PEER REVIEW REPORT ON **CLODINAFOP** 30.07.2005

(based on the variant clodinafop-propargyl)

TABLE OF CONTENTS

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
1(1)	General comment	**EFSA:** For clarification purposes, in stead of the code CGA 193469 the ISO common name clodinafop should be used.	ii) CGA 193469 is a metabolite of clodinafop-propargyl and is indeed clodinafop (ISO name). For clarification if this metabolite is mentioned the name clodinafop can be added between brackets where relevant. The DAR will be amended accordingly.	IIA/ IIIA Open point 1.1 RMS to add 'clodinafop' to the code CGA 193469 in the List of endpoints. (see also 1(11)) Evaluation Meeting (25.05.2004): RMS to amend the list of end points. Open point still open.
1(2)	Vol. 1, p. 4, 1.1 Purpose for which the monograph was prepared	**EFSA:** For clarification purposes, it should be stated here that the active substances is clodinafop (according to the ISO/TC 81 common name for pesticides and other agrochemicals) and clodinafop-propargyl is a variant of it. It is may be also helpful to mentioned that all data relied on the variant unless it is otherwise specified.	ii) This is open for discussion. Looking at other examples as e.g. glyfosaat, glyfosate-trimesium and metsulfuron-methyl there seems to be no standardised way how to deal with esters. From the point of physical chemical properties there are differences between the ester and the acid, but for the other aspects it is depending on the stability of the ester. Also it will be very confusing to use	Open point 1.2 RMS to amend the DAR and list of endpoints This issue could be taken into account in the expert group which will discuss and develop proposals (templates) for improving and harmonisation the DAR.

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1(2)	*continued* Vol. 1, p. 4, 1.1 Purpose for which the monograph was prepared		both names in the monograph. A proposal could be to put in volume 1 an additional comment on this topic to avoid confusion.	(see also 1(10)) Evaluation Meeting (25.05.2004): RMS to revise the draft assessment report. RMS to amend the list of end points. Open point still open.
1(3)	Vol. 1, point 4.1 Justification for the high level of specification for impurities related to the 5-batch analysis of CGA 268087 is required.	**Syngenta**: CGA 268087 is present in significant amounts of [redacted] As it was present in the tox-batches [redacted] it is fully tested. Therefore there is no safety risk to list it in the specification [redacted]	ii) As the tox-batches did not show any problem this explanation is acceptable.	Addressed RMS to consider including in a revised DAR the justification for the high level of specification for impurities related to the 5-batch analysis of CGA 268087. Evaluation Meeting (25.05.2004): RMS to provide an

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1(3)	*continued* Vol. 1, point 4.1 Justification for the high level of specification for impurities related to the 5-batch analysis of CGA 268087 is required.			addendum to the draft assessment report. Open point still open.
1(4)	Vol. 1, point 4.1 In the new batches the content of nitrosamines is not determined	**Syngenta**: On the basis of the chemical structure of clodinafop-propargyl and of the reaction conditions the formation of nitrosamines is not expected. [redacted] Therefore a repetition of the nitrosamine analysis is not considered to be necessary.	ii) This clarification is acceptable. The results from the nitrosamines determination in the batches from the former production site where all below [redacted] The validation of the method used is already included in the DAR.	Addressed

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1(5)	Vol. 1, point 4.5 1) The method is not validated for impurity CGA 268087, [redacted]	**Syngenta**: CGA 268087 has the following chemical structure: [redacted]	ii) This explanation is acceptable as the compound is comparable with compounds [redacted]	Addressed RMS to consider including in a revised DAR the explanation regarding the impurity CGA 268087. Evaluation Meeting (25.05.2004): RMS to provide the explanation concerning the validation of the analytical method for the determination of CGA 268087 in a revised DAR or in an corrigendum / addendum.

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	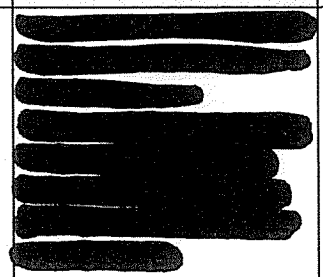			
1(6)	Vol. 1, point 4.5 2) Validated methods for the determination of residues of the major (>10%) soil metabolite CGA 302371 in drinking water and groundwater were not submitted but should be provided in case this compound is considered to be a relevant metabolite (also B 5.5 Analytical methods in water)	**Syngenta**: This data will be available in May 2004	ii) Study not yet received (April 2004). After submission of the study an addendum will be prepared.	IIA 4.2.3 Data requirement 1.1 Validated methods for the determination of residues of the major (>10%) soil metabolite CGA 302371 in drinking water and groundwater should be submitted. Evaluation Meeting (25.05.2004): The notifier will submit the relevant information in June 2004. RMS to provide an addendum to the draft assessment report.

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1(6)	*continued* Vol. 1, point 4.5 2) Validated methods for the determination of residues of the major (>10%) soil metabolite CGA 302371 in drinking water and groundwater were not submitted but should be provided in case this compound is considered to be a relevant metabolite (also B 5.5 Analytical methods in water)			Data requirement still open.

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1(7)	Vol. 1, point 4.5, 3) In the report for the confirmatory method for CGA 193469 residues in wheat grain, the tables for wheat grain and wheat straw should be checked on the fortification level of ppm (instead of ppb?).	**Syngenta**: This refers to method MS 247 (SAM CGA 184927/4928) which was added later as a confirmatory method for CGA 193469 in cereals. The error between ppm and ppb in two of the summary tables in this method has been corrected and an amended version of the report is attached here.	ii) This point was mainly to check the tables in the report. The adjusted report is correct and acceptable.	IIA 4.2.1 Addressed RMS to consider including in a revised DAR (Vol. 1)
1(8)	Vol. 1, point 4.5 4) A confirmatory method to demonstrate specificity is required for measuring CGA 193469 residues in wheat grain	**Syngenta**: MS 247 uses LC-MS-MS with multiple reaction monitoring to detect and quantify the analytes. For CGA 193469, the mass transition being monitored is mz/ 312 to 266, which occurs at a known retention time from the LC. It is therefore considered that this method is highly specific for each of the analytes included in the scope of the method, including CGA 193469. Additionally, European Commission document SANCO/825/00 rev.6 (20/06/00) states that an additional confirmatory method is not required where the original method is highly specific (eg. HPLC-MS-MS). In this	ii) In volume 3 in the DAR the method MS 247 was already accepted as an confirmatory method. Volume 1 was by mistake not adjusted accordingly. There was an additional question about this validation (see point 1(7)), but that has now been answered. Point closed.	IIA 4.2.1 Addressed RMS to consider including in a revised DAR (Vol. 1). (see also 1(9))

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1(8)	*continued* Vol. 1, point 4.5 4) A confirmatory method to demonstrate specificity is required for measuring CGA 193469 residues in wheat grain	case, it is the confirmatory method that uses this methodology, confirming the specificity of this method. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.		
1(9)	Vol. 1, point 2.2.3 Vol. 1, point 3.1	**Syngenta**: All the points raised regarding analytical methods have been addressed in previous correspondence with the RMS. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) See answer at point 1(8).	Addressed (see also 1(8))
1(10)	Vol. 1, p. 4 and 5, 1.3.2 – 1.3.6	**EFSA:** It is may be helpful to mention these data also for the active substance and not only for the variant.	ii) See comment 1(2)	Open point See 1 (2)
1(11)	Vol. 1, p. 13, 2.2.3 Analytical methods for residue analysis	**EFSA:** For clarification purposes, in stead of the code CGA 193469 the name clodinafop should be used (see also comment to 1.1 and 1.3.2ff).	ii) See comment 1(1)	Open point See 1 (1)

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1(12)	Vol 3, point B5.3.3, analytical methods in air	**RMS:** By mistake a word is missing in the assessment for the analytical method in air; an CONFIRMATORY method for the determination of clodinafop-propargyl in air is not required if an acceptable method for water is available. This means that there is still a data gap for an validated analytical method in air.	ii) Agreed. Data requirement for a validated analytical method in air.	IIA 4.2.4 Data requirement 1.2 A validated analytical method in air should be submitted. (see also 1(19) Evaluation Meeting (25.05.2004): The notifier will submit these data in November 2004. Data requirement still open.
1(13)	Vol. 1, p. 13, 2.2.3 Analytical methods for residue analysis	**EFSA:** The assessment of the methods for the determination of residues in food of plant origin should be modified because sufficient methods for post-monitoring purposes seem to be available. The method of Mair (2000, 319/00; SAM No. 4755) seems to be acceptable as enforcement method. The included ILV performed by Lütolf can be accepted as ILV, provided the independency is granted (see comment 12). For confirmatory	ii) This is correct (see also comment at point 1(8))	IIA 4.2.1 Open point 1.3 RMS to provide a revised assessment of the methods for the determination of residues in food of plant origin in an addendum. Evaluation Meeting (25.05.2004): DE tabled at the meeting a proposal regarding a new

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1(13)	*continued* Vol. 1, p. 13, 2.2.3 Analytical methods for residue analysis	purposes, the method of McLean (2002, Report NO MS 247) can be used.		residue definition which shopuld be taken into account provided that the expert meeting on residues will confirm this proposal. Open point still open.
1(14)	Vol. 1, p. 13, 2.2.3 Analytical methods for residue analysis	**EFSA:** The evaluation of the methods for the determination of residue in food of animal origin seems not to be necessary, because no residue definition is proposed.	ii) This is correct. However these methods are taken up in the DAR to prevent all MS to assess them if at MS-level another use is proposed for which a residue definition in animal origin is proposed.	Open point 1.4 RMS to amend the list of endpoints (for clarification purposes) with a statement that analytical methods for the determination of residues in food of animal origin are not required. This issue should be taken into account in the expert group which will discuss and develop proposals (templates) for improving and harmonisation the DAR. Evaluation Meeting (25.05.2004): RMS to include in the list of

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1(14)	*continued* Vol. 1, p. 13, 2.2.3 Analytical methods for residue analysis			end points a note that no method is required. Open point still open.
1(15)	Vol. 1, p. 13, 2.2.3 Analytical methods for residue analysis	**EFSA:** It is not possible that a residue analytical method for the determination of residue in water covers the necessity for an analytical method for air. Provided, the method for air does not meet the requirement a new or an improved method must be submitted. In the previous ECCO meeting there was an agreement that provided acceptable methods for soil and water were available; there is no need for a confirmatory method for air, unless the same analyte will be determined.	ii) This is correct, and a data requirement has already been set (see 1(12))	Addressed See 1 (12)
1(16)	Vol. 3, p. 6, B.2.1.23 Oxidising properties	**EFSA:** It should be mentioned whether the result comes from performing the EEC A17 test or from a justification based on the theoretical consideration of the chemical structure.	ii) As the EEC method 17 is named as the method used (and not a statement) this is already clear from the DAR	Addressed However, the method EEC A17 includes also the possibility for a statement based on the chemical structure. Therefore, an additional remark would be helpful.

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1(17)	Vol. 3, p. 42, B.5.2 Analytical methods	**EFSA:** The independency of both laboratories described in the study 319/00 (SAM No. 4755) should be stated more precisely to decide whether the validation in the second laboratory can be accepted as an ILV.	ii) The comment from the notifier was that "both laboratories are located at Novartis in Basel... It is explicitly stated that no communication with the developers of the method was required by lab 2 to carry out the analysis. .. therefore the ILV of method 138.10 is considered to have been conducted in accordance with the current guidance on this issue " (sanco/825/00 rev 6). This can be accepted.	Addressed RMS to consider in a revised DAR
1(18)	Vol. 3, p. 46ff and 63ff, Tables B.5.2 and B.5.3	**EFSA:** For clarification purposes, only the validation data for the accepted methods should be given.	ii) We do not agree, as it was decided that the complete dossier would be assessed. It is however possible to mark the not acceptable data, e.g. by making the letter type italics	Addressed RMS to consider in a revised DAR This issue should be taken into account in the expert group which will discuss and develop proposals (templates) for improving and harmonisation the DAR.

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1(19)	Vol. 3, p. 71, B.5.5 Evaluation and assessment	**EFSA:** It is not possible that a residue analytical method for the determination of residue in water covers the necessity for an analytical method for air (see also comment 1(15)	ii) This is correct, and a data requirement has already been set (see 1(12)).	Addressed See 1 (12)
1(20)	Vol. 3, p. 72, B.5.6 References relied on	**EFSA:** The references of analytical methods which are clearly unacceptable or not necessary (e.g. methods for food of animal origin) should be removed.	ii) We do not agree that the references which are not used for the endpoints are removed. This is also in contrast with earlier decisions. By removing the references but keeping the assessment it is not possible to be sure which reference is used for which assessment. What is possible, but that has to be discussed first, is to mark the references in question.	Open point 1.5 The proper way of referencing analytical methods not relied on to be discussed in the expert meeting: In previous ECCO meeting the list of references relied on were double-checked during the meeting. All method which do not meet the requirements (and therefore they are “no references relied on”) were marked and deleted from following reference lists. The complete list of references is still available in Volume 2. This issue should also be

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1(20)	*continued* Vol. 3, p. 72, B.5.6 References relied on			taken into account in the expert group which will discuss and develop proposals (templates) for improving and harmonisation the DAR. Evaluation Meeting (25.05.2004): The proper way of referencing analytical methods not relied on will be discussed in the expert meeting developing DAR templates. Open point closed for clodinafop RMS to consider in a revised DAR.

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1(21)	Vol. 4, p. 5, C.1.2 Detailed specification of the active substance	**EFSA:** None of the specified limits is reliable according to the submitted batch analyses. A new specification or a justification is required. It seems to be that the applicant has been provided some explanations. These should be assessed and mentioned in an addendum of Volume 4.	ii) The original specifications were already lowered to those in the DAR, e.g 5 compounds are removed from the specifications. Also there are no guidelines for setting specifications. The explanations of the notifier may be addressed in a addendum. Although the specifications are sometimes high the RMS feels that at this moment they are acceptable. See also point 1(3)	IIA 1 Open point 1.6 RMS to prepare an addendum with the explanations of the notifier regarding the detailed specification of the active substance. As guideline for setting a specification the FAO/WHO Manual on development and use of FAO and WHO specifications for pesticides can be used. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point needs to be discussed in an expert meeting after submission of the addendum. Open point still open.

Additional comments received just before or during the evaluation meeting				
1(22)	Vol. 1, 2.2.3, Analytical methods for residue analysis Vol. 3, B.5.5, Evaluation and assessment	DE: We do not agree with the statement that a method in air need not be provided if a validated method in water is available. Up to now trapping efficiency/break through can not be evaluated.	--	Evaluation Meeting (25.05.2004): It was agreed to discuss trilaterally between the DE, RMS and EFSA to clarify whether this comment still needs to be addressed further, probably in the relevant expert meeting. RMS to initiated discussion.
1(23)	Vol. 1, 2.4.1, Definition of residues relevant to MRLs	DE: Residue definition should be “parent” since the chosen metabolite does not occur in grain but only in fodder. Residues of metabolite in fodder are not transferred to foodstuffs of animal origin.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)
1(24)	Vol. 3, B.5.3.2, Residues in water	DE: Data Requirement: For determination of CGA 193468 and CGA 302371 primary and confirmatory methods in drinking and surface water are missing and should be provided.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)
1(25)	Vol. 3, B.5.3.2, Residues in water	DE: A method to confirm positive findings with the accepted method of analysis (Robinson, 2003) is missing.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)

1(26)	Vol. 3, B.5.3.2, Residues in water	DE: A description of the method of Mair (1999) listed in Table B.5.3 and in B.5.6 (References relied on) is missing.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)
1(27)	Vol. 3, B.5.3.3, Residues in air	DE: Data Requirement: The method of Tribolet (1999) should be sufficiently validated according to SANCO/825/rev.6. Furthermore, a confirmatory method is required.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)
1(28)	Vol. 3, B.5.3.3, Residues in air	DE: AOEL from the List of Endpoints is 0.026 mg/kg bw/d, and so a LOQ of 7.8 µg/m³ is calculated.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)
1(29)	Conclusion	DE: We agree with RMS, that sufficiently validated methods are not supplied by the notifier for monitoring of parent residues in wheat according to SANCO/825/rev.6. Therefore, an inclusion of Clodinafop-propargyl into Annex I without the required new studies will not be supported.		Evaluation Meeting (25.05.2004): See general conclusion to 1(22)

2. Mammalian toxicology

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2(1)	Vol. 1, Level 2, Overall Conclusions, 2.1.4, Classification and labelling	**SE:** In addition to the proposed classification and labelling of clodinafop-propargyl the risk phrase R48/22 should be added.	ii) No classification with R48/22 was proposed since based on mechanistic data it was concluded that humans are considered to be non-responsive to the liver growth effects of peroxisome proliferators. However, considering the haematological effects observed at low doses in short-term toxicity studies, one might consider R48/22. We propose to discuss this further at an expert-meeting.	Open point 2.1 The classification of the active substance with R48/22 to be discussed at an expert meeting. Final classification of the active substance to be agreed at ECB, Ispra. (see also 2(2)) Evaluation Meeting (25.05.2004): Open point needs to be discussed in an expert meeting. Final decision should be made by Ispra. Open point still open.

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2(2)	Vol. 1, 2.1.4 Classification and labelling:	**DK:** We propose a R48/22 classification. We suggest that this matter should be discussed at the ECB, Ispra.	ii) see response at 2(1).	Open point See open point 2.1
2(3)	Vol. 1, Level 2, Overall Conclusions, 2.1.4, Classification and labelling	**SE:** In addition to the proposed classification and labelling of the preparation (TOPIC 100 EC) the risk phrase R43 should be added.	ii) Classification with R43 was not considered necessary considering the results of the available studies. However, additional data on the sensitising properties of TOPIC were requested since accuracy of the test substance concentrations chosen for the main study could not be verified. If data cannot be provided or data indicate that the concentrations were not accurate, the formulation needs to be labelled with R43.	Data requirement 2.1 Additional data on the sensitising properties of TOPIC should be submitted. Open point 2.2 RMS to consider the classification of the active substance with R43 in revision of DAR and updated list of endpoints (see also 2(9), 2(21)) Evaluation Meeting (25.05.2004): Data requirement 2.1: The notifier will submit further data on sensitising properties as soon as possible (by the end of July 2004 at the latest).

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2(3)	*continued* Vol. 1, Level 2, Overall Conclusions, 2.1.4, Classification and labelling			Data requirement still open. Open point 2.2: RMS to amend the list of end points and to consider in a revised DAR. Open point still open.
2(4)	Vol. 1, point 2.1.4 Vol. 3, point B.4.1 Removal of justification for R63 proposal regarding human health effects	**Syngenta**: As no R63 is proposed (see evaluation in Volume 3, B.6.6.3 Summary), please delete "R63 - Based on the presence of developmental effects in the absence of maternal toxicity in a teratogenicity study in rats."	ii) The sentence "R63 - Based on the presence of developmental effects in the absence of maternal toxicity in a teratogenicity study in rats" will be deleted in Vol. 1, point 2.1.4 and B.4.1.	Addressed RMS to delete the sentence "R63 - Based on the presence of developmental effects in the absence of maternal toxicity in a teratogenicity study in rats" in Vol. 1, point 2.1.4 and B.4.1. in a revised DAR (see also 2(5), 2(21) and 2(36)) Evaluation Meeting (25.05.2004):

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2(4)	*continued* Vol. 1, point 2.1.4 Vol. 3, point B.4.1 Removal of justification for R63 proposal regarding human health effects			The classification with R63 needs to be discussed in an expert meeting. The notifier to submit relevant data on the teratogenicity study and for rat developmental study in advance of the expert meeting in September 2004. Data requirement and open point set.
2(5)	Vol. 1, 2.1.4 Classification and labelling: Justification for the proposal	**DK:** Under the paragraph *human health effects* a R63 classification is not mentioned, while just below under justification for the proposal: R63 is warranted. This seems inconsistent.	ii) The sentence "R63 - Based on the presence of developmental effects in the absence of maternal toxicity in a teratogenicity study in rats" will be deleted in Vol. 1, point 2.1.4.	Addressed See 2(4)
2(6)	Vol. 1, Appendix 3, List of end-points	**SE:** It is stated that the rate and extent of excretion is 23-34% in urine and 80-90% in faeces within 24 hrs. A misprint? The given values seem to be the total excretion in males and females, respectively.	ii) Text was incorrectly copied from Vol. 3. The following text is included in the list of end-points: Urinary: 16-27% in males, 77-87% in females in 24 h; faecal 7-9% in males and 2-5% in females in 24 h.	Addressed

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2(7)	Vol. 1, point 4.6, Toxicology and metabolism, Active substance Vol. 3, point 6.6.1 2-generation reproduction study in the rat (Muller 1991). A tentative NOAEL was derived for parental toxicity in a 2-generation reproduction study in rats, because no histopathology was performed on liver and kidneys of the intermediate dose groups.	**Syngenta**: The histopathology on kidney and liver in intermediate doses was performed and the data are available. These data are contained in an addendum to the 2 generation reproduction report. Summaries of the histopathology data on the kidney and liver are included in the MII Section 3 summary of the study (Table 5.6.1-5 'Two-generation study with clodinafop-propargyl – Necropsy findings of parental generation F0' and Table 5.6.1-6 'Two-generation study with clodinafop-propargyl – Necropsy findings of parental generation F1'). These data do not alter the proposed parental NOAEL of 50ppm (4.6 mg/kg bw/day). The report addendum was mistakenly not included in the original submission. It is attached here and has subsequently been included in the updated dossier at KIIA 5.6.1/02	ii) Additional data on histopathology on kidney and liver were evaluated. Based on this addendum the summaries in Vol. 1, point 4.6 and Vol. 3 point 6.6.1 will be amended. Furthermore, the request for additional information in Vol. 1, level 4 will be removed.	Open point 2.3 RMS to provide evaluation of additional data on histopathology on kidney and liver (2-generation reproduction study in the rat) in an addendum. RMS to amend Vol. 1, level 4 in an revised DAR Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.

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2(8)	Vol. 1, Level 4, Demand for further information, Toxicology and metabolism, Plant protection products	**SE:** No studies were conducted on the main metabolite CGA 193469 though this metabolite was found in high amounts (>10% of administered dose). Please, make a justification why no further data has been required.	ii) Since metabolite CGA 193469 was a metabolite in rats, no further studies were requested. It is assumed that if the parent compound is given to rats, the animals will have been exposed to CGA 193469 as well. Therefore, no further testing is considered necessary.	Addressed RMS to consider justification in a revision of DAR
2(9)	Vol. 1, point 4.6, Toxicology and metabolism, Plant protection products. Vol. 3, point 6.11.2 Skin sensitisation study (Maximisation test) on the preparation (Besson 1991). The reporting of the study was not considered acceptable	**Syngenta**: It is not possible for Syngenta to adequately supplement the information in this report. Therefore if required for risk assessment Syngenta will undertake an additional study. However, Syngenta believes that the existing data; this study and the Beuhler sensitisation report also submitted and evaluated (Ullmann et al, 1990) provide an adequate dataset and use of test animals to generate further data is not justified.	ii) The available Maximisation test was not considered suitable for the evaluation of the skin sensitising properties of TOPIC 100 EC, since the accuracy of the test substance concentrations chosen for the main study could not be verified It should be noted that a Maximisation test or LLNA is preferred as it is considered a more sensitive test than the non-adjuvant Buehler test. If no data are provided, TOPIC 100 EC should be labelled with R43, due to the sensitising properties of clodinafop-propargyl.	See data requirement 2.1 and open point 2.2

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2(10)	Vol. 3, B.6.2.1 Acute toxicity	**SE:** The animals in the acute inhalation toxicity study were not tested up to 5 mg/l (limit test). The highest dose tested was 2.3 mg/l. One female rat died during the treatment. Was this death substance-related? If so, a LC_{50} value below 5 mg/l may be expected and the substance should be classified in the category of danger Harmful with the risk phrase R 20.	ii) The dose tested was the highest attainable concentration. Methods for generation the exposure atmosphere was accurate. Therefore it is not to be expected that animals will be exposed to higher levels than 2.3 mg/L. No test substance related clinical signs were noted during the study in all animals, including the female that died during the study. No treated related findings were noted at pathology. Since no treatment-related effects were noted, most probably the animal died due to technical reasons. Since the highest attainable concentration was tested, since only one female died at the end of the exposure period (10% mortality), and since no test substance related effects were noted, no classification was proposed.	Addressed

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2(11)	Vol 3, B6.3 Tables – general point	**UK:** The use of semi-qualitative information (increased / decreased) in the tables makes it difficult for an independent interpretation to be performed. For end-points critical to the overall assessment the RMS should consider providing actual values.	ii) If parameters are critical for the establishment of the NOAEL, percentages (compared to control) were given in paragraph „conclusions“ at each study. It is considered to be more organised to give already an evaluation of the numbers/values of the study report within the evaluation table, than to present all the data from the study report.	Addressed
2(12)	Vol 3, B6.3.2.1 28 day dermal study	**UK:** If body weight did not change why did relative liver weight values not increase in line with absolute values?	ii) Both absolute and relative liver weights were increased in the 200 and 1000 mg/kg bw/day groups. Body weight was very slightly reduced in both dose groups, 94-96% when compared to controls in week 4. Since the reduction in body weight was only slight, not dose-related and not consistent over the study period, it was not reported as a treatment-related finding. At 50 mg/kg bw/day the body weight was slightly increased: 103% when compared to controls. Above observation might explain why relative liver weights did not increase in line with absolute values.	Addressed RMS to consider justification in a revision of the DAR

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(13)	Vol 3, B6.3.2.2 21 day dermal study with Topic	**UK:** The local irritant effects are probably related to concentration, not applied dose and should be expressed accordingly.	ii) Since AOEL are not derived for local effects, and since TOPIC is already classified as irritating to skin, the summary is not adapted.	Addressed
2(14)	Vol 3, B6.3.4.1 13 week rat study	**UK:** In the recovery phase there are dose-related reductions in erythrocyte parameters at 15ppm. As 15ppm is the proposed NOAEL, the significance of the erythrocyte effects needs to be discussed.	ii) At conclusions the following is included: ”Changes in haemoglobin, red blood cell count and haematocrit at 15 mg/kg food and haemoglobin at 2 mg/kg food, occurred only at the end of the recovery period and were only slight (95-97% of control values) and were considered of no toxicological significance and unlikely to be related to treatment.“	Addressed RMS to consider justification in a revision of DAR

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(15)	Vol. 3, B.6.3.4. Study 5: 13 week oral toxicity study. Dog.	**DK:** We propose a NOAEL of 10 ppm.	ii) Probably DK mean study 4, since in study 5 the highest dose level was 50 mg/kg food. In study 4 indeed slight skin effects were noted in males given 50 and 200 mg/kg food and females given 200 mg/kg food. However, these skin effects did not occur consistently during the study: in one male of the 50 mg/kg food group, skin effects were noted in week 6 and during week 10-13. In another male of the 50 mg/kg food group, skin effects were noted in week 2 only. In two males of the 200 mg/kg food group, skin effects were noted during week 2 and a part of week 3. In one female of the 200 mg/kg food group skin effects were noted during week 2 and a part of week 3. Since skin effects in animals of the 50 and 200 mg/kg food group were only slight and did not occur consistently during the study period, the effects were not considered to be adverse. Therefore the NOAEL was set at 50 mg/kg food, based on changes in haematology and biochemistry.	Open point 2.4 The setting of the NOAEL from 13 week oral toxicity dog study to be discussed at an expert meeting (see also 2(16)) Evaluation Meeting (25.05.2004): Open point needs to be discussed in an expert meeting. The setting of the NOAEL should also been mentioned in the consultation report. Open point still open.

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(16)	Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity	**DK:** We propose a NOAEL of 1 ppm for males.	ii) There are several reasons for setting the NOAEL at 10 mg/kg food: (A) The increased incidence of hepatocellular hypertrophy and pigment accumulation in the epithelia of the renal tubules was only slight. (B) Within the chronic study, no changes in functional liver parameters were noted at 10 mg/kg food. (C) Within the chronic study, no changes in functional kidney parameters were noted at 10 mg/kg food. (D) No further histopathological findings were noted in kidneys at 10 mg/kg food in the chronic study, and no kidney effects were noted in short-term studies. For peroxisome proliferators, effects do not depend on the duration of exposure (short-term versus chronic exposure). Based on an evaluation of liver pathology data from short-term toxicity studies, no adverse liver effects due to peroxisome proliferation are expected at a level of 10 mg/kg food in a chronic study. For both findings, hepatocelluar	Open point See open point 2.4

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(16)	*continued* Vol. 3, B.6.5.1 Chronic toxicity and carcinogenicity continued		hypertrophy and pigment accumulation in the epithelia of the renal tubules, no historical control data were available. If above considerations are not sufficient for MS DK, the notifier should submit the historical control data for both findings for an additional evaluation. Based on above considerations, the increased incidences in hepatocelluar hypertrophy and pigment accumulation in the epithelia of the renal tubules were not considered to be adverse effects. Therefore, the RMS proposes to keep the NOAEL at 10 mg/kg food (0.32 mg/kg bw/day).	
2(17)	Vol 3, B6.5.1 Chronic rat study	**UK:** In Table 6.5.1.1 there is an increased incidence of hypertrophy of hepatocytes and renal tubule pigmentation at 10 ppm. These findings appear to be statistically significant (Fisher exact rest). As 10ppm is proposed as the NOAEL the RMS should give a reason for discounting these findings. 1. In Table 6.5.1.1 the pathology findings re presented as being from 80 animals. Could the RMS confirm if the 80 includes the	ii) Reasons for discounting the effects in liver and kidneys at 10 mg/kg food was given at point 2(16). With regard to the presentation of the pathology data, the comment of MS UK is considered justified. The pathology data of 80 animals, included 10 animals/sex /dose of the interim sacrifice after 1 year treatment. An additional table will be included with terminal sacrifice data only. Taking the terminal sacrifice data into account the incidence of hypertrophy	Addressed RMS to amend the description of chronic rat study in a revision of the DAR

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(17)	*continued* Vol 3, B6.5.1 Chronic rat study continued	interim sacrifice animals. If so, the results should be re-presented in terms of the animals in the chronic phase only. 2. Until the above points have been addressed it is not possible to confirm the NOAEL from this study – and hence the ADI cannot be defined.	of hepatocytes was as follows: 0/47, 0/46, 4/38, 43/49 and 48/49 in males and 1/42, 0/41, 1/45, 41/49 and 45/47 in females for the respective dose groups. Taking the terminal sacrifice data into account the incidence of renal tubule pigmentation was as follows: 0/47, 0/46, 0/38, 14/49 and 13/49 for males and 3/42, 4/41, 8/45, 17/49 and 20/47 for females for the respective dose groups. The terminal sacrifice data do not change the overall conclusion for this study. Incidences of neoplastic lesions in liver, prostate and ovary remain within the historical control range and the carcinomas of the mammary gland remain outside the historical control range. Separate data for the interim group were not provided since this would not have influenced the conclusion of the study. No dose-related mortality was noted.	

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2(18)	Vol 3, B6.5.1 Chronic mouse study	**UK:** The pathology results in Table 6.5.1.2 the survival results are presented for 50 animals but the pathology is for 60 animals. Could the RMS confirm if the 60 includes the interim sacrifice animals. If so, the results should be re-presented in terms of the animals in the chronic phase only.	ii) Since the majority of deaths occurred during the last 4 weeks of the study, it was not considered necessary to present the pathology results for scheduled sacrifice and moribund sacrifice or animals found death separately. No interim sacrifice was performed. 60 animals/sex/dose were examined for microscopical findings. 10 animals/sex/dose were not included in the group mortality data. These animals were in a specific group for evaluation of haematological and blood chemistry parameters. Within this group several animals died, without a dose related response, probably as a result of over exposure to anaesthetic.	Addressed

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(19)	Vol. 3, B.6.6.1 Reproductive toxicity	**DK:** We propose a NOAEL of 500 ppm for reproductive effects.	ii) Changes in physical development and reduced viability index were considered to be developmental effects and no reproductive effects. The reduced viability index was statistically significant at 1000 mg/kg food during late lactation (day 14 p.p. to day 21 p.p.). Therefore, the NOAEL for reproductive effects was set at ≥ 1000 mg/kg food. The NOAEL for developmental effects was set at 50 mg/kg food.	Addressed
2(20)	Vol 3, B6.6.1 Reproduction study	**UK:** Delayed incisor eruption is seen in the F2 generation at 50 ppm and is discounted based on the small magnitude of the delay. It would be helpful if additional details e.g. mean values, ranges and historic control ranges were presented to support the conclusion.	ii) A delay in incisor eruption was only noted at day 9 to 11 p.p. The following group mean percentages of pups with incisor eruption were reported for the F2a generation for the dose groups 0, 5, 50, 500 and 1000 mg/kg food: Day 8: 7.3, 7.5, 4.7, 2.9 and 6.3 Day 9: 47.6, 38.4, 15.9, 13.8 and 14.1 Day 10: 89.7, 74.5, 52.1, 38.3, and 30.6 Day 11: 97.4, 89.7, 77.6, 67.8 and 62.9 Day 12: 98.8, 98.8, 96.2, 86.1 and	Addressed RMS to consider further details regarding reproduction study in a revision of the DAR Evaluation Meeting (25.05.2004): The notifier will submit the data prior to the expert meeting in September 2004.

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(20)	*continued* Vol 3, B6.6.1 Reproduction study		79.1 Day 13: 100, 100, 100, 95.7 and 91.4 Historical control data were not available. The delay in incisor eruption during days 9 to 11 was not considered to be an adverse effect. Therefore, the NOAEL for developmental effects was set at 50 mg/kg food.	Data requirement set.
2(21)	Vol. 3, B.6.6.2 Teratogenicity studies	**SE:** We propose a classification of the substance as Toxic for reproduction in Category 3 with the risk phrase R63 ("Possible risk of harm to the unborn child"). **SE:** In the developmental toxicity study in rats skeletal and visceral findings were noted in offsprings at ≥40 mg/kg bw/day. The findings in offsprings at 40 mg/kg bw/day was within historical control range according to RMS. Please, specify the historical control data.	ii) Skeletal and visceral findings at 40 mg/kg bw/day were within the historical control range: Incomplete ossification of right and left metacarpals: incidence in study 39%, historical control range 8.1-56.2%. Incomplete ossification of interparietal: incidence in study 26%, historical control range 3.9-41.4%. Incomplete ossification of squamosals: incidence in study 7%, historical control range 0-14.6%. Bilateral distension of ureters: incidence in study 15%, historical control range 4.9-62.6%. Bilateral ureter torsion: incidence in	Addressed See 2(4) and 2(5)

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(21)	*continued* Vol. 3, B.6.6.2 Teratogenicity studies		study 17%, historical control range 7.7-57.2%. Since potentially critical effects of the test substance (on liver and red blood cells) were not studied in maternal animals, and considering the NOAELs observed for females in short-term toxicity studies (e.g. NOAEL ≤ 5 mg/kg bw/day, gavage), no classification with R63 was proposed.	
2(22)	Vol 3, B6.6.2 Rat developmental study	**UK:** The fetal effects at 40 mg/kg bw/d show a consistent pattern of developmental delay, and are discounted based on a comparison with historic control data. Can the RMS confirm that the historic data are from the same laboratory and strain and are contemporary e.g. 1987 – 1991. If not, the assessment should be performed with appropriate historic control data.	ii) The historic control data were compiled from 22 studies from Hazleton. The data were compiled from studies performed from 1985 to 1986. The data are from the same rat strain as used for the teratology study with clodinafop-propargyl.	Addressed
2(23)	Vol 3, B6.10.3 ADI	**UK:** Before the ADI can be defined, the NOAEL from the rat chronic study needs to be confirmed (see comments on B6.5.1 above)	ii) See discussion at 2(16) and 2(17).	Open point 2.5 The setting of the ADI to be discussed at an expert

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2(23)	*continued* Vol 3, B6.10.3 ADI			meeting Evaluation Meeting (25.05.2004): Open point needs to be discussed in an expert meeting. Open point still open.
2(24)	Vol 3, B6.10.4 Acute reference dose	**UK:** The findings in the reproduction study appear to be more related to repeated dosing than single dosing. The maternal toxicity findings in the rabbit teratology study are evident just after the commencement of dosing and might be a more suitable basis for the ArfD.	ii) Critical effects of the test substance (e.g. haematological effects) were not studied in teratogenicity study in rabbits, the maternal NOAEL is not considered suitable for the derivation of the ArfD. Since no more suitable studies are available, the ArfD should be based on the NOAEL of 4.63 mg/kg bw/day.	Addressed Evaluation Meeting (25.05.2004): The setting of the ARfD should be discussed in an expert meeting. (see also 2(40)) Open point set.
2(25)	Vol. 3, B.6.10.5 AOEL	**SE:** The acceptable operator exposure level (AOEL) proposed by the RMS is based on the 1-year oral toxicity study in dogs. Instead, we propose the	ii) The NOAEL of 0.92 mg/kg bw/day is indeed the lowest NOAEL from semichronic toxicity studies. However, since comparable NOAELs	Addressed

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2(25)	*continued* Vol. 3, B.6.10.5 AOEL	NOAEL from the 90-day oral toxicity study in rats to be used for the setting of AOEL.	and LOAELs were noted in semichronic studies with rats and dogs, the most relevant NOAEL was chosen, based on a comparison of NOAELs and LOAELs. The NOAEL of 3.4 mg/kg bw/day from the 1-year study in dogs was lower than the LOAELs established in other semichronic studies, and therefore considered to be suitable for the derivation of the AOEL.	
2(26)	Vol 3, B6.10.5 AOEL	**UK:** The RMS proposal for using an oral systemic AOEL is supported. The dermal and oral values are reasonably similar, but the larger number of assumptions in deriving the dermal AOEL make it less reliable.	ii) Agreed.	Addressed
2(27)	Vol 3, B.6.12.1	**DK :** The dermal absorption of clodinafop-propargyl is 45 % and 24 % (the 24 h time point including the residue at the treated skin site)	ii) All animals were exposed to the test substance for 6 hours. The text in the DAR was not very clear. First it was concluded that the potentially absorbed dose should be taken for risk assessment purposes. However, in the conclusion the systemically available dose was given as a measure of dermal absorption.	Open point 2.6 Dermal absorption value to be discussed at an expert meeting (see also 2(28), 2(29), 2(30), 2(31), 2(42), 2(43))

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2(27)	*continued* Vol 3, B.6.12.1		Part of the material in the skin seems to be firmly bound in the stratum corneum. Whether all of this material will not be available for absorption is not sure. However, if some of it becomes available, than this will be a very slow process. A lower dislodged dose was noted for the high animals at 24 hours, most probably due to less efficient washing which might explain the higher values measured in the treated skin of these animals. Therefore, data at 24 hours were not considered suitable for risk assessment purposes. Therefore, finally, the systemically available dose at 72 hours was taken as a worst-case measure of exposure.	Evaluation Meeting (25.05.2004): Open point needs to be discussed in an expert meeting. Open point still open.
2(28)	Vol 3, B6.12.1 Rat in vivo dermal penetration	**UK:** The dermal penetration value from the rat in vivo study is supported. The skin residue at 72 hours should not be included as this is inconsistent with the derivation of the AOEL, which is on a 24 hour basis.	ii) See comment at 2(27).	See open point 2.6

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2(29)	Vol. 3, point 6.12.2 Dermal absorption in vitro (Hassler 2001c). The rapporteur considered the percentages of dermal absorption to calculate the human/rat ratio and proposed a factor of 4 by which dermal absorption is greater through rat than human skin	**Syngenta**: The scientific approach is to compare the penetration rates through rat and human skin membranes at the linear range. Otherwise, by considering percentages it might be influenced by the duration of the lack phase before penetration starts and the shape of the absorption curve. Therefore, Syngenta still recommends to consider the flux. By considering the flux the absorption through rat skin is 10 (concentrate) and 11 fold (dilution) greater than through human skin. However, if percentage is considered the corresponding factors are 5 for the dilution and 11 for the concentrate after 24 hours. Therefore, if percentages are taken then Syngenta suggests to consider theses values of 5 and 11 instead of a factor of 4.	ii) The choice for percentages was based on the presence of significant amounts of label in the skin at the end of the exposure period. The factor 4 is derived from the dermal absorption data in table 6.12.1.3. In Table 6.12.1.4 dermal absorption percentages were given, however, these were without the amount in the skin membranes., Since no “infinite” dose levels were used and considering the fact that full thickness skin was used (no blood flow) and the short study duration, dermal absorption percentages (percentage radiolabel in receptor medium plus skin membrane) at 24 hours (table 6.12.1.3) should be used to make a comparison of rat and human dermal absorption.	See open point 2.6
2(30)	Vol 3, B6.12.2 and 6.12.3 Dermal penetration	**UK:** Using the concentrate (924ug/cm^2) human skin appears to be approximately 10 fold less permeable to clodinafop (based on a number of end-points). It is unclear why a correction of 4 was used for both concentrate and dilution when	ii) The factor 4 is derived from the dermal absorption data in table 6.12.1.3. In Table 6.12.1.4 dermal absorption percentages were given, however, these were without the amount in the skin membranes., Since no “infinite” dose levels were used and considering	See open point 2.6

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
	continued	extrapolating from rat in vivo data.	the fact that full thickness skin was used (no blood flow) and the short study duration, dermal absorption percentages (percentage radiolabel in receptor medium plus skin membrane) at 24 hours (table 6.12.1.3) should be used to make a comparison of rat and human dermal absorption.	
2(30)	Vol 3, B6.12.2 and 6.12.3 Dermal penetration			
2(31)	Vol. 3, B.6.12.3 Overall conclusion dermal absorption. AOEL-internal calculated via the dermal route	**DK:** Dermal absorption for the high dose should be ~6 % and ~11 % at the low dose	ii) See comments above. A dermal absorption of 2.5% should be considered for high doses and 9.75% for low doses.	See open point 2.6
2(32)	Vol. 3, B.6.13 Toxicological data on non active substances	**SE:** It is stated that cloquintocet-mexyl needs no classification for acute oral, dermal or inhalation toxicity. Please, add data e.g. LD_{50}/LC_{50} values to support the conclusion.	ii) Oral LD50: > 5000 mg/kg bw Dermal LD50: > 2000 mg/kg bw LC50: > 935 mg/m3 (highest attainable concentration)	Addressed Evaluation Meeting (25.05.2004): RMS to provide information in a revised DAR or an addendum / corrigendum. Open point still open.

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(33)	Vol. 3, B.6.13 Toxicological data on non active substance	**SE:** The acute reference dose (ARfD) for cloquintocet-mexyl proposed by the RMS is based on the teratogenicity study in rats. Instead, we propose the NOAEL from the teratogenicity study in rabbits to be used for the setting of ARfD for cloquintocet-mexyl.	ii) The NOAEL of 60 mg/kg bw/day is indeed the lowest NOAEL for developmental toxicity. However, since comparable NOAELs and LOAELs were noted in teratogenicity studies in rats and rabbits, the most relevant NOAEL was chosen, based on a comparison of NOAELs and LOAELs. The NOAEL of 100 mg/kg bw/day from the teratogenicity study in rats was lower than the LOAEL established in the teratogenicity study in rabbits, and therefore considered to be suitable for the derivation of the AOEL. Differences only occur due to the choice of dose levels.	Addressed

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
Additional comments received just before or during the evaluation meeting				
2(34)	Vol. 1, 2.1.4 and Vol. 3, B.4.1, Classification and labelling	DE: After the re-evaluation of the reproductive toxicity studies (2-gen., rat, teratogenicity, rats) DE agrees that there is a need to discuss a classification (R63) for development effects. Note: The classification for developmental toxicity (R63) as recommended by the RMS is not formally proposed (and not mentioned in the list of endpoints) although a respective justification is given.	--	Evaluation Meeting (25.05.2004): Will be to be discussed as open point in expert meeting Refer to 2(4)
2(35)	Vol. 1, 2.1.4 and Vol. 3, B.4.1, Classification and labelling	DE: The occurrence of ovarial and prostate adenoma and mammary gland carcinoma in the long-term study in rats was also discussed in relation with the national authorisation in 1997. Additional mechanistic studies and explanations of the notifier finally lead to the decision not to classify the active substance with respect to cancerogenic effects.	--	--

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2(36)	Vol. 1, 2.1.4 and Vol. 3, B.4.1, Classification and labelling	DE: In view of the proposals for the active substance [see 2(34)], for the classification and labelling of Topic 100 EC the risk phrase R63 has to be considered additionally.	--	Evaluation Meeting (25.05.2004): Will be to be discussed as open point in expert meeting Refer to 2(4)
2(37)	Vol. 3, B.6.6.1, Reproductive toxicity	DE: Histopathological examination of liver and kidney tissues at the low and intermediate dose groups in the two-generation study in rats should be considered if possible	--	Evaluation Meeting (25.05.2004): RMS will provide an addendum to the draft assessment report Refer to 2(7)
2(38)	Vol. 3, B.6.6.2, Teratogenicity studies	DE: Data requirement: After a re-evaluation of the teratogenicity study in rats, a comment of the notifier on the findings in the fetuses at 40 and 5 mg/kg bw/d is required..	--	Evaluation Meeting (25.05.2004): Data requirement is set

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(39)	Vol. 3, B.6.8, Further toxicological studies	DE: After a re-evaluation of the repeat-dose studies a possible immunotoxic action of the active substance and the need for additional investigations should be discussed.	--	Evaluation Meeting (25.05.2004): Open point A possible immunotoxic action of the a.s. and the need for additional investigations to be discussed in expert meeting
2(40)	Vol. 1, 2.3.3 and Vol. 3, B.6.10.4, Acute Reference Dose (ARfD),	DE: Comment of the RMS is required on a proposed ARfD of 0.034 mg/kg bw from the 1-yr dog study.	--	Evaluation Meeting (25.05.2004): Will be to be discussed as open point in expert meeting Refer to 2(24)
2(41)	Vol. 1, 2.3.5, Drinking water limit	DE: Since the maximum permissible concentration for active substances is 0.1 µg/L according to EU legislation, it is not appropriate to derive a separate "drinking water limit" that is higher by about 96 times.	--	Evaluation Meeting (25.05.2004): Open point RMS to amend list of endpoint (drinking water limit)

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
2(42)	Vol. 3, B.12, Dermal absorption	DE: **Comment of the RMS is required** on the dermal absorption rates of 6 % (concentrate) and 12 % for the diluted formulation.	--	Evaluation Meeting (25.05.2004): Will be to be discussed as open point in expert meeting Refer to 2(27)
2(43)	Vol. 1, 2.3.6, Impact on human and animal health and Vol. 3, B.6.14, Exposure data	DE: On the basis of the proposed dermal absorption rates of 6% and 12 % [see (11)] and considering the proposed additional Risk phrases [R 63], a new risk assessment should be carried out.	--	Evaluation Meeting (25.05.2004): Will be to be discussed as open point in expert meeting Refer to 2(27)
2(44)		BE: We agree with RMS for disregarding the oncogenic effects of the a.s. in prostate and ovaries in the rat but questions remains about the mammary gland carcinoma. There seems to be an increased incidence at top dose, which could be related to aromatase induction.	--	Evaluation Meeting (25.05.2004): Open point Increased incidence regarding mammary gland carcinoma in rat study to be discussed in expert meeting

3. Residues

Originally no comments were received for this section.

One late comment was received for residues. Evaluation by RMS wasn't possible anymore.

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
3(1)	Vol. 1, 2.4.1, Definition of residues relevant to MRLs	DE: Residue definition should be "parent" since the chosen metabolite does not occur in grain but only in fodder. Residues of metabolite in fodder are not transferred to foodstuffs of animal origin. It is expected, that the supply of enforcement laboratories with the metabolite will cause problems. Further the determination of residues by GC methods is possible with proposed new residue definition only.	-	Open point 3.1 Definition of residues for monitoring purposes to discuss in an expert meeting

4. Environmental fate and behaviour

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(1)	Vol.1 Fate Vol. 3. B8. General	**EFSA:** For clarity CGA 163469 should be named by its name: clodinafop.	ii) CGA 193469 is a metabolite of clodinafop-propargyl and is indeed clodinafop (ISO name). For clarification if this metabolite is mentioned the name clodinafop can be added between brackets where relevant. The DAR will be amended accordingly. See also 1(1).	IIA/ IIIA Addressed RMS to consider adding 'clodinafop' to the code CGA 193469 in a revision of the DAR.
4(2)	Vol 1. Fate. Vol 3. B.8.	**EFSA:** Identity and chemical structure of metabolite CGA 193468 is given neither in Vol 1 nor in B.8. Please, amend for clarity.	ii) Agreed. DAR will be amended accordingly.	IIA 7 Addressed RMS to consider identity and chemical structure of metabolite CGA 193468 in a revision of the DAR.
4(3)	Vol. 1, point 2.5.2 Fate and behaviour in soil. Soil accumulation trials Vol. 3, point B.8.1.2 Field Studies For each study the RMS has noted the absence of storage stability data for parent and metabolites in soil	**Syngenta**: Data on long-term stability in stored soil and water samples was submitted in a response to the RMS on 16 June 2003.	ii) Storage stability data is included in the information of the notifier (June 2003). Further clodinafop-propargyl is very unstable and therefore a study to demonstrate stability is very difficult to perform. However the degradation product CGA-193469, which is the environmentally relevant substance, has been shown to be stable under frozen storage. This is agreed by RMS.	Addressed

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(4)	Vol. 1, point 2.5.3 Fate and behaviour in water, Biodegradability, Anaerobic water/sediment studies Further information requested	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the rebuttal dated 16 June 2003. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) Two new aqueous photolysis studies have been conducted to EPA guidance in 2002 and 2003 (Anderson W 2002 Syngneta No. 82-00 and Anderson W 2003 Syngenta No. 19-02 provided separately). In these studies, no unknowns exceed 6.5% applied radioactivity. Syngenta proposes that these new studies should replace the older studies. The notifier presented two summaries of new studies (Anderson W 2002 Syngneta No. 82-00 and Anderson W 2003 Syngenta No. 19-02 provided separately). DAR will be amended accordingly.	IIA 7.2.1.2 Open point 4.1 These two new studies seem to have been already summarised in the DAR (Vol 3 B.8.4.2. pp 419- 426), however, photolysis studies are not expected to address the data requirement on further information requested for the anaerobic water /sediment study. Need of this data requirement may be discussed by MS. Evaluation Meeting (25.05.2004): The RMS states that the notifier has to clarify this point sufficiently. No data requirement set because the main issue is addressed in other points of the evaluation table. Open point fulfilled.

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(5)	Vol 1. p.47. Column leaching./ Vol 3. B8. 2.2.1 p. 390 (Keller, A. 1989e).	**EFSA:** Acceptability of column leaching studies should be clearly stated and a data requirement for the missing data proposed if necessary.	ii) The notifier gave an adequate reaction on this point of the DAR. The result is that the study is fully acceptable so this paragraph will be amended.	IIA 7.1.3.1 Open point 4.2 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding 'column leaching' to include the information provided by the notifier. Evaluation Meeting (25.05.2004): EFSA states that if there is more information available in the study it should be make more transparent. RMS to provide an addendum to the draft assessment report. Open point still open.
4(6)	Vol.1 p.48. Field monitoring.	**EFSA:** Acceptability of field study on leaching dissipation should be clearly stated. If not acceptable they should be not included in the list of endpoints.	ii) The notifier gave an adequate reaction on this point of the DAR. The result is that the study is fully acceptable so this paragraph will be amended. It is not necessary to amend the list of endpoints.	IIA 7.1.3.3 Open point 4.3 Evaluation meeting to discuss the need for an amendment of DAR or an addendum 'field monitoring' to include the information provided by the notifier Evaluation Meeting

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(6)	*continued* Vol.1 p.48. Field monitoring.			(25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
4(7)	Vol.1. p. 56. Water sediment studies./ Vol 3. B.8.4.4. Water-sediment studies. Keller A. 1993b and Reischmann F.-J. 1996	**EFSA:** Acceptability of water sediment studies should be clearly stated. Data requirement should be specified if necessary.	ii) The notifier gave an adequate reaction on this point of the DAR. The result is that the study is fully acceptable so this paragraph will be amended.	IIA 7.2.1.3 Open point 4.4 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding 'water sediment studies' to include the information provided by the notifier. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(8)	Vol.1 List of endpoints. p. 114.	**EFSA:** Soil accumulation studies should not be reported in the list of endpoints if soil accumulation study is not considered fully acceptable.	ii) The notifier gave an adequate reaction on this point of the DAR. The result is that the study is fully acceptable so it is not necessary to amend the list of endpoints.	Open point 4.5 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding “soil accumulation studies” to include the information provided by the notifier. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
4(9)	Vol 3. B.8. p. 351 Keller, A. 1992 b.	**EFSA:** Specificity of CO_2 identification should be clarified for aerobic degradation studies, including study with metabolite 302371 (Jonas, W. 1999).	ii) This point will be checked and addressed.	Open point 4.6 RMS to address specificity of CO_2 identification for aerobic degradation studies, including study with metabolite 302371 (Jonas, W. 1999). If no sufficient data is available in the dossier new data may need to be required to the notifier. Evaluation Meeting

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(9)	*continued* Vol 3. B.8. p. 351 Keller, A. 1992 b.			(25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
4(10)	Vol 3. B.8.1.2 Field studies.	**EFSA:** Acceptability of field soil dissipation studies should be clearly stated.	ii) The notifier gave an adequate reaction on this point of the DAR. The result is that the study is fully acceptable so this paragraph will be amended.	IIA 7.1.3. 3 Open point 4.7 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding 'field studies' to include the information provided by the notifier. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(11)	Vol. 3, point B.8.1.3 Summary Soil photolysis 'The acceptation of the data on soil photolysis is subject to the condition that the applicant submits representative and properly annotated chromatograms'	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the rebuttal submitted 3 February 2003. The comment has been removed from the individual study reviews. If the RMS agrees with this comment then please remove the remaining statement in the DAR referring to this.	ii) The notifier has provided the chromatograms. The chromatograms show adequate separation. The study is completely accepted and presented in the list of endpoints. The results will be confirmed in the DAR.	Addressed RMS to consider to include in a revision of the DAR a statement on the chromatograms (soil photolysis). Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
4(12)	Vol 3. B.8.2.1.2 Adsorption desorption of major metabolites. D) Hill, A.D. 1994b	**EFSA:** Range of pH in the soils tested is very short: 7.0, 7.1, 7.3. Dependence of adsorption on soil pH may not be assessed.	ii) Agreed but because of this, the results are considered worst case for leaching with respect to pH.	Data requirement 4.1. Degradation product CGA 193469 is ionisable and probably a zwitterion at pH 7. Notifier to address pH adsorption dependence of metabolite CGA 193469. Evaluation Meeting (25.05.2004): The notifier states that the pH

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(12)	*continued* Vol 3. B.8.2.1.2 Adsorption desorption of major metabolites. D) Hill, A.D. 1994b			was tested in a worst case study, with analysing in all relevant pH's. The notifier should provide this as a statement to the RMS. The RMS will evaluate this in an addendum to draft assessment report. Data requirement still open.
4(13)	Vol. 3 B.8.2.4 Predicted concentrations in groundwater (Ann IIIA 9.2.1)	**UK**: The FOCUS PEARL modelling supports the proposed GAP for application in the spring. MS will need to consider autumn application	ii) RMS agrees that autumn application can be considered at MS level.	Addressed. Autumn applications are not covered by EU assessment and should be dealt at MS level.
4(14)	Vol. 3, point B.8.4.1, Hydrolysis Studies c) Jonas W(2000), comment (1) by RMS.	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the rebuttal dated 16 June 2003 (~~attached here~~, removed by EFSA). If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) The statement provided is agreed by RMS. The statement will be confirmed in the DAR.	IIA 7.2.1 Open point 4.9 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding the hydrolysis study from Jonas (2000) to include the information provided by the notifier. RMS to advise notifier to add statement for updating the dossier.

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(14)	*continued* Vol. 3, point B.8.4.1, Hydrolysis Studies c) Jonas W(2000), comment (1) by RMS.			<u>Evaluation Meeting (25.05.2004):</u> RMS to provide an addendum to the draft assessment report. Open point still open.
4(15)	Vol. 3, point B.8.4.2, Aqueous photolysis d) Phaff (1995a), acceptation of study relies on recalculation of quantum yield	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the environmental fate rebuttal dated 16 June 2003. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) The notifier presented modifications due to a wrong molar absorption. The results are in line with the results of RMS. The results will be confirmed in the DAR.	IIA 7.2.1.2 <u>Open point 4.10</u> Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding a statement on aqueous photolysis (study from Phaff; 1995a). See also comment 4(21) <u>Evaluation Meeting (25.05.2004):</u> RMS to provide an addendum to the draft assessment report. Open point still open.

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(16)	Vol. 3, point B.8.4.2, Aqueous photolysis f) Purghart (2002), acceptation of study relies on recalculation of quantum yield	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the environmental fate rebuttal dated 16 June 2003. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) The notifier presented modifications due to a wrong molar absorption. The results are in line with the results of RMS. The results will be confirmed in the DAR.	IIA 7.2.1.2 Open point 4.11 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding a statement on aqueous photolysis (study from Purghart; 2002). See also comment 4(21) Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
4(17)	Vol. 3, point B.8.4.2, Aqueous photolysis g) Purghart (2001), acceptation of study relies on method of calculation of photolysis half-life	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the environmental fate rebuttal dated 16 June 2003. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) The notifier presented modifications due to a wrong molar absorption. The results are in line with the results of RMS. The results will be confirmed in the DAR.	IIA 7.2.1.2 Open point 4.12 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding a statement on aqueous photolysis (study from Purghart; 2001). See also comment 4(21)

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

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4(17)	*continued* Vol. 3, point B.8.4.2, Aqueous photolysis g) Purghart (2001), acceptation of study relies on method of calculation of photolysis half-life			Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
4(18)	Vol. 3, point B.8.4.5.1 Summary of Clodinafop-propargyl, Photolysis, information concerning the studies on quantum yield.	**Syngenta**: The DAR includes comments by the RMS which Syngenta believe have been addressed in the environmental fate rebuttal dated 16 June 2003. If the RMS agrees with this comment then please insert a statement to the DAR confirming this.	ii) The notifier presented modifications due to a wrong molar absorption. The results are in line with the results of RMS. The results will be confirmed in the DAR.	IIA 7.2.1.2 Open point 4.13 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding a statement on photolysis, information concerning the studies on quantum yield. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.

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

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
4(19)	Vol 3. B.8.4.2 Photolytic degradation in water. Keller A, 1990c.	**EFSA:** Photoproducts U-6.1 max. 33.2 %, U-7.2 max. 25.9 %, U-8.3 max. 24.4 % and U-5.2 max. 12.9 % should be characterized and identified.	ii) The notifier gave an adequate reaction including 2 studies (Anderson 2002 and 2003) on this point of the DAR. The result is that the new studies are fully acceptable and the Keller study is not fully acceptable so this paragraph will be amended.	IIA 7.2.1.2 Open point 4.14 Evaluation meeting to discuss the need for an amendment of DAR or an addendum regarding 'photolytic degradation in water' (Keller, 1990c) to include and statement on the acceptability of this study. Evaluation Meeting (25.05.2004): RMS to revise the draft assessment report. Open point still open.
4(20)	Vol 3. B.8.4.2 Photolytic degradation in water. Anderson W. 2003b.	**EFSA:** CGA-193468 may need to be considered a relevant phoproduct in water.	ii) PEC sw values for risk assessment are provided in the DAR	Addressed.

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

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4(21)	Vol 3. B.8.4.2 Photolytic degradation in water. Phaff, R. 1995a, Purghart V. 2002, Purghart, 2001.	**EFSA:** The RMS requires several data or further information for the acceptation of these studies. However, no specific data requirement appears in Vol 4. Please clarify.	ii) The notifier gave adequate reactions to all point mentioned in the DAR. The result is that all points are addressed and no data requirements are required. See also 4(15), 4(16) and 4(17).	See open points 4.10, 4.11 and 4.12.

5. Ecotoxicology

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
5(1)	Vol. 3, B.9	**EFSA:** Preferably studies should be summarized in a more extensive way indicating e.g. temperature, pH, oxygen content, observations made etc. (see e.g. B.9.2). This summary should preferably be presented in a structural way and not in a descriptive way. The acceptability of a study should always be clearly stated.	ii) This general comment will be kept in mind for future monographs.	-
5(2)	Vol. 3, B.9.1.5.1	**EFSA:** Why were not the FIR/bw values from the SANCO/4145/2000 document used in the risk assessment.	ii) The risk assessment is based on the guidance in the draft version of SANCO/4145/2000 of February 2001. It is questionable if the guidance of the final version of SANCO/4145/2000 is compulsory as the dossier was declared complete before this document was accepted in October 2002.	Open point 5.1: EFSA proposes that the RMS makes a risk assessment for birds and mammals available according to SANCO/4145/2000 final (September 2002) in an addendum using the present data available. See also comments 5(3), 5(6), 5(7) and 5(9). Evaluation Meeting (25.05.2004):

section 5 – Ecotoxicology (B.9)

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
5(2)	*continued* Vol. 3, B.9.1.5.1			RMS to provide an addendum to the draft assessment report. Open point needs to be discussed in an expert meeting. Open point still open.
5(3)	Vol. 3, B.9.1.5.1	**EFSA:** A risk assessment for an insectivorous bird is considered necessary.	ii) Based on the draft version of SANCO/4145/2000 of February 2001 the risk assessment can be restricted to a medium sized herbivorous bird for early cereals. See also 5(2).	See open point 5.1 Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point needs to be discussed in an expert meeting. Open point still open.
5(4)	Vol. 3, B.9.1.5.1, Table B.9.38	**EFSA:** on which studies were the LogPow values of the metabolites	ii) These values were calculated.	Open point 5.2: RMS to make LogPow

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
5(4)	*continued* Vol. 3, B.9.1.5.1, Table B.9.38	based.		calculations available in an addendum. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
5(5)	Vol. 3, B.9.1.6	**EFSA:** Preferably the endpoints for mammals are mentioned in a tabular format at the start of the risk assessment, indicating the observations on which the endpoints are based and the references to the studies.	ii) This general comment will be kept in mind for future monographs.	-
5(6)	Vol. 3, B.9.1.6.1	**EFSA:** FIR/bw values from the SANCO/4145/2000 document should be taken into account as these lead to a higher ETE estimation.	ii) The risk assessment is based on draft version of SANCO/4145/2000 of February 2001. It is questionable if the guidance of the final version of SANCO/4145/2000 is compulsory as the dossier was declared complete before this document was accepted in October 2002.	See open point 5.1 Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report.

section 5 – Ecotoxicology (B.9)

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
5(6)	*continued* Vol. 3, B.9.1.6.1			Open point needs to be discussed in an expert meeting. Open point still open.
5(7)	Vol. 3, B.9.1.6.1	**EFSA:** A risk assessment for an insectivorous mammal is considered necessary.	ii) Based on the draft version of SANCO/4145/2000 of February 2001 the risk assessment can be restricted to a herbivorous mammals for early cereals. See also 5(6).	See open point 5.1 Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point needs to be discussed in an expert meeting. Open point still open.
5(8)	Vol. 3, B.9.1.6.1	**EFSA:** The refinement of the long term risk assessment should preferably be established with quantified refinement factors based on available studies as e.g. measured residues.	ii) The comment is not clear as the long term risk was refined with a DT50 <1d based on measured residues and leading to a TER_{lt} >13.	Open point 5.3: RMS to make the refinement of the risk assessment for mammals more transparent (e.g. indicating refined f_{twa} values

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
5(8)	*continued* Vol. 3, B.9.1.6.1			used) in an addendum. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
5(9)	Vol. 3, B.9.1.6.1	**EFSA:** Risk assessment for earthworm eating mammals should be based on a 10 g mammal eating 14 g fresh material per day instead of 11 g fresh material per day. Similarly the risk assessment for a fish eating mammals should be based on a 3000 g mammal eating 390 g fresh fish per day instead of 346 g fresh fish per day (see SANCO/4145/2000).	ii) The risk assessment is based on draft version of SANCO/4145/2000 of February 2001. It is questionable if the guidance of the final version of SANCO/4145/2000 is compulsory as the dossier was declared complete before this document was accepted in October 2002.	See open point 5.1 Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point needs to be discussed in an expert meeting. Open point still open.

section 5 – Ecotoxicology (B.9)

No.	Column 1 Data point based on draft assessment report or comments from MS	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (i) Co-rapporteur, and (ii) Rapporteur	Column 4 Data requirement or Open Point (if data point not addressed or fulfilled) (Annex point)
5(10)	Vol. 3, B.9.1.6.2	**EFSA:** The available acute toxicity study with the preparation (see section B.6.11) should be taken into account.	ii) This is correct. If necessary the end point from the study with the formulation will be taken into account in a revision of the DAR.	IIA 8.1 IIIA 7.1 Open point 5.4 RMS to provide addendum with a risk assessment for mammals taking into account the endpoint from the acute toxicity study with the preparation. Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
5(11)	Vol. 1, List of Endpoints, toxicity data for aquatic species	**EFSA:** The acute LC_{50} for fish is subject to the condition that the applicant provides acceptable information on the method of analysis of the test substance in test media. Was this information received and can the study be regarded as acceptable?	ii) RMS received the document for method of analysis. Based on the delivered document design of the analytical method plus validation criteria, recovery and repeatability are considered appropriate and the study results were considered acceptable. The DAR will be revised based on the additional information.	IIA 8.2 Open point 5.5 RMS to include additional information on the method of analysis regarding the toxicity to fish in an addendum. Evaluation Meeting (25.05.2004): RMS to provide an

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5(11)	*continued* Vol. 1, List of Endpoints, toxicity data for aquatic species			addendum to the draft assessment report. Open point still open.
5(12)	Vol. 3, Table B.9.21	**EFSA:** Why was the claimed limit solubility in the test by Rufli H. (1988a) only 2.5 mg/L?	ii) The value of 2.5 mg/L is the claimed limit of solubility in the study report. One can expect a lower solubility at 20°C compared to the solubility of 4,0 mg/L at 25°C mentioned in the list of end points. Based on our evaluation criteria the study could have been classified as unreliable since test concentrations are up to more than 10 times the solubility. This strict approach was not used since based on the results for the lower test concentrations a conservative EC_{50}/NOEC can be derived. Results for the test concentrations above water solubility are considered not reliable for deriving the end point as homogeneity of the test media was not tested and therefore not proven. Syngenta accepted our position.	Addressed.

section 5 – Ecotoxicology (B.9)

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5(13)	Vol. 3, point B.9.2.3.1.3 Effects on sediment dwelling organisms (IIA 8.2.7) The study is classified as unreliable since stock solutions were used with a concentration far above solubility.	**Syngenta**: For this dossier, we agree with the conclusion to use a NOEC of 2.5 and an EC50 > 2.5 mg/L based on the solubility limit in water. However Syngenta would like to change the 2nd comment stated in paragraph B.9.2.3.1.3. to 'this study must be seen as acceptable with the previous restriction as described in the CTB's response (NOEC = 2.5, EC50 > 2.5 mg/L)'. Furthermore, this statement will now be in line with the conclusions of paragraph 9.2.3.3.3 (effects on metabolites).	ii) The value of 2.5 mg/L is the claimed limit of solubility in the study report. One can expect a lower solubility at 20°C compared to the solubility of 4.0 mg/L at 25°C mentioned in the list of end points. Based on our evaluation criteria the study could have been classified as unreliable since test concentrations are up to more than 10 times the solubility. This strict approach was not used since based on the results for the lower test concentrations a conservative EC_{50}/NOEC can be derived. Results for the test concentrations above water solubility are considered not reliable for deriving the end point as homogeneity of the test media was not tested and therefore not proven. Syngenta accepted our position.	Open point 5.6: RMS to clarify if the study can be regarded as acceptable or not given the comment made by the notifier. Evaluation Meeting (25.05.2004): The RMS states that the study is now acceptable. The Meeting agrees on that this point needs to be discussed in an expert meeting. Open point still open.

section 5 – Ecotoxicology (B.9)

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5(14)	Vol. 3, Table B.9.28	**EFSA:** It is noted that the representative formulation was not tested on aquatic plants but instead a study with another formulation is available. The aquatic plant species tested differs from the species tested with the active substance. Although no argumentation on the comparability of both formulations or testing of different species is given.	ii) Both the tested formulation and the representative formulation are EC formulations. If necessary, an argumentation on the comparability of the formulations and the tested species will be added to the DAR.	IIIA 10.2.1 Open point 5.7 RMS to include in an addendum a statement on the comparability of the formulations and the tested species (aquatic plants). Evaluation Meeting (25.05.2004): RMS to provide an addendum to the draft assessment report. Open point still open.
5(15)	Vol. 3, B.9.4, p. 507	**EFSA:** At the top of p 507 it is stated that the study on bees with the active substance is acceptable. At the bottom of the same page it is stated that this study is not acceptable as no toxic standard was included in the test design. The second statement should be followed and accordingly the acute oral LD50 for bees of >93.7 µg as/bee has to be deleted from the list of endpoints.	(ii) These are indeed contradictionary statements in the DAR. For reasons of consistancy we propose to consider the study with the active substance as acceptable. As stated in the DAR separate toxic standards were not performed at the time of the study. Such older studies have been accepted for other active substances. Nevertheless, preference can be given to the more recent study with the formulation in the risk	IIA 8.3.1 Open point 5.8 Acceptability of the acute bee toxicity study to be discussed in an expert meeting. See also comment 5(16) Evaluation Meeting (25.05.2004):

section 5 – Ecotoxicology (B.9)

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5(15)	*continued* Vol. 3, B.9.4, p. 507		assessment as this study included possible effects of co-formulants and the safener (see also data point 5.17).	Open point needs to be discussed in an expert meeting. Open point still open.
5(16)	Vol. 3, point B.9.4.2.1 Bees, acute risk of the active substance	**Syngenta**: Proposal: delete 3rd sentence: "The study performed with …. using a toxic standard.". Comment: this sentence no longer in line with the new statement of acceptability of this acute bee study (see conclusions of B9.4.1.1).	(ii) Agreed, see 5(15).	See open point 5.8 Evaluation Meeting (25.05.2004): Open point needs to be discussed in an expert meeting. Open point still open.
5(17)	Vol. 3, point B.9.5.3.2 Bees, risk assessment of the safener	Syngenta**: Add the following sentence: "However the toxicity studies conducted on TOPIK 100 EC take also into account the potential toxicity of the safener'.**	(ii) We support this suggestion, see 5(15).	Addressed RMS to consider in a revision of the DAR.
5(18)	Vol. 3, B.9.8	**EFSA:** A study with the major soil metabolite CGA 193469 is considered necessary as the concentration of CGA 193469 was not analytically verified during the study with the	ii) We do not consider a separate study with metabolite CGA 193469 necessary as all available studies show that clodinafop is (nearly) quantitatively converted to CGA	Open point 5.9: The need for further studies on soil non-target micro-organisms with the metabolites CGA 193469

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5(18)	*continued* Vol. 3, B.9.8	parent. Additionally a second study with a duration exceeding 28 days with the metabolite CGA 302371 is considered necessary as more than 25% effect was seen on the nitrate formation after 28 days.	193469 in natural soils. Although not verified it is highly unlikely that such a complete conversion to CGA 193469 was not the case in the study with the parent. ii) With regard to CGA 302371 additional information was supplied by Syngenta and the DAR states: “The pattern of nitrate formation during the study was plotted in a graph. Between day 0 and day 7 denitrification took place in treatments as well as in the control. Nitrate formation in the treatments was lower compared to the control between day 7 and 14 but higher compared to the control between day 14 and 28. Given this pattern there is enough confidence that the difference between treatments and control will be less than 25% after 100 days.” Based on this argumentation further data are not considered necessary.	and CGA 302371 to be discussed in an expert meeting. Evaluation Meeting (25.05.2004): Open point needs to be discussed in an expert meeting. RMS to provide an addendum to the draft assessment report with regard to CGA 193469. Open point still open.