effects, the exposure and monitoring periods studied should be of sufficient duration to pick up any longer term impacts.	
(7)	Vol 3, B.9.5.3 Risk to other non-target arthropods	UK: Given the IGR mode of action of spirodiclofen and the remaining uncertainty about the precise mode of toxicity/action it would be helpful to have some further clarification about the specificity of activity. Is there for example any further information from screening studies that might be helpful in this respect?	

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9. 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
		No comments	

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section 2 - Mammalian toxicology (B.6)

10. 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
		No comments	

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section 3 - Residues (B.7)

11. 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
		No comments	

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

12. 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 8.1.1.1 b (Oi, M. 1999a), Aerobic studies Vol. #, <<data point>>, <<description>>	PL: The RMS comment on the reliability of the results (i.e. „The lack of data points would result in values, which are considered less reliable than those from the previous study") is not very clear (it is somehow contradictory and thus confusing). Please explain its meaning.	

section 5 - Ecotoxicology (B.9)

13. 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
		No comments	

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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, 2.6.3.2 Other arthropod species	Could you please confirm that the most appropriate route of uptake has been used in the terrestrial arthropod studies? Testing with other IGRs has revealed that in some cases uptake through food is a more appropriate route of uptake. That does not necessarily need to be the case with spirodiclofen but could you please confirm this.	
(2)	Vol. 3, 2.6.3.2 Other arthropod species	The test conducted with ground dwelling arthropods (i.e. *Poexilus* and *Pardosa*) only investigated effects on mortality and food consumption. These are not typical endpoints for IGR, rather effects on fecundity may be much more sensitive and according to ESCORT 2 such endpoints should be studies for IGR. Can you please comment on that?	

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. 3, 2.6.3.2 Other arthropod species	We don not think that the risks for non target arthropods in off-field habitats have been fully evaluated. The TER values indicate that sensitive species may be affected in off field habitats at distances of < 20 m from treated fields. According to our interpretation of the data presented in the DAR only *Typhlodromus* and *Chrysoperla* (*Aphidius* is not a suitable species for IGRs according to ESCORT 2 p 15 and comment 2 above) have been tested using endpoints appropriate for IGRs. Hence very little information on the sensitivity of other NTA is available. Further, we do not agree with the conclusion that the field studies with Typhlodromus demonstrate that the off-crop risk is acceptable. We agree with that one year may be an acceptable time to recovery in-field, however regarding off-field effects a recovery period of one year cannot be considered acceptable. If an acceptable risk for NTA in off-crop areas cannot be demonstrated then a buffer zone should be considered.	

15. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5); Vol. 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, 1.3.1, Name and address of applicant p. 4	Notifier: New address: Bayer CropScience AG Research and Development Global Regulatory Affairs Alfred-Nobel-Str. 50 D-40789 Monheim am Rhein	Notifier: Please replace the former address by the new one.
(2)	Vol. 1, 1.3.5, CAS, EEC and CIPAC numbers p. 5	Notifier: New **CIPAC** number: 737	Notifier: Please add the newly assigned CIPAC number
(3)	Vol. 1, 1.3.7, Manufacturer of the active substance p. 5	Notifier: New address: [redacted]	Notifier: Please replace the former address by the new one.
(4)	Vol. 1, 1.4.1, current, former and proposed trade names; p. 6	Notifier: Development code number: BAJ 2740 SC 240 proposed trade name: **Envidor** SC 240	Notifier: Please list the proposed trade name in addition to the development code number.
(5)	Vol. 1, 2.2.2, analytical method for the formulation analysis p. 14	Notifier: Interferences should be added, so that the last sentence reads: The method was validated with respect to the parameters: precision, linearity, accuracy, specificity and **interferences**.	Notifier: The interference was listed correctly in Vol. 3, B.5.1.1, methods for the determination of the pure active substance in the active substance as manufactured and in the formulated product. Therefore it should also be mentioned in Vol. 1, 2.2.2, analytical method for the formulation analysis.

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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
(6)	Vol 1, 2.2.3 p. 15	Notifier: Method 00568 is considered valid for determination of residues in **grapes**. To support the explanations in Column 3 the notifier will subject an extra sample from the grape metabolism study (stored frozen until today) to the Method 00568. Extraction efficiency will be compared with the result from the metabolism study. The extract will be subjected to chromatographic analysis to check whether the pattern of active substance and metabolites is the same as reported in the metabolism study. If so it confirms storage stability. If the extraction efficiency with both methods is the same and the storage stability is given then the question of the RMS is also answered experimentally. Results will be available by end of September 2004.	Residues on grapes and apples are mainly (ca. 96-98 %) located on the surface as unchanged parent compound and are shown to be removed by washing with dichloromethane and acetonitrile/water (see table below). Hence, the amount of incurred residues in the fruits is low (4-8 %). Possible incomplete extraction of these incurred residues by using acetonitrile/water would have no meaningful influence on the overall amount of BAJ 2740 and could not explain the differences between the height of residues in metabolism and residue study. The differences between these two studies can be explained by different application procedures. The aim of the application in the metabolism study was to produce residues as high as possible to have enough material available for elucidation of metabolism. Hence, it was taken care to spray the grapes intensively and to avoid spraying the leaves. Moreover the grapes were smaller than in the residue study and due to the relatively higher surface/volume ratio the residues expressed in mg/kg are relatively higher.

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		
(6) continued			**Study/method**	**Surface washing/ extraction with**	**Result/remark**
			Apple metabolism study	Dichloromethane/ acetone	98 % of TRR in surface washings (96 % in dichloromethane, 2 % in acetone)
			Grape metabolism study	Dichloromethane/ methanol, water	96 % of TRR in surface washings
			Radiovalidation	Acetonitrile/water	92 and 97 % extracted from homogenised apple
			Residue method 00568	Acetonitrile/water	extraction method identical with radiovalidation
			Enforcement method S19	acetone	88-93,4 % of the TRR extracted from apple

* 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.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(7)	Vol 1, 2.2.3 p. 15	Notifier: **No MRLs and no enforcement method for animal matrices** are necessary, because the cattle feeding study clearly shows that no residues are to be expected in milk, animal tissues and organs at the 1.7 and 5.1-fold overdose (1.38 and 4.14 mg/kg feed). In addition in the goat metabolism study no residues were found in goat tissues above 0.01 mg/kg considering the applied overdose.	
(8)	Vol 1, 2.4.1 , p. 29	Notifier: The notifier is convinced that no residue definition in animal tissues is needed (see argumentation above (7)). Besides this, the notifier does not agree with the argumentation for the proposed residue definition in animal products. Spirodiclofen was not found in the goat. The results from the goat metabolism study not support the inclusion of spirodiclofen into the residue definition.	Vol 1, 2.4.1
(9)	Vol 1, 2.4.4, p. 30	Notifier: For grapes a provisional MRL of 0.2 mg/kg is proposed by the rapporteur (0.1 in this chapter is probably a typing error)	Vol 1, 2.4.4

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, 2.4.4, p. 30	Notifier: No MRLs for animal matrices are considered necessary, because the cattle feeding study clearly shows that no residues are to be expected in milk, animal tissues and organs at the 1.7 and 5.1-fold overdose (1.38 and 4.14 mg/kg feed). In addition in the goat metabolism study no residues were found in goat tissues above 0.01 mg/kg considering the applied overdose.	Vol 1, 2.4.4
(11)	Vol. 1, Appendix 3, List of Endpoints; p. 86	Notifier: New CIPAC number: 737	Notifier: Please add the newly assigned CIPAC number
(12)	Vol. 1, Appendix 3, List of Endpoints; p. 87	Notifier: Henry's law constant: at 20°C <2 x 10^{-3} Pa m^3mole^{-1}	Notifier: Please correct the typing error
(13)	Vol. 1, list of endpoints, Chapter 2.2. p. 91	Notifier: No enforcement method for animal matrices is considered necessary, because the cattle feeding study clearly shows that no residues are to be expected in milk, animal tissues and organs at the 1.7 and 5.1-fold overdose (1.38 and 4.14 mg/kg feed). In addition in the goat metabolism study no residues were found in goat tissues above 0.01 mg/kg considering the applied overdose.	
(14)	Vol 1, list of endpoints, Chapter 2.4. p. 97	Notifier: MRL in peach and whole peach group should be 0.2 mg/kg (0.1 in this chapter is probably a typing error)	

* 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.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(15)	Vol. 1, Level 4, demand for further information, 4.1 Identity of the active substance p. 126	Notifier: 1. A 5 batch analysis of the large scale production is under preparation 2. A confirmatory method is in preparation Both studies will be submitted as soon as possible.	
(16)	Vol, 1, level 4, 4.5.1 p. 126	Notifier: No enforcement method for animal matrices is considered necessary, because the cattle feeding study clearly shows that no residues are to be expected in milk, animal tissues and organs at the 1.7 and 5.1-fold overdose (1.38 and 4.14 mg/kg feed). In addition in the goat metabolism study no residues were found in goat tissues above 0.01 mg/kg considering the applied overdose.	
(17)	Vol, 1, level 4, 4.5.2 p. 126	Notifier: additional validations at levels up to 1 mg/kg spirodiclofen in dry apple pomace will be conducted.	

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 4, 4.5.3 and 4.5.5 p. 127	Notifier: Method 00568 is considered valid for determination of residues in grapes. To support the explanations in Column 3 the notifier will subject an extra sample form the grape metabolism study (stored frozen until today) to the Method 00568. Extraction efficiency will be compared with the result from the metabolism study. The extract will be subjected to chromatographic analysis to check whether the pattern of active substance and metabolites is the same as reported in the metabolism study. If so it confirms storage stability. If the extraction efficiency with both methods is the same and the storage stability is given then the question of the RMS is also answered experimentally. Results will be available by end of September 2004.	Residues on grapes and apples are mainly (ca. 96-98 %) located on the surface as unchanged parent compound and are shown to be removed by washing with dichloromethane and acetonitrile/water (see also comment number (6), Vol. 1, 2.2.3). Hence, the amount of incurred residues in the fruits is low (4-8 %). Possible incomplete extraction of these incurred residues by using acetonitrile/water would have no meaningful influence on the overall amount of BAJ 2740 and could not explain the differences between the height of residues in metabolism and residue study. The differences between these two studies can be explained by different application procedures. The aim of the application in the metabolism study was to produce residues as high as possible to have enough material available for elucidation of metabolism. Hence, it was taken care to spray the grapes intensively and to avoid spraying the leaves. Moreover the grapes were smaller than in the residue study and due to the relatively higher surface/volume ratio the residues expressed in mg/kg are relatively higher.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(19)	Vol 1, level 4, 4.5.4 p. 127	Notifier: laboratory method MR-694/98 is identical with method 00568. The laboratory method MR-694/98 was validated as method 00568 in a separate document under report no. MR-351/99.	
(20)	Vol 1, level 4, 4.5.6 p. 127	Notifier: additional validations in animal matrices and milk for analytical method 109720 will be conducted.	
(21)	Vol. 1, level 4, 4.5.7 p. 127	Notifier: No MRLs and hence no enforcement method for animal matrices is considered necessary, because the cattle feeding study clearly shows that no residues are to be expected in milk, animal tissues and organs at the 1.7 and 5.1-fold overdose (1.38 and 4.14 mg/kg feed). In addition in the goat metabolism study no residues were found in goat tissues, milk and organs above 0.01 mg/kg considering the applied overdose.	

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(22)	Vol. 1,level 4, 4.7.1 p. 127	Notifier: identification of metabolite M06 has been described previously in a position paper by BCS which has been accepted by the rapporteur (Memo of [redacted], CTB, to [redacted], Bayer CropScience 19-02-03 as answer on: commentaar van notifier op openstaande vragen monografie spirodiclofen onderdeel residuen (RIVM october 2002)	- The identity of M06 was confirmed by bridging from oranges to lemons where M06 was identified - by co-chromatography with authentic reference compound - concentration was below 0,05 ppm which is the trigger for identification. - Percentage is below 10% of the TRR which is the trigger for identification
(23)	Vol. 2, A.1, Identity p. 3	Notifier: Reference IIA, 4.1.1/01; Ruengeler, W.; 2000; **confidential information**; 1. please delete this reference from this list and add it to Vol.4 Annex C, Confidential information; 2. the reference to the annex points IIA, 1.10, IIA, 1.11, IIA, 4.1.2 and IIA, 4.1.3 should be added to reference Ruengeler, W., 2000; 3. the reference to the annex point, IIA, 4.1.1 should be removed from reference Ruengeler, W., 2000;	Notifier: Please add "**confidential information**"; as this reference contains confidential information. Therefore this reference should be deleted from Vol. 2 and inserted in Vol. 4, Annex C, Confidential information, C.3 References relied on. The confidential report contains data relevant for the annex points IIA, 1.10, IIA, 1.11, IIA, 4.1.2 and IIA, 4.1.3. Therefore it should be listed in the reference list accordingly. The report provides also information relevant to annex point, IIA, 4.1.1. However this information is given by a non confidential report as well (see below point No. 17). For practical reasons the non confidential report should be referred to in annex point, IIA, 4.1.1 instead of the confidential report.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(24)	Vol. 2, A.2, Physical and chemical properties, references for the active substance p. 3	Notifier: The report Eberz, A., 1998 (reference IIA, 2.11.1/01) fulfils also requirements of the annex points IIA, 2.11.2 and 2.13; please add those in the reference list accordingly: Annex Point IIA, 2.11.2/01: ⇒ IIA, 2.11.1/01 Annex Point IIA, 2.13/01: ⇒ IIA, 2.11.1/01	
(25)	Vol. 2, A.2, Physical and chemical properties, references for the active substance p. 3	Notifier: The reference Kaußmann, M., 2000 was amended. Therefore it should read: Spectral Data Set of BAJ 2740 Bayer AG, Report No.: 15-600-2116 Date: 2000-03-09, **amended 2000-09-01** GLP, unpublished	
(26)	Vol. 2, A.2, Physical and chemical properties, references for the active substance p. 3	Notifier: The report Krohn, J., 1997 (reference IIA, 2.1.1/01) is also the reference of the other annex points listed in column 3;	please add the list accordingly: Annex Point IIA, 2.1.3/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.2/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.3.1/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.3.2/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.4.1/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.4.2/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.6.2/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.7/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.8/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.9.4/01: ⇒ IIA, 2.1.1/01 Annex Point IIA, 2.14/01: ⇒ IIA, 2.1.1/01

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(27)	Vol. 2, A.2, Physical and chemical properties, references for the plant protection product p. 4	Notifier: The report Eberz, A., 1998 (reference IIIA, 2.2.1/01) is also the reference of the annex point IIIA, 2.3/01; please add the list accordingly: Annex Point IIIA, 2.3/01: ⇒ IIIA, 2.2.1/01	
(28)	Vol. 2, A.2, Physical and chemical properties, references for the plant protection product p. 5	Notifier: The report Hess, T., 1998 (reference IIIA, 2.1/01) is also the reference to other annex points listed in column 3; please add the list accordingly.	Notifier: Please add: Annex Point IIIA, 2.4.2/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.5.2/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.5.3/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.6.1/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.8.2/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.8.3/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.8.5/01: ⇒ IIIA, 2.1/01 Annex Point IIIA, 2.8.8.2/01: ⇒ IIIA, 2.1/01
(29)	Vol. 2, A.2, Physical and chemical properties, references for the plant protection product p. 5	Notifier: New reference: Gueldner, W. IIIA, 2.4.2/02 2002 Determination of pH value (1% and undiluted) of BAJ 2740 SC 240 (Article no.: 05304954) Bayer CropScience report no. 1410505220 Date: 2002-05-16 GLP, unpublished Data protection claimed: Y Owner: BCS	Notifier: Please add the new reference.

* 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.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(30)	Vol. 2, A.2, Physical and chemical properties, references for the plant protection product p. 5	Notifier: The report Zimmermann, M., 2000 (reference IIIA, 2.7.1/01) is also the reference of the annex point IIIA, 2.7.3/01; please add the list accordingly: Annex Point IIIA, 2.7.3/01: ⇒ IIIA, 2.7.1/01	
(31)	Vol. 2, A.5, Methods of analysis p. 7	Notifier: 1. Reference IIA, 4.1.1/01; Ruengeler, W.; 2000; **confidential information**; 2. please delete this reference from this list and add it to Vol.4 Annex C, Confidential information; 3. the reference to the annex points 4.1.2 and IIA, 4.1.3 should be added to reference Ruengeler, W., 2000; 4. the reference to the annex point, IIA, 4.1.1 should be removed from reference Ruengeler, W., 2000;	Notifier: Please add "**confidential information**"; as this reference contains confidential information. Therefore this reference should be deleted from Vol. 2 and inserted in Vol. 4, Annex C, Confidential information, C.3 References relied on. The report Ruengeler, W., 2000 contains data relevant for the annex points IIA, 4.1.2 and IIA, 4.1.3. Therefore it should be listed in the reference list in Vol. 4, Annex C, Confidential information, C.3 References relied on. The report provides also information relevant to annex point, IIA, 4.1.1. However this information is given by a non confidential report as well (see below point No. 17). For practical reasons the non confidential report should be referred to in annex point, IIA, 4.1.1 instead of the confidential report.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(32)	Vol. 2, A.5, Methods of analysis p. 7	Notifier: New reference: Ruengeler, W. IIA, 4.1.1/01 2000 BAJ 2740; Assay of technical active ingredient; HPLC - Internal standard Bayer CropScience report no. 2005-0010101-99E Date: 2000-02-07 non GLP, unpublished Data protection claimed: Y Owner: BCS	Notifier: This report is a part of the confidential report Ruengeler, W., 2000. It does not contain any data which may exceed the information of the confidential document; please insert this reference instead of the confidential reference.
(33)	Vol. 2, A.5, Methods of analysis p. 7	Notifier: New reference: zur Muehlen, U. IIA, 4.1.3/02 2000 Validation report VB1-2005-0010101-99E ; BAJ 2740 Technical, HPLC - internal standard; Bayer CropScience report no. VB12005-0010101-99 Date: 2000-02-07 non GLP, unpublished Data protection claimed: Y Owner: BCS	Notifier: This report is a part of the confidential report Ruengeler, W., 2000. It does not contain any data which may exceed the information of the confidential document; please add this reference.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(34)	Vol. 3, B.1.3, References relied on p.1	Notifier: Reference IIA, 4.1.1/01; Ruengeler, W.; 2000; **confidential information**; 1. please delete this reference from this list and add it to Vol.4 Annex C, Confidential information; 2. the reference to the annex points IIA, 1.10 and IIA, 1.11 should be added to reference Ruengeler, W., 2000; 3. the reference to the annex point, IIA, 4.1.1 should be removed from reference Ruengeler, W., 2000;	Notifier: Notifier: Please add "**confidential information**"; as this reference contains confidential information. Therefore this reference should be deleted from Vol. 3 and inserted in Vol. 4, Annex C, Confidential information, C.3 References relied on. The report Ruengeler, W., 2000 contains data relevant for the annex points IIA, 1.10 and IIA, 1.11. Therefore it should be listed accordingly in the reference list in Vol. 4, Annex C, Confidential information, C.3 References relied on. Please remove this report from the reference list to the annex point, IIA, 4.1.1, because it is replaced by a non confidential report (see above point No. 16 and 17)
(35)	Vol. 3, B.2.1.4, relative density p. 3	Notifier: The correct reference is Krohn, J., 1997 ⇒ IIA, 2.1.1/01	Notifier: Please correct the reference
(36)	Vol. 3, B.2.1.6, volatility, Henry's law constant p. 3	Notifier: Henry's law constant: at 20°C <2 x 10^{-3} Pa m^3mole^{-1}	Notifier: Please correct this typing error
(37)	Vol. 3, B.2.2.10, pH p. 10	Notifier: Additional data: pH 5.3 (1% dilution)	Notifier: The additional data were already submitted and the value was correctly quoted in Vol. 1, 2.1.2, Physical and chemical properties. Therefore it should also be listed in Vol. 3, B.2.2.10, pH.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(38)	Vol. 3, B.2.3.1, Active substance p. 13	Notifier: The sentence "The log P_{OW} (5.83) is not pH dependable..." should be replaced by "The log P_{OW} (5.83) was measured at pH 4 only due to substance instability at higher pH values...."	Notifier: Due to substance instability in the neutral and alkaline pH range the log P_{OW} could be tested at pH 4 only. Therefore a statement on the pH dependency of the substance is not possible. Please change the sentence as proposed in column 2.
(39)	Vol. 3, B.2.4, References for the active substance p. 14	Notifier: The reference Kaußmann, M., 2000 was amended. Therefore it should read: Spectral Data Set of BAJ 2740 Bayer AG, Report No.: 15-600-2116 Date: 2000-03-09, **amended 2000-09-01** GLP, unpublished	
(40)	Vol. 3, B.2.4, References for the plant protection product p. 16	Notifier: New reference: Gueldner, W. IIIA, 2.4.2/02 2002 Determination of pH value (1% and undiluted) of BAJ 2740 SC 240 (Article no.: 05304954) Bayer CropScience report no. 1410505220 Date: 2002-05-16 GLP, unpublished Data protection claimed: Y Owner: BCS	

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(41)	Vol 3, B.5.5.2.2 p. 61	Notifier: Method 00568 is considered valid for determination of residues in grapes. To support the explanations in Column 3 the notifier will subject an extra sample form the grape metabolism study (stored frozen until today) to the Method 00568. Extraction efficiency will be compared with the result from the metabolism study. The extract will be subjected to chromatographic analysis to check whether the pattern of active substance and metabolites is the same as reported in the metabolism study. If so it confirms storage stability. If the extraction efficiency with both methods is the same and the storage stability is given then the question of the RMS is also answered experimentally. Results will be available by end of September 2004.	Residues on grapes and apples are mainly (ca. 96-98 %) located on the surface as unchanged parent compound and are shown to be removed by washing with dichloromethan and acetonitrile/water (see table point (6), Vol 1, 2.2.3). Hence, the amount of incurred residues in the fruits is low (4-8 %). Possible incomplete extraction of the incurred residues by using acetonitrile/water would have no meaningful influence on the overall amount of BAJ 2740 and could not explain the differences between the height of residues in metabolism and residue study. The differences between these two studies can be explained by different application procedures. The aim of the application in the metabolism study was to produce residues as high as possible to have enough material available for elucidation of metabolism. Hence, it was taken care to spray the grapes intensively and to avoid spraying the leaves. Moreover the grapes were smaller than in the residue study and due to the relatively higher surface/volume ratio the residues expressed in mg/kg are relatively higher.
(42)	Vol 3, B.5.5.2.2 p. 63	Notifier: Method 00568: Additional recovery experiments in apple pomace up to 1.0 mg/kg spirodiclofen will be conducted. Results will be available end of 2004/beginning 2005.	

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(43)	Vol. 3, B.5.6, References relied on p. 65	Notifier: Reference IIA, 4.1.1/01; Ruengeler, W.; 2000; this reference should be replaced by the new reference Ruengeler, W. IIA, 4.1.1/01 2000 BAJ 2740; Assay of technical active ingredient; HPLC - Internal standard Bayer CropScience report no. 2005-0010101-99E Date: 2000-02-07 non GLP, unpublished Data protection claimed: Y Owner: BCS	Notifier: This report is a part of the confidential report Ruengeler, W., 2000. It does not contain any data which may exceed the information of the confidential document; please insert this reference instaed the confidential reference.
(44)	Vol. 3, B.5.6, References relied on p. 65	Notifier: Reference IIA, 4.1.2/01; Ruengeler, W.; 2000; **confidential information**; please delete this reference from this list and add it to Vol.4 Annex C, Confidential information;	Notifier: Please add "**confidential information**" as this reference contains confidential information. Please delete this reference from Vol. 3 and insert it in Vol. 4, Annex C, Confidential information, C.3 References relied on.
(45)	Vol. 3, B.5.6, References relied on p. 65	Notifier: Reference IIA, 4.1.3/01; Ruengeler, W.; 2000; **confidential information**; please delete this reference from this list and add it to Vol.4 Annex C, Confidential information;	Notifier: Please add "**confidential information**" as this reference contains confidential information. Please delete this reference from Vol. 3 and insert it in Vol. 4, Annex C, Confidential information, C.3 References relied on.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(46)	Vol. 3, B.5.6, References relied on p. 65	Notifier: New reference: zur Muehlen, U. IIA, 4.1.3/02 2000 Validation report VB1-2005-0010101-99E ; BAJ 2740 Technical, HPLC - internal standard; Bayer CropScience report no. VB12005-0010101-99 Date: 2000-02-07 non GLP, unpublished Data protection claimed: Y Owner: BCS	Notifier: This report is a part of the confidential report Ruengeler, W., 2000. It does not contain any data which may exceed the information of the confidential document; please add this reference.

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
	Vol. 1; 2.3 p. 15 – 28 and list of endpoints	Notifier: For certain studies differences are evident between the assessments of the RMS and those of BCS as presented in the dossier: subacute feeding rat, subacute dermal rat, subchronic feeding mouse and rat, oncogenicity mouse, chronic combined rat, reproduction rat. Several of these discrepancies have relevance when setting the NOAEL for the studies concerned. A detailed justification supporting the BCS assessments has been provided specifically for each study in response to Volume 3 of B.6 "Toxicology and Metabolism". These justifications apply also for the study summaries of Volume 1 and should be implemented here and in the list of endpoints as well.	

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
(1)	Vol. 3, B.6.3.1, NOAEL of the subacute feeding study in rats, p. 84 - 86	BCS comment: BCS proposes a **NOAEL of 500 ppm** based on changes in clinical chemical parameters at 5000 ppm.	With regard to a possible effect on haematological parameters (total no. of leukocytes, percentage of lymphocytes and neutrophils) it should be noted that the differences between the control group and the mid and high dose group are very slight and it remains questionable if there is really a treatment related effect. In any case, the small deviations observed are not regarded as „adverse effect“ and their toxicological relevance is assessed to be low, also because white blood cell parameters are generally known to show high limits of variation even under physiological conditions. Higher ECOD values are not seen as an adverse effect but as a physiological adaptation of the liver to an increased metabolic burden in order to efficiently detoxify the xenobiotic. Also the slight effects on non-standard immune cell parameters are regarded as variations within physiological limits and not as an adverse effect so that these parameters should not be considered for setting the NOAEL.

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.6.3.2, NOAEL of the subacute dermal toxicity study in rats, p. 88-89	BCS comment: BCS proposes a **NOAEL of 1000 mg/kg bw** based on the absence of adverse effects at this dose level.	The slight body weight differences between control and treatment group seen only in female animals are regarded not to be treatment related but to result from an accidental inhomogeneous distribution of animals. Two animals in the control group (no. 12 and 14) did not gain any body weight at all during the study period while in the treatment group three animals had a slightly higher body weight already at the beginning of the study and later on this differences were enlarged. The alleged lower food consumption must be seen in relation to the slight body weight differences: on a „g/animal/day"-basis the food intake in the treatment group was not different to that of the control group. It should also be stressed that in other rat studies such findings were not obtained and that under general considerations it is unlikely that reduced feed intake could be associated with an increased body weight gain. Also the slight differences for red blood cell parameters (haemoglobin and haematocrit) between control and treated males are regarded not to be compound related but to result from an accidental inhomogeneous distribution of animals. For both parameters three control animals (no. 2, 3, 4) showed rather high values which are considered to represent the upper limit of the historical control range or even exceeding it. Even the values of the treatment group were higher than the historical control means so that a reduction of HB and HCT can be excluded (see page 21 of the report). The small decrease of ALAT activity is not considered to be an adverse toxicological effect since only increases are taken as indicator for liver cell damage. Regarding triglycerides it is physiologically quite normal that female rats have substantially lower levels than males. The finding that in comparison to control animals lower triglycerides levels were established for treated males is not seen as treatment related since females did not show a similar decrease and since the level was well within the historical control range. It should be noted that in this study only five animals were used per treatment group so that a high degree of variation is unavoidable for certain parameters. It is also a common finding that in comparison to males, female rats

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
(3)	Vol. 3, B.6.3.3, NOAEL of the subchronic feeding study in mice, p. 90-92	BCS comment: BCS has proposed a **NOAEL of 100 ppm** based on Leydig cell hypertrophy and cytoplasmic vacuolation of the adrenal cortex at 1000 ppm. We agree that with regard to effects on the liver, the no-observed effect level is < 100 ppm, but the centrilobular hepatocellular hypertrophy seen at this dose level is not considered to be an adverse effect.	Hypertrophy of liver cells was the only treatment-related effect seen at 100 ppm. This, however, should not be considered as “adverse” but rather as a morphological correlate to a physiological adaptation of the organ to an increased metabolic activity. It is proposed to differentiate between no-observed effect level (NOEL < 100 ppm) and NOAEL (100 ppm) for this study.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(4)	Vol. 3, B.6.3.3, NOAEL of the subchronic feeding study in rats, p. 92-94	Based on an increased incidence of adrenal cortical vacuolation in males, the RMS considers the NOAEL to be < 100 ppm. BCS comment: BCS has proposed a **NOAEL of 500 ppm** for males and 100 ppm for females based on effects on lipid metabolism (cholesterol, triglycerides), liver (increased transaminase activities) and adrenals (cortical vacuolation).	For the following reasons, the NOAEL for the finding in the adrenals "vacuolation small/cortex" is considered to be 500 ppm for male rats: The average severity grade was presented in this study as average grade per number of animals in the groups and also as average grade per number of affected tissues / animals. With both calculations a distinct increase of the severity score for small adreno-cortical vacuolation is observed first at 2500 ppm and above. In these two high dose groups, the severity scores 3 (moderate), 4 (severe) or even 5 (massive) were used frequently to characterise the lesion while in controls and males of the 100 or 500 ppm groups, the adreno-cortical lesion was scored predominantly grade 1 (minimal) or grade 2 (slight). Furthermore, there was no dose-dependent increase from 100 to 500 ppm in this study with respect to incidence and severity score. Fine vesicular vacuolation of adreno-cortical cells ("Vacuolation small/cortex") represents a physiological status of the normal adrenal activity which is visible in the histological slide and can be seen to a variable degree even among untreated controls. The average severity score varies roughly between 1 and 2 in the control groups. Lesions of that type are considered to represent the physiological background vacuolation in male rat adreno-cortical tissue corresponding to normal steroid biosynthesis. Our interpretation is in-line with the results from other rat studies with even longer treatment duration and similar dose levels in male Wistar rats. These studies are the two-generation study and also the combined study on chronic toxicity and carcinogenicity. In these studies adreno-cortical vacuolation and/or hypertrophy were restricted to the high dose levels which were 1750 ppm or 2500 ppm respectively. Neoplastic or preneoplastic lesions of the adrenal cortex like focal hypertrophy or focal hyperplasia and adenomas were absent in the two year bioassay. In summary, the absence of a dose-dependent increase of small adreno-cortical vacuolation between 100 and 500 ppm in the respective study and also the lack of an increase after prolonged treatment, support our setting of the NOAEL. With regard to all feeding studies, the overall NOAEL for induced adreno-cortical lesions in male Wistar rats should be established as stated in our report at 500 ppm BAJ 2740.

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, B.6.5.1, NOAEL of the oncogenic study in mice, p. 104 - 107	BCS comment: Whereas the RMS concludes that the NOAEL in this study is < 25 ppm, BCS considers this dose level to be tolerated without **adverse** effects. Only at 3500 ppm treatment-related changes were seen.	**Adrenal Cortical Vacuolisation** Vacuolation of the adrenal cortex was noted at significant levels in 3,500 and 7,000 ppm mice of both sexes (M: 0, 0, 31*, 37*; F: 1, 6, 49*, 48*[1]). Average severity was higher in the 7,000 ppm group for both sexes as well, when compared with the 3,500 ppm group. The pattern of vacuolation was slightly different between sexes; although, the difference was not apparent in more pronounced cases. In males, the vacuolation appeared to be seen earliest in the zona glomerulosa; while in females, the initial vacuolation appeared deeper in the cortex. All levels of the cortex were ultimately affected. The changes seen are isolated in the 3500 and 7000 ppm groups. There is no significant incidence at 25 ppm in either sex, and there is a significant difference between the incidence at 25 ppm and at 3500 ppm for both sexes. The background in females was higher than in males, as indicated by the presence of the change in the female control. Since this is a common change in adrenals, is not significantly increased over control levels in females at 25 ppm, and does not occur at all in males at 25 ppm, the 25 ppm group is not regarded as affected by compound administration (NOEL established at 25 ppm). **Adrenal Corticomedullary Pigmentation** A statistically flagged incidence of increased pigmentation at the adrenal corti-comedullary junction was noted in 7,000 ppm mice of both sexes, and in 3,500 ppm and 25 ppm females (M: 7, 5, 11, 27*; F: 11, 20*, 45*, 42*). A certain amount of pigment at the corticomedullary junction is normal. In this study there was a prominent amount of pigment as background, as shown by the control values, above. Historically, in two studies where the frequency of this background lesion was coded, the combined frequency of pigmentation was 20 - 32 % in control males and 24 - 50 % in control females. Due to the background level of the change in the control groups, and the fact that the female frequency at 25 ppm is consistent with the historical control values, we consider the increase in pigmentation to be increased only in the 7000 ppm groups and the 3500 ppm female group. Also supporting this opinion is the large jump between the 25 ppm frequency and the 3,500 ppm frequency.

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) cont.	Vol. 3, B.6.5.1, NOAEL of the oncogenic study in mice, p. 104 - 107	BCS comment: *continued*	**Hepatocyte Enlargement/Hepatocytomegaly** In the liver, hepatocytomegaly, an increase in the size of hepatocytes, was significantly increased over control levels in 3,500 and 7,000 ppm males. The change was essentially not seen in females (M: 2, 6, 17*, 21*; F: 0, 0, 0, 1). This finding correlates well with organ weight data in males. The change of hepatocytomegaly is a common response to metabolism of a xenobiotic, and is a normal response. It is considered to be an effect, but not an adverse effect, as it is generally due to proliferation of endoplasmic reticulum needed to metabolise the test material. The liver is not changed in a degenerative manner: there is no necrosis, only increased normal activity. In addition, there was a background level noted in control males (2/50) and the frequency at 25 ppm was 6/50, not significantly increased over the control level, and since this finding has a high variability, the frequency at 25 ppm is not regarded as affected by treatment. Since the change is not statistically increased over control in the 25 ppm group, and is a normal response of the liver in any case, we believe the change is compound related only in the 3500 and 7000 ppm males groups (NOEL established at 25 ppm). **Amyloidosis** Since there is no treatment-related increase in the number of animals with amyloid, because the increases in frequency in selected organs are not statistically different from control, and because amyloid is a common background change in CD-1 mice, we regard the amyloidosis noted in the study as not compound related.

[1] *=Statistically significantly different from control at p#0.05

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, NOAEL of the chronic combined feeding study in rats, p. 107 - 110	BCS comment: On basis of alleged thymus and ovary weight changes at 350 ppm, the RMS considers 100 ppm to be the NOAEL for this study; BCS still proposes **350 ppm as a NOAEL**.	With regard to the thymus and ovary weights it is concluded by the RMS that these were increased dose-related in the two highest dose groups (350 and 2500 ppm). **Thymus weights** at interim and final necropsy are evaluated to be comparable to control weights, because there was neither a clear dose correlation nor any treatment-related histological findings in this organ. The only significantly different mean thymus weights were those related to body weight in high dose rats (females at interim necropsy, males at final necropsy). These rats had body weight reductions up to 11% in males and up to 8% in females. The differences in relative thymus weights of these animals are thus seen in the context of the lower body weights. In addition, the value of these mean weights were about the same as that at 50 ppm of the same sex at the same necropsy, showing the incidental scattering range for thymus weights within unaffected study groups. The figures indicating the mean weights including minimum and maximum values for the respective groups support further the lack of any dose correlation. **Ovary weights** of all treated females were comparable to controls at interim and final necropsy. There were no statistically significant differences at any dose level. Somewhat higher absolute and relative ovary weights at 2500 ppm at final necropsy are seen in the context of metastases of uterine adenocarcinoma. There were neither treatment-related histological findings nor a change of incidence of primary ovarian neoplasms.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(7)	Vol. 3, B.6.6.1, NOAEL of the 2-generation reproduction study in rats, p. 114 - 117	BCS comment: The RMS considers 70 ppm to be an effect level (effects on body weights, brain and liver weights, triglycerides and cholesterol) whereas BCS still proposes a **NOAEL of 70 ppm.**	As outlined on page 40 of the study report we think that the slightly and transiently lower (only week 1 – 6) **body weights** of the 70 ppm dose group males in the F0 generation are not related to treatment: It should be noticed that at study begin this group incidentally had a lower mean body weight in comparison to the control group and that with regard to body weight gain no statistically differences occurred during week 2 – 6. Furthermore, no significantly reduced body weights were seen in F1 rats of this dose level both, absolutely and when body weight gain is considered. Taken together 70 ppm is regarded to be a NOAEL for body weight effects in parent F0 and F1 animals. Apparently, the **liver weights** of all treatment groups were slightly lower in comparison to control animals. However, when considering the facts that differences were rather small, that a dose response relationship did not exist, that in F1 males no significant deviations with regard to liver weights were seen at ≤ 350 ppm and that morphological correlates in the liver were absent up to the highest dose level, a toxic effect is not assumed up to the dose of 350 ppm. Possible differences in body weights (see above) which had to be measured on different days along the period of necropsy could be the reason for these differences. There were 6% increased relative **brain weights** at 70 and 350 ppm in F0 males in comparison to controls. Because these differences are minimal and there was no treatment effect on this parameter in F1 males up to 350 ppm, this deviation does not reflect a toxic effect. As it is true for the liver weight deviations, differences in body weights might be the reason for this result. It should be noted that absolute brain weights do not correlate with body weight changes. The plasma levels of **triglycerides** and **cholesterol** were dose dependently lower than that of the concurrent control group in all treated F1 males. These findings must be seen as a direct consequence of the “pharmacological/insecticidal” action of spirodiclofen on lipid metabolism and should not be considered as an “adverse” effect. Additionally, as outlined in the study report (page 57) for the 70 and 350 ppm dose groups all individual values are covered by historical control data, which show the generally high

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. 3, B.6.8.1, Immu-notoxicological and mechanistic studies, p. 137	RMS: ”Incubation of commercially available purified enzymes resulted in BAJ 2510-induced inhibition of mitochondrial malate dehydrogenase (MD), whereas malic enzyme was not affected.” (also on further pages). BCS comment: Both mitochondrial and cytosolic malate dehydrogenase were inhibited by BAJ 2510. It is proposed to modify the sentence as follows: "Incubation of commercially available enzymes resulted in BAJ 2510-induced inhibition of mitochondrial **and cytosolic** malate dehydrogenase (MD), whereas malic enzyme was not affected.	
(9)	Vol. 3, B.6.8.1, Immu-notoxicological and mechanistic studies, p. 143	RMS: ” It cannot be excluded that this effect may contribute to reduction of testosterone synthesis in Spirodiclofen treated testicular tissue.” BCS comment: Spirodiclofen was never detected in the plasma of laboratory animals. In order to stress this point, it should be indicated that this statement refers to the *in vitro* situation only.	

* 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.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(10)	Vol. 3, B.6.10.5, AOEL, p. 152	BCS comment: *Systemic AOEL / enteral absorption*: The RMS used a correction factor of 0.58 to reflect an allegedly incomplete absorption of spirodiclofen from the gastro-intestinal tract. This value obviously originates from a single dose study (3 mg/kg bw) where renal excretion was ca. 58 % in male rats and 75 % in females. A correction factor of 0.58 is regarded to be over-conservative as it does not include spirodiclofen excreted via bile. In a bile cannulation experiment ca. 12 % of the radioactivity was identified in the bile fluid. This finding and the fact that in a repeated dose study > 70 % of the radioactivity were excreted in the urine of males and females, support an overall correction factor of 0.7. Therefore, BCS proposes an **AOEL of 0.01 mg/kg bw/day.**	The compilation of all absorption studies after oral admin. at low dose levels at 1 – 3 mg/kg bw. **clearly indicated a higher absorption than 70 %** when considering significant excretion via bile e.g. 12 % in 24 hrs when 24 % were excreted via urine: **Koester (2000),** Report No.: MR-227/00, Edition No: MO-01-012780: **59** % of 3 mg/kg bw. via urine of male in 48 hrs plus x % via bile plus x % beyond 48 hrs plus x % remaining in the carcass **Andersch & Koester (2000a)** Report No.: MR-136/00, Edit No.: MO-00-015111 **57-62** % of 1 x 2 mg/kg bw. via urine of male in 48 hrs **67** % of 2 mg /kg bw. in urine in 48 hrs.(14 days pre-treated with 2 mg/kg b.w. followed by 1 x 2 mg/kg bw.) **74** % of 1 x 2 mg/kg bw. via urine of female in 48 hrs all plus x % via bile plus x % beyond 48 hrs plus x % remaining in the carcass (extra bile cannulation experiment with male rats and 1 mg/kg b.w.: **12** % via bile in **24 hrs** 24 % urine in 24 hrs 31 % faeces in 24 hrs **Andersch and Koester (2000b)** Report No.: MR-610/99, Edition Number: MO-00-015018 : Sub-chronic non-labelled pre-treatment at 50 ppm in diet for 15 weeks followed by 2 mg/kg bw. radiolabelled active substance: **72** % of 2 mg/kg bw. via urine of male in 48 hrs **75** % of 2 mg/kg bw. via urine of female in 48 hrs plus x % via bile plus x % beyond 48 hrs plus x % remaining in the carcass.

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
(11)	Vol. 3, B.6, p. 114&148	BCS comment: R 40 labelling of the active ingredient: The actual wording for R 40 is **„Limited evidence of a carcinogenic effect“** and no longer “Possible risk of irreversible effects”, please change everywhere in the DAR.	

typing errors:
page 89, line 2: ..with the following deviat**i**on ...
page 92, line 13: ...the NOAEL **is** 100 ppm; line 15: in accordance with the opinion of the study author, **is** set at 100 ppm
page 101, STUDY 2, table: Brendler-S**ch**waab
page 123, NOAEL: 70 mg/kg bw/dag**y**
several pages: the term “jejenum” should be changed to “jejunum”

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. 3, B.7.6.1, p. 206	Notifier: Method 00568 is considered valid for determination of residues in grapes. (see Vol. 3, B.5.5.2.2) To support the explanations in Column 3 the notifier will subject an extra sample form the grape metabolism study (stored frozen until today) to the Method 00568. Extraction efficiency will be compared with the result from the metabolism study. The extract will be subjected to chromatographic analysis to check whether the pattern of active substance and metabolites is the same as reported in the metabolism study. If so it confirms storage stability. If the extraction efficiency with both methods is the same and the storage stability is given then the question of the RMS is also answered experimentally. Results will be available by end of September 2004.	Residues grapes and apples are mainly (ca. 96-98 %) located on the surface as unchanged parent compound and are shown to be removed by washing with dichloromethane and acetonitrile/water (see first table of comments, point (18), Vol., 1, level 4, 4.5.3 and 4.5.5) Hence, the amount of incurred residues in the fruits is low (4-8 %). Possible incomplete extraction of these incurred residues by using acetonitrile/water would have no meaningful influence on the overall amount of BAJ 2740 and could not explain the differences between the height of residues in metabolism and residue study. The differences between these two studies can be explained by different application procedures. The aim of the application in the metabolism study was to produce residues as high as possible to have enough material available for elucidation of metabolism. Hence, it was taken care to spray the grapes intensively and to avoid spraying the leaves. Moreover the grapes were smaller than in the residue study and due to the relatively higher surface/volume ratio the residues expressed in mg/kg are relatively higher.

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
(2)	Vol. 3, B.7.6.1, p. 206	Notifier: Method 00568: Additional recovery experiments in apple pomace at 1.0 mg/kg spirodiclofen required (see Vol 3, B.5.5.2.2) Study will be conducted. Results will be available end of 2004/beginning 2005	
(3)	Vol 3, B.7.16.3.2, p 250.	Residue definition animal products Notifier: No residue definition in animal tissues is needed, because the cattle feeding study clearly shows that no residues are to be expected in milk, animal tissues and organs at the 1.7 and 5.1-fold overdose (1.38 and 4.14 mg/kg feed). In addition in the goat metabolism study no residues were found in goat tissues above 0.01 mg/kg considering the applied overdose. Besides this, the notifier does not agree with the argumentation for the proposed residue definition in animal products. Spirodiclofen was not found in the goat. The results from the goat metabolism study do not support the inclusion of spirodiclofen into the residue definition.	

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)		No comments from the notifier in this section.	

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. 1, 2.6.3.2. (p. 59)	Notifier: The rate tested in the laboratory glass plate test on *T. pyri* is **58** g a.s./ha, not 53.3. g a.s./ha	Typing error
(2)	Vol. 3, B.9.1.3, Table B.9.4 (p. 328), line 22, and Table B.9.5, (p. 329)	Notifier: Number of 14-days chicks as percent of hatchlings as given in the dossier is 94.**8**%, not 94.6%	Typing error
(3)	Vol. 3, B.9.1.5.1 (p. 330)	Notifier: The DFI as given in the dossier is **10.05** g material/day, not 10.3 g material/day	Typing error
(4)	Vol. 3, Table B.9.12 (p. 336)	Notifier: ETE as given in the Dossier is **11.6**, not 11.7 mg/kg bw/d, resulting TER > **216**, not 214	Typing error
(5)	Vol. 3, B.9.2.2.1.1 (p. 346)	Notifier: The citation has to be "DORGERLOH, M., **2001**", not "2000"	Typing error
(6)	Vol. 3, B.9.2.2.1.2 (p. 347)	Notifier: Concentrations in the 2nd paragraph have to be corrected from 49.3 and 70.7 **m**g a.s./L into 49.3 and 70.7 **µ**g a.s./L	Typing error

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(7)	Vol. 3, B.9.2.3.1.2 Longterm Risk (Active substance) p. 357	BCS comment: BCS proposes TERs for chronic risk assessment for fish which consider the TWA PEC for the same period of time (65 days) as the **sensitive** period of the ELS test (65 days of the 97 days). This means for example for Orchard use early and buffer zone of 20 m 1.95 µg/L NOEC TER = ---------- = 60.9 0.032 µg/L TWA(65d) PEC In case the above recommendation is followed, supported by the justification in Column 3, then all the TERs in Vol. 1 p. 109 ff. and the list of endpoints need to be recalculated. This would change all recommendations for buffer zones, which can be improved further with additional mitigation measures.	**A) Justification from data in the submitted dossier and the DAR:** As given in the GD Sanco/3268/2001 rev.4 (final), 17 October 2002 the approach is recommended to compare chronic NOEC with the respective TWA considering the time to onset of effects for the relevant endpoints and the fate of the residues in water. The fact that no acute toxicity was observed at the maximum water solubility > 35 µg/L indicates that there is no fast translocation of the residues in water to sensitive sites within the fish for any significant effects. However, the dissipation of the active substance with the very high adsorption coefficient of 31371 L/kg from the water phase (DT-50 = 0.3 d) is very fast followed again by a very fast degradation in the sediment (< 4 days). There is no direct or indirect indication for irreversible toxicity mechanism which caused the effects on the most sensitive parameter of growth rate and fish weight which may have occurred in the most sensitive period of a few days. Even if there is a relevance of the initial peak concentration it is in the case of Orchard use, early and buffer zone of 20 m the initial PEC (= 1.3 µg/L) is still below the chronic NOEC, the permanently established concentration of 1.95 µg/L in the ELS study. **B) Justification from data out of an additional study (not submitted yet but announced to the RMS in direct discussions; the study will be submitted as soon as possible)** (Dorgerloh, M. Sommer, H., 2002) Chronic effects of BAJ 2740 on selected early life stages of rainbow trout (*Oncorhynchus mykiss*) under more realistic conditions of exposure.

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
(7) continued	Vol. 3, B.9.2.3.1.2 Longterm Risk (Active substance) p. 357		The chronic toxicity of BAJ 2740 to Rainbow Trout was determined for the most sensitive early life stage (between 60 and 70 days old fry, PHD 25-35) in a static indoor microcosm (water/artificial sediment-system) after a single application (pulse) of the test item on study day 0 into the water phase. 61 days old (PHD 27) fry were exposed over a total duration of 42 days. The overall chronic NOEC for BAJ 2740 on the most sensitive early life stage of rainbow trout under more realistic conditions of exposure is 20.0 µg a.s./L (based on growth effects) and the LOEC is 40.0 µg a.s./L. In this study relative to the submitted study 2 parameters were different pulse versus constant exposure and sediment microcosm versus water flow-through only. This additional study clearly indicates that in reality with sediment and a pulse exposure with the high initial PEC not the same no effect level of 1.95 µg/L was observed but a 10-fold more favourable one 20 µg/L. **Consequently, the proposed consideration of the TWA for comparison with the chronic NOEC is justified.**

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. 3, B.9.2.3.2.1, Table B.9.26 (p. 360)	Notifier: EC_{50} algae: For the risk assessment, the E**r**C50 should be used rather than the E**b**C50, as it will be done in the revised OECD 201 and ISO 8692 (See also: DORGERLOH, M. (2004): How to Express Growth Effects on Algae under 91/414/EEC? Poster presentation, SETAC 2004 (Prague). Therefore a value of **> 100 mg/L** should be used instead of 82.8 mg/L.	
(9)	Vol. 3, B.9.4.1.3 Evaluation of the study of SCHUR (2002) (p. 368)	Notifier: RMS does not accept the Notifier's conclusion of the lack of effects at the drift rate of 45 g a.s./ha, since, according to the DAR, there was no significant effect of the toxic standard observed in this study. However, in the 2nd run of the study (2001), there was a clearly increased number of dead pupae observed in the toxic standard, which is a typical symptom of the effects of Insegar. Thus, it can be stated that at least in this run there was a clear evidence of exposure of the bee brood. Therefore, bee safety of the 45 g a.s./ha can be shown in this trial.	

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(10)	Vol. 3, B.9.4.2.2 (p. 369)	Notifier: The risk mitigation measure of a **warning label** (no application into flowering, bee-attractive cultures) was already proposed by the Notifier.	
(11)	Vol. 3, B.9.5.1, Table B.9.35 (p. 370)	Notifier: The rate tested in the laboratory glass plate test on *T. pyri* is **58** g a.s./ha, not 53.3. g a.s./ha	Typing error
(12)	Vol. 3, B.9.6.1.4.1 (p. 383)	Notifier: The LC_{50} for earthworms of the SC 240 formulation is not 226 mg a.s./kg, but **245** mg a.s./kg	Typing error
(13)	Vol. 3, study of MOSER (2001b) (p. 393)	Notifier: RMS reduces the NOEC from 100 mg a.s./kg to 6.25 mg a.s./kg based on a remark just qualitatively annotating that the juveniles were smaller in the treatment than in the control groups. The Notifier considers this not appropriate: the NOEC should not be based on a not quantifiable, non-standard endpoint which was just subjectively reported as a side observation, and which is neither defined in terms of statistical nor of biological significance. The NOEC should thus be considered to be 100 mg a.s./kg, as originally fixed.	

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

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
		No comments	

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
		No comments	

* 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.

22. 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.7.15.1, Table B.7.15.1a (Indicative calculation of TMDI …) and Table B.7.15.1b (Indicative calculation of NTMDI …), page 246	AT: Only a formal supplementation in the headline of the mentioned tables: There is written: "…. and an ADI of 0.015 mg/kg bw" There should be called: "…. and an ADI of 0.015 mg/kg bw**/d**"	

section 5 - Ecotoxicology (B.9)

23. 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
		No comments	

24. 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
		No comments	

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

25. 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)		No comments.	

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section 2 - Mammalian toxicology (B.6)

26. 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 6.1.6, Toxicokinetics, absorption.	DK: In the summary and conclusions it is stated, that the absorption is at least 64% in males and 76% in females, but the absorption is stated as 58% in the list of End-Points.	
(2)	Vol. 3, B6.1.6. Toxicokinetics, Metabolism.	DK: There is a big difference in the metabolites of spirodiclofen found in urine of male an female rats. Is there any explanation for this?	

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section 3 - Residues (B.7)

27. 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)		No comments	

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

28. 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)		No comments	

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section 5 - Ecotoxicology (B.9)

29. 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)		No comments	

30. 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)	General	EFSA: It should be noted that references of studies which are unacceptable or not necessary in the light of Directives 94/37/EC and 96/46/EC (Annex IIA and IIIA of 91/414/EEC) should be removed from the chapter "References relied on", because it is not possible to rely on these references.	
(2)	Vol. 1, p. 31, Proposed EU MRLs in relation to analytical methods	EFSA: Clarification is needed regarding the proposed MRL for food of animal origin. From the analytical point of view it is unclear why the MRL should be set at the limit of detection (LOD). However, it seems to be that this is a typing error, due to the fact that the given values are in line (except for milk) with the limit of quantification (LOQ), mentioned in Vol. 3 (p. 50, Table B.5.2.4). The proposed MRLs should be confirmed.	
(3)	Vol. 1, p. 86, List of endpoints, Minimum purity	EFSA: For transparency, it should be indicated (e.g. with an asterisk) that the specification is based on the results of a pilot plant.	

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
(4)	Vol. 1, p. 86, List of endpoints, Identity of relevant impurity	EFSA: Clarification is needed regarding the statement that the technical material does not contain any relevant impurity. Taken the given residue definition for monitoring purposes for soil and water into account, it seems to be that one of the mentioned compounds is also an impurity in the technical material. Therefore it is unclear, why on one hand this compound is regarded as toxicological and/or ecotoxicological relevant (only for such compounds an enforcement method is required) and on the other hand the same compound is regarded in the technical material as not relevant.	
(5)	Vol. 1, p. 87, List of endpoints, temperature of decomposition	EFSA: A value or a range for the temperature of decomposition should be given (as mentioned in Vol. 3, table B.2.1). Also in the row "boiling point" it is stated that spirodiclofen decomposes. The statement that spirodiclofen is stable at the melting point is meaningless in this context.	
(6)	Vol. 1, p. 87, List of endpoints, relative density and Vol. 3, p. 3, B.2.1.4 Relative density	EFSA: For transparency, it should be mentioned that the density rather than the relative density was determined.	
(7)	Vol. 1, p. 87, List of endpoints, dissociation constant	EFSA: For clarification, it should be considered whether a statement such "*no dissociation is expected based on the chemical structure*" would be more helpful.	

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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
(8)	Vol. 1, p. 89, Summary of intended uses	EFSA: For transparency and better comprehensibility, instead of the "summary of intended uses", the list of representative uses evaluated, as mentioned in EPCO Manual E4, should be used.	
(9)	Vol. 1, p. 126, 4.5 Methods of analysis 2.	EFSA Clarification is needed regarding the requirement for further validation data for dry apple pomace at levels up to 1.0 m/kg. It seems to be that no MRL is proposed, which support this requirement in respect to enforcement methods. It seems to be that this is rather an issue concerning data generation methods and should therefore be mentioned in chapter B.7. The same is also applicable to the requirements concerning the extraction efficiency.	
(10)	Vol. 3, p. 4ff, Determination of pH depending properties (e.g. solubility in water and partition co-efficient)	EFSA: Clarification is needed regarding the non submission of data at higher pH values than pH 4. Taken the given DT_{50} values from the hydrolysis study into account, it seems to be that measurements at pH 7 are possible and reasonable.	
(11)	Vol. 3, p. 7, B.2.1.21 Flash point	EFSA: Being aware that the determination of the flash point is not applicable for spirodiclofen, this should be indicated in the table B.2.1.	

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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
(12)	Vol. 3, p. 7 and 10, General point, oxidising properties	EFSA: It should be discussed in an expert meeting as a general point whether it is acceptable to address both annex points on oxidising properties (for the active substance and the formulation) only with justifications based on a theoretical assessment.	
(13)	Vol. 3, p. 10, B.2.2.10 pH value	EFSA: Clarification is needed regarding the comment that "*result for a 1% dispersion is required*". It seems to be that this requirement does not appear in Level 4 of Volume 1.	
(14)	Vol. 3, p. 31, B. 3.4.2.1 and p. 38, B.3.5.6.2 Controlled incineration	EFSA: Being aware that the annex point is addressed, it should be noted just for clarification purposes that in principle the content of halogens should be taken into account and not only the content of chlorine. Furthermore, the statement on page 38 that "*spirodiclofen contains no halogens at all*" is incorrect.	
(15)	Vol. 3, p. 64, B.5.5.3 Analytical methods (residue) soil, water, air	EFSA: Clarification is needed regarding the assessment of the analytical method for soil. Taken the given residue definition for monitoring into account (Vol. 1, p. 31, 2.5.1) it seems to be that these metabolites are regarded as relevant. For clarification purposes, the residue definition and the relevance of the metabolites, respectively, should be confirmed.	

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section 2 - Mammalian toxicology (B.6)

31. Mammalian toxicology (B.6)

No comments are available at this stage.

section 3 - Residues (B.7)

32. 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. 1, Level 4	EFSA: ESFA confirms the following data requirements by the RMS: The identity of metabolite M06 (2,4-dichloro-mandelic acid) in the orange and lemon metabolism study is not shown. The notifier is requested to submit identification data on metabolite M06.	
(2)	Vol. 1, Level 4	EFSA: ESFA confirms the following data requirements by the RMS: The notifier should submit the following study reports for evaluation: Krolski, M.E. 2000. BAJ 2740 240 SC. Magnitude of the residue in orange processed commodities. Bayer AG Div Report No. 109726.De Haan, R.A. 2000. BAJ 2740 240 SC. Magnitude of the residue in apple processed commodities. Bayer AG Div Report No. 110025.	
(3)	Vol.3, B.7. General	EFSA: Acceptability of a study should be clearly stated. It becomes not always clear from the conclusion if a study is deemed to be acceptable, e.g. for processing studies reported under B.7.7.2 and B.7.7.4 (citrus and stone fruits). Studies deemed as not acceptable for evaluation have to be removed from the list of references relied on (B.7.17).	

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
(4)	Vol.3, B.7.12.4 MRL and STMR proposals in animal products	EFSA: EFSA agrees that the proposal of the RMS to define the residue in animal products as partly fat soluble should be discussed in an expert meeting.	

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

33. 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 General.	EFSA: Acceptability and reliability of each of the studies should be clearly indicated in the DAR.	
(2)	Vol.3. B.8.1.1.1. b) Oi, M. , 1999a	EFSA: Whereas, the study could not be used to derive reliable DT50, it should be considered reliable with respect to establishing the route of degradation since label position is placed in a different position to address formation of potential metabolites not identified in the Oi, M. and Bornatsch, W., 1999.	
(3)	Vol 3. B.8.2.3 Babczinsky, P., 2000a.	EFSA: It should be clarified if the study is acceptable and if it is used in the risk assessment.	
(4)	Vol 3. B.8.4.2. a) Hellpointer, E. 1998a.	EFSA: It should be clarified if the photolysis study Hellpointer, E. 1998a. is reliable.	
(5)	Vol 3. B.8.4.2. c) Babczinski, P. 2000c	EFSA: Efforts to identify M4 and the other non identified photolysis compounds should be reported.	
(6)	Vol 3. B.8.4.3. Ready biodegradability.	EFSA: Since the water sediment study indicates that Spirodiclofen is not ready biodegradable, either the R53 should be proposed or a ready biodegradability test required.	
(7)	Vol 3. B.8.9. Definition of the residue.	EFSA: It should be clarified if metabolite BAJ 2740-enol is also proposed to form part of the residue definition in ground water.	

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section 5 - Ecotoxicology (B.9)

34. Ecotoxicology (B.9)

No comments are available at this stage.

Vol. 1, level 2 (overall conclusions) and level 4 (Demand for further information) and Vol. B9 (Ecotoxicology)

35. Vol. 1, Level 2, Overall conclusions

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Point 2.1.4. Classification and labelling	Prof.Dr.Jacob.Peter. van Praagh As the proposed use involves a single seasonal application only (see p. 56 for instance), the label should include a phrase stating that only a single application is authorised.	Following restriction should be added on the label This product is toxic to honey bees through direct contamination of pollen and nectar. The persistence of residues suggests the possibility of chronic toxic risk to hey bee larvae and the eventual stability of the hive. Do not apply to blooming, pollen-shedding or nectar-producing parts of plants if bees forage on the plants.
(2)	Point 2.3. Impact on human health	Prof.Dr.Jacob.Peter. van Praagh The substance is considered carcinogenic for inducing liver tumors in mouse and testes or uterus tumors in rats. Which are the effects of such substances on mammals at long term (for instance 10 years)?	I would point out that workers in orchards and vineyards are already more frequently affected by cancers than other people. Some studies performed in Belgium and France show, for instance, that cancer of the urinary tract are more common among these workers (see for instance Viel et al. Bladder 1995: *Bladder cancer among French farmers: does exposure to pesticides in vineyards play a part?* Occupational and Environmental Medicine, 52: 587 – 592); cancer incidences is increased around the orchards of St Truiden, Belgium, following the Flemish cancer cadastral survey)

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Vol. 1, level 2 (overall conclusions) and level 4 (Demand for further information) and Vol. B9 (Ecotoxicology)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Point 2.5. Fate and behaviour in the environment.	Prof.Dr.Jacob.Peter. van Praagh Systemicity and persistence of Spirodiclofen and Spirodiclofen-enol in plants should be assessed.	The dossier includes an assessment of degradation routes and DT50 in soil and water. No persistence assessment is provided for plant residues except for MRLs definition (point 2.4.1). We ask the EFSA to require the applicant to provide further data on BAJ 2740 and BAJ 2740-enol residues in plants. Leaf-air exchanges are a possible route for hydrophobic substances systemicity in plants. Leaf-air exchange and BAJ 2740/BAJ 2740-enol persistence in plants should be assessed (please refer to Villa, S., Vighi, M., Finizio, A., Bolchi Serini, G., 2000: *Risk assessment for honeybees from pesticide-exposed pollen,* Ecotoxicology, 9: 287-297 and Paterson, S. and Mackay, D., 1991: *Correlation of the equilibrium and kinetics of leaf-air exchange of hydrophobic organic chemicals*, Environ. Sci.Technol., 25, 866-871, for leaf-air exchange assessment and risk for honeybees from pesticide exposure via pollen).
(4)	Point 2.5.2. Fate and behaviour in soil.	Prof.Dr.Jacob.Peter. van Praagh Low values of DT50 in soil are quite surprising since DT50 in water is 1119,6d or 52,1d at pH 4 and 7 respectively, when hydrolysis is a major degradation pathway in soil. Which was the soil pH in the trials related in point 5.2? Trials for acid soils should be provided.	

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36. Vol. 1, level 4: Demand for further information

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Point 4.9	Prof.Dr.Jacob.Peter. van Praagh The applicant is required to submit further data to address the effects on bee brood (e.g. field tests or to include a warning phrase on bees on the label. We ask the EFSA to require the applicant to provide lab tests and reliable field tests.. The effects on bee brood, be it an “in crop effect” or due to the not clearly investigated drift rate of 45 g a.s./ha, can not be accepted, considering also the know weak standards of the used tests considering validation of the data. (ICPBR-Symposium Boekarest 2008).	Lab tests should be performed in order to obtain a reliable measurement of the sprirodiclofen toxicity for bee brood, that is to say to define the acute LD50 and a chronic LD 50 if necessary (please refer to point 2.5 about the substance and metabolites persistence and systemicity in plants). For lab test method: please refer to Aupinel, P., Fortini, D., Michaud, B., Marolleau, F., Tasei, J.N. and Odoux, J-F. : Toxicity of dimethoate and fenoxycarb to honey bee brood (Apis Mellifera) using a new in vitro standardized feeding method, Pest Manag Sci 63: 1090-1094. In field tests, the actual bees exposure must be considered; a toxic standard should be used. Several replications should be performed because the exposure cannot be exactly measured even when a toxic standard is used. About the warning phase on the label: if the substance can be authorized, the label phrase should include a waiting time between the application and the plant flowering, based on the residue persistence in plants (please refer to our concerns bout point 2.5). The phrase should include particular warning for drifts and for weed flowering.

37. Vol. B.9. Ecotoxicology

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Point B.9.4.1, last §:	Prof.Dr.Jacob.Peter. van Praagh Applicant's argument (reference substance fenoxycarb not valid) is not admissible as emphasized by the RMS. The substance is really hazardous for bee brood and further studies should be provided in order to define risk mitigation measures at least.	
(2)	Point B.9.4.2.2.	Prof.Dr.Jacob.Peter. van Praagh The point conclusion is: In crop effects on bees are not acceptable. What about drift effects? We would point out that drift effects assays are not valid since the toxic standard didn't give adequate response. Further studies about effects at the drift rate should be provided.	

Vol. 1, level 2 (overall conclusions) and level 4 (Demand for further information) and Vol. B9 (Ecotoxicology)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Point B.9.4.1.3	Prof.Dr.Jacob Peter van Praagh The comments by RMS are very correct. Leaving the test colonies confined for just 6 days (+6DAT) allows the nurse bees to use other -non contaminated- pollen more or less during the whole test, as indicated by the pollenstorages at -1DAT and all days post application.. I expect this study to underestimate the real effects of Spirodiclofen on honeybee larvae & pupae.	As there is no Tier 1 test for a validated estimation of LD 50 values for bee brood, the semi-field test presented only allows for a rough estimation of the risks of Spirodiclofen. The still missing accepted tests for substances with an IGR-related mode of action, more than 20 years after the mis-judgement of Insegar (fenoxycarb), makes very clear that at the introduction of substances with a new mode of action for inclusion in the Annex I of Council Directive 91/414/EEC not only the methods of analysis should form a part of the DAR-Data, but also internationally accepted tests for the honeybee colony toxicity considering the "new" way of action. Now-a-days valuable honeybee-tests are developed after the introduction of the first new substances. The "Insegar-story is a good example of the actual practice. As long as the available tests are not adequate for the fate of the substances in the colony, the decision of the European Commission and the local governments can only be based upon non-adequat risk assesments. Those assessment lack the real scientific description of the risks to expected, as these are not being investigated using adequat tests.

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Comments of J. Kievits on behalf of the European beekeepers coordination on the draft assessment report on Spirodiclofen

Vol. 1, level 2 (overall conclusions) and level 4 (Demand for further information) and Vol. B9 (Ecotoxicology)

38. Vol. 1, Level 2, Overall conclusions

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Point 2.1.4. Classification and labelling	European beekeepers coordination As the proposed use involves a single seasonal application only (see p. 56 for instance), the label should include a phrase stating that only a single application is authorised.	.
(2)	Point 2.3. Impact on human health	European beekeepers coordination The substance is considered carcinogenic for inducing liver tumors in mouse and testes or uterus tumors in rats. Which are the effects of such substances on mammals at long term (for instance 10 years)?	We would point out that workers in orchards and vineyards are already more frequently affected by cancers than other people. Some studies performed in Belgium and France show, for instance, that cancer of the urinary tract are more common among these workers (see for instance Viel et al. Bladder 1995: *Bladder cancer among French farmers: does exposure to pesticides in vineyards play a part?* Occupational and Environmental Medicine, 52: 587 – 592); cancer incidences is increased around the orchards of St Truiden, Belgium, following the Flemish cancer cadastral survey)

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Vol. 1, level 2 (overall conclusions) and level 4 (Demand for further information) and Vol. B9 (Ecotoxicology)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Point 2.5. Fate and behaviour in the environment.	European beekeepers coordination Systemicity and persistence of Spirodiclofen and Spirodiclofen-enol in plants should be assessed.	The dossier includes an assessment of degradation routes and DT50 in soil and water. No persistence assessment is provided for plant residues except for MRLs definition (point 2.4.1). We ask the EFSA to require the applicant to provide further data on BAJ 2740 and BAJ 2740-enol residues in plants. Leaf-air exchanges are a possible route for hydrophobic substances systemicity in plants. Leaf-air exchange and BAJ 2740/BAJ 2740-enol persistence in plants should be assessed (please refer to Villa, S., Vighi, M., Finizio, A., Bolchi Serini, G., 2000: *Risk assessment for honeybees from pesticide-exposed pollen,* Ecotoxicology, 9: 287-297 and Paterson, S. and Mackay, D., 1991: *Correlation of the equilibrium and kinetics of leaf-air exchange of hydrophobic organic chemicals*, Environ. Sci.Technol., 25, 866-871, for leaf-air exchange assessment and risk for honeybees from pesticide exposure via pollen).
(4)	Point 2.5.2. Fate and behaviour in soil.	European beekeepers coordination Low values of DT50 in soil are quite surprising since DT50 in water is 1119,6d or 52,1d at pH 4 and 7 respectively, when hydrolysis is a major degradation pathway in soil. Which was the soil pH in the trials related in point 5.2? Trials for acid soils should be provided.	

39. Vol. 1, level 4: Demand for further information

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Point 4.9	European beekeepers coordination The applicant is required to submit further data to address the effects on bee brood (e.g. field tests or to include a warning phrase on bees on the label. We ask the EFSA to require the applicant to provide lab tests and reliable field tests..	Lab tests should be performed in order to obtain a reliable measurement of the sprirodiclofen toxicity for bee brood, that is to say to define the acute LD50 and a chronic LD 50 if necessary (please refer to point 2.5 about the substance and metabolites persistence and systemicity in plants). For lab test method: please refer to Aupinel, P., Fortini, D., Michaud, B., Marolleau, F., Tasei, J.N. and Odoux, J-F. : Toxicity of dimethoate and fenoxycarb to honey bee brood (Apis Mellifera) using a new in vitro standardized feeding method, Pest Manag Sci 63: 1090-1094. In field tests, the actual bees exposure must be considered; a toxic standard should be used. Several replications should be performed because the exposure cannot be exactly measured even when a toxic standard is used. About the warning phase on the label: if the substance can be authorized, the label phrase should include a waiting time between the application and the plant flowering, based on the residue persistence in plants (please refer to our concerns bout point 2.5). The phrase should include particular warning for drifts and for weed flowering.

40. Vol. B.9. Ecotoxicology

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Point B.9.4.1, last §:	European beekeepers coordination Applicant's argument (reference substance fenoxycarb not valid) is not admissible as emphasized by the RMS. The substance is really hazardous for bee brood and further studies should be provided in order to define risk mitigation measures at least.	
(2)	Point B.9.4.2.2.	European beekeepers coordination The point conclusion is: In crop effects on bees are not acceptable. What about drift effects? We would point out that drift effects assays are not valid since the toxic standard didn't give adequate response. Further studies about effects at the drift rate should be provided.	