PEER REVIEW REPORT ON **PROQUINAZID** 29 09 2009

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1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

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	Section 1 Open points: ***7*** Points for clarification: ***0*** Data requirement: ***4***			Section 1 Open points: ***0*** Points for clarification: ***0*** Data requirement: ***1***
	Open point: 0.1 RMS should consider to use the current harmonised version of the list of end points. See reporting table 0(1)	**DuPont:** We have no comment to add regarding the format of the list of end points.	The endpoints are updated in the current harmonised format with the exception of the fate & behaviour which will be revised immediately after the expert meeting. RMS (27 May 2009) LOEP updated	PRAPeR 66 (21 – 24 April 2009): Open point still open: RMS to update the LoEP according to the agreed template Written procedure: Open point fulfilled LoEP was updated
	Open point: 1.1 The new specification and supporting data in the addendum to Vol 4 should be considered by a meeting of experts. See reporting table 1(1)	**DuPont:** Documentation supporting the revised specification of proquinazid based on the analysis of commercially produced technical material has been submitted to the RMS. This data was evaluated by the RMS and their conclusions are reported in the Addendum to Volume 4 of the proquinazid DAR. DuPont are in agreement with the conclusions of the RMS.	RMS agrees that the revised specification taking into account "full scale" production should be considered in a PRAPeR expert meeting. The evaluation is presented in the most recent revised Annex C to the DAR dated March 2009. This Addendum to the confidential volume replaces in its entirety the original Annex C and the earlier Addendum to Volume C, dated December 2007. The revised Annex C is made available in the confidential area of CIRCA. RMS (27 May 2009) RMS will clarify with applicant	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled New data requirement: Applicant to provide justification for the limits of certain impurities and the minimum purity or a revised specification

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	New data requirement 1.5: Applicant to provide justification for the limits of certain impurities and the minimum purity or a revised specification			PRAPeR 66 (21 – 24 April 2009): Data requirement open Written procedure: Data requirement still open Applicant to provide justification for the limits of certain impurities and the minimum purity or a revised specification
	Open point: 1.2 The suppliers and purity of all starting materials are missing. The rapporteur stated that the information was included in the addendum but this was not the case. See reporting table 1(4)	**DuPont:** Report DuPont-21127: Technical grade proquinazid (DPX-KQ926): Manufacturing description and formation of impurities – EU submission, Hartzell, S. (2007) which was submitted with the documents supporting the notification of the commercial production site for proquinazid contains details of the supplies and specifications of all starting materials.	This information was omitted from the addendum in error. It is now included in the revised Annex C to the DAR dated March 2009. This Addendum to the confidential volume replaces in its entirety the original Annex C and the earlier Addendum to Volume C, dated December 2007. The revised Annex C is made available in the confidential area of CIRCA.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled
	Data requirement 1.1: How was the identity of the impurities confirmed. See reporting table 1(10)	**DuPont:** The principle technique for the analysis of commercially produced proquinazid samples is high performance liquid chromatography (HPLC) with ultraviolet visible (UV) diode array detection (DAD). [redacted]	The additional information provided has been considered and is evaluated in the revised Annex C to the DAR dated March 2009. This Addendum to the confidential volume replaces in its entirety the original Annex C and the earlier Addendum to Volume C, dated December 2007. The revised Annex C is made available in the confidential area of CIRCA.	PRAPeR 66 (21 – 24 April 2009): Data requirement closed

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		[redacted] HPLC/UV DAD spectral data are presented to confirm the identities of the active and registered impurities for a commercially produced proquinazid sample in the following report: DuPont-19009 Supplement No. 1, Revision No. 1 The identity of the impurities was further confirmed using HPLC/MS spectral data: DuPont-19009 Supplement No. 2		
	Data requirement 1.2: The boiling point and temperature of decomposition needs to be addressed. See reporting table 1(21)	**DuPont**: The boiling point and temperature of decomposition were assessed by Differential Scanning Calorimetry. A sharp exotherm, due to decomposition, was observed with a mean peak temperature of 367.63°C. A boiling point was not observed due to the decomposition of proquinazid. DuPont-23153	A new study has been submitted by the Notifier. This has been evaluated and presented in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR. The RMS agrees with the information presented by the Notifier in Column B of this evaluation table.	PRAPeR 66 (21 – 24 April 2009): Data requirement closed
	Data requirement 1.3: Applicant to address the absence of a temperature/time curve in	**DuPont:** The report has been revised to include a temperature/time curve in Appendix 1.	The information has now been provided by the Notifier in a revised study report.	PRAPeR 66 (21 – 24 April 2009): Data requirement closed

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	the Gravell 1997 study auto-flammability. See reporting table 1(29)	AMR 4223-96 RV 1		
	Open point: 1.3 Please state the concentration at which the surface tension was determined. It has been stated that this has been done in the end points however, this is not the case. See reporting table 1(31)	**DuPont:** The surface tension was determined at a concentration of 1 g/L (DuPont-12183 – submitted with original dossier)	The RMS apologises for omitting this information– the LOEP have now been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled
	Data requirement 1.4: Two year shelf-life study. See reporting table 1(38)	**DuPont:** The 2 year storage stability study is reported in DuPont-12184 and DuPont-12186. The formulation was found to be stable when stored for 2 years at ambient conditions in both HDPE/EVOH and PET containers.	New studies have been submitted by the Notifier. These have been evaluated and presented in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.	PRAPeR 66 (21 – 24 April 2009): Data requirement closed
	Open point: 1.4 The GAP should be clarified. Given the comment from the applicant. See reporting table 1(43)	**DuPont:** In the DAR the minimum application rate for Italy and Germany is cited as 40 g a.s./ha and the minimum application rate for Greece is cited as 25 g a.s./ha. These rates equate to the maximum rate that could be applied at the first application based on the bird and mammal risk evaluation. On the basis of the proposed use rate of a 5 g/hL dilution applied at a volume of 300 – 1500	A revised GAP table has been provided by the Notifier and the changes are highlighted in the list of endpoints. The only changes to the rates are to the minimum rate of a.s./ha. There is no impact on the risk assessment.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled

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		L/ha for Greece and Italy and at 400 – 1500 L/ha for Germany the minimum rate that could be applied based on the minimum spray volume at the first application timing is 15 g a.s./ha in Greece and Italy and 20 g a.s./ha in Germany. A revised GAP table is provided		
	Open point: 1.5 The method for plants should be considered by a meeting of experts. The full validation data is on the GC-ECD, ILV with a reduced data set is with GC-MS and the ILV is also the confirmatory method. See reporting table 1(45)	**DuPont:** The GC-ECD and the GC-MS methods involve the same sample extraction and cleanup. Additionally, chromatographic analyses both use GC. The only difference is the use of different detectors, i.e., ECD and MSD (MSD is more selective and is appropriate for quantification when interference is present). The GC-ECD data satisfied validation requirement, thus, should be considered. GC-MS validation data for wheat and barley straw (dry), grain (oily), and immature plant (watery) generated from MOR studies DuPont-5857 and DuPont-5858 (previously submitted) will be used as additional data. These data proved further that the GC-MSD method is suitable as an enforcement method.	The RMS believes that although the validation data available is not considered complete in line with current guidance the weight of evidence indicates that the method is suitable for use as an enforcement method.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled
	Open point: 1.6 The analytical method for milk should be considered by a meeting of experts given	**DuPont:** Results of animal metabolism studies indicated that no MRL is necessary for proquinazid in food of animal origin and no MRL was	As the Notifier has already stated a method for products of animal origin is not required as no MRLs are required and no residues definition has been	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled New open point:

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	the poor recoveries. The egg method should also be considered given the high RSD. See reporting table 1(47)	proposed. (Furthermore based on the levels of proquinazid in animal feed items there is no expectation of significant intake of proquinazid by livestock.) Therefore an enforcement method is not necessary	proposed. RMS (27 May 2009) LOEP updated	RMS to amend list of endpoints to give the matrices covered by the residue method
	New open point 1.7: RMS to amend list of endpoints to give the matrices covered by the residue method			PRAPeR 66 (21 – 24 April 2009): Open point open Written procedure: Open point fulfilled LoEP updated
	New open point 1.8: RMS to amend the list of end points according to the discussions during thef PRAPeR 66 meeting.			PRAPeR 66 (21 – 24 April 2009): Open point open Written procedure: Open point fulfilled LoEP updated
	Message from section 1 to sections 2 and 5: Please consider the new specification given in Addendum 2 to Annex C (March 2009) The definitive specification is that given in Table C 1.1 (it should be mentioned that Section 1 set a new data requirement to be provide justification for the limits of certain impurities and the minimum purity or a revised			PRAPeR 69 (4 – 8 May 2009): Answer from section 2 to section 1: Message noted and discussed by experts. See Addendum to Annex C (Table C.1.8) for full details. PRAPeR 68 (4 – 8 May 2009): Answer from section 5 to section 1: Message noted, action will be taken if necessary when the specification is

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	specification)			confirmed
	Message from section 3 to section 1: An analytical method for monitoring will be necessary if MRLs in food of animal origin according to the proposed residue definition for monitoring (sum of proquinazid and metabolites IN-MU210 expressed as proquinazid) will be set.			Written procedure: If MRLs in food of animal origin according to the proposed residue definition for monitoring (sum of proquinazid and metabolites IN-MU210 expressed as proquinazid) will be set a data gap for an analytical method for monitoring will have to be set

2. Mammalian toxicology

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	Section 2 Open points: ***4*** Points for clarification: ***0*** Data requirements: ***0***			Section 2 Open points: ***0*** Points for clarification: ***0*** Data requirements: ***0***
	Open point: 2.1 MSs to agree on the relevant NOAEL of the 1-year dog study, taking into account the occurrence of ocular discharge and its toxicological relevance. See reporting table 2(2)	**DuPont:** The applicant proposed a NOAEL of 15 mg/kg/day for males and 60 mg/kg/day for females, based on body weight losses and/or reductions in body weight gains at higher doses. The increased incidence in ocular discharge in females at 15 mg/kg bw/day is not considered to be an adverse effect because it was only a slight increase compared with the highest control incidence at the time of dosing and with no evidence for the effect lasting through to the next day. A NOAEL of 15 mg/kg bw/day is proposed based on effects seen on reduced body weight gain in males at 60 mg/kg bw/day. DuPont agrees with the NL comment, that a value of <15 mg/kg bw/day is too conservative, although as already mentioned, this NOAEL does not affect risk assessment.	**Toxicological relevance of ocular discharge in dogs** There was a substance-related increase in the incidence of ocular discharge in both the one-year dog study (capsule dosing) and in the 90-day dog study (dietary administration). For ease of reference, ocular discharge findings, and associated commentary, from the DAR are reproduced on p 17 et seq of Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR. In the DAR the RMS concludes that: “as ocular discharge in dogs was most frequent at the time of test substance administration (dietary or capsule) it suggests that ocular discharge was principally due to direct (non systemic) ocular contact with the test substance at the time of	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. In the 1 year dog study the NOAEL in males is 15 mg/kg bw/d (based on reduced body weight gain). In females the 15 mg/kg bw/d is considered to be a LOAEL based on increased incidence of ocular discharge.

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			dosing. However systemic exposure of the eye to the test substance/metabolites may have contributed to the ocular irritation seen at other times." **Since the cause of this consistent and frequent finding in dogs exposed to proquinazid is unclear, and there was some evidence for ocular discharge in rodents at high doses, a precautionary approach is justified when considering the relevance of ocular discharge in dogs for human risk assessment.** **NOAELs in 1-year dog study** **Males**: RMS proposes same value for the NOAEL as the applicant, ie 15 mg/kg bw/d based on reduced body weight gain at 60 mg/kg bw/d (see DAR). **Females**: RMS agrees that the NOAEL of < 15 mg/kg bw/d proposed in the DAR is conservative. This proposal was made following advice from the UK ACP members	

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			who were concerned about the ocular discharge in females at 15 mg/kg bw/d. Prior to obtaining ACP advice the RMS had considered the increased incidence in ocular discharge in females at 15 mg/kg bw/d to be not an adverse effect because it was only a slight increase compared with the highest control incidence at the time of dosing and with no evidence for the effect lasting through to the next day (ie based on data for clinical examination before dosing). **To conclude: The RMS can agree to a NOAEL of 15 mg/kg bw/day for females (based on increased ocular discharge at 60 mg/kg bw/d) if this is the view of the PRAPeR meeting toxicology experts (but does not support raising the NOAEL for females to 60 mg/kg bw/d as proposed by the applicant)**.	
	Open point: 2.2 MSs to discuss the ARfD value. See reporting table 2(8)	**DuPont:** Regardless of whether the ARfD is set at 0.2 or 0.3 mg/kg bw the short term dietary exposure based on the NESTI is <<100% indicating that proquinazid when used according to the proposed GAP does not represent an acute dietary risk to sensitive	In the DAR the RMS proposed an ARfD of 0.2 mg/kg bw based on ocular discharge in one dog at the time of first exposure to 19 mg/kg bw in the 90-day study (full copy of ARfD proposal section from DAR is at page 25 of Addendum 2, dated March 2009,	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. ARfD = 0.2 mg/kg bw

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		population groups.	to Annex B (Volume 3) of the DAR. DAR table B.6,33a which shows first occurrence of ocular discharge for each dog in the 90 day study is reproduced at page 20 of Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.) In the reporting table, **DE** proposed an ARfD of 0.3 mg/kg bw based maternal toxicity seen over the first 2 days of dosing at 60 mg/kg bw/d in the developmental rat study (see full **DE** comments reproduced on page of Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR). **RMS acknowledges the concerns expressed by DE, and can accept the DE proposal for an ARfD of 0.3 mg/kg bw because 0.2 mg/kg bw may be too conservative (precautionary), see the Addendum. However the views of other members of the PRAPeR toxicology meeting are welcomed.**	
	Open point: 2.3 MSs to discuss dermal absorption of proquinazid representative formulation.	**DuPont:** We accept the RMS interpretation of the dermal penetration studies presented in the DAR and agree with the proposed penetration values of 2% (concentrate) and 12% (dilution).	Dermal absorption of proquinazid from Proquinazid 200 g/L EC (lead product) was investigated *in vitro* using rat and human skin and *in vivo* in the rat. Tests were conducted with the undiluted formulation and with a 1.3	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled Dermal absorption:

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	See reporting table 2(9)		g/L aqueous dilution. The tested dilution was however not as dilute as the proposed in-use spray dilutions (0.05-0.5g/l). **RMS proposed dermal absorption values of 2% (concentrate) and 12% (dilution).** These proposals were calculated from values determined in the *in vivo* rat study, with adjustment for relative absorption through rat and human skin *in vitro.* In the *in vivo* study with a 6 h exposure there considerable delayed absorption. The RMS therefore considered the percentage of dose absorbed by rats *in vivo* relevant to operator risk assessment to be the amount absorbed over the first 24h (amount in tissues, excluding dosed skin, and excreta) plus the amount excreted over the next 24h (excretion was maximal over the first 48h). The rat: human adjustment factor was based on the difference in the percentage absorption calculated *in vitro* for rat and human skin (and took account of radiolabel in tape strips of the stratum corneum). **DE** considered (see reporting table)	2% for the concentrate 12% for the dilution

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			that worst-case assumptions based on the outcome of *in vivo* and *in vitro* studies should be used. At least, these assumptions should cover the absorbable dose in the *in vitro* study with human skin. **Therefore 3% (concentrate) and 15% (dilution) were suggested** (ie the amount in receptor fluid plus tape stripped human skin at the end of the 6h exposure). RMS notes some uncertainties in the dermal absorption data provided (e.g. dilution tested was not as dilute as the intended in-use dilutions). However, the RMS approach is considered to be sufficiently precautionary. RMS does not support the DE proposal because the data clearly show that for rat skin the absorbable dose of proquinazid was much greater when determined *in vitro* than when determined *in vivo*. Hence it would seem likely that the absorbable dose of proquinazid through human skin *in vitro* would over estimate absorption through human skin *in vivo*. **To conclude, RMS still considers dermal absorption values of 2% (concentrate) and 12% to be**	

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			appropriate for use in the risk assessment of Proquinazid 200 g/L EC. To aid discussion at PRAPeR some information/comments additional to those in the DAR are presented in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.	
	Open point: 2.4 MSs to agree on the input parameters and models to calculate operator, worker and bystander exposure. See reporting table 2(11)	**DuPont:** The operator exposure assessment presented by DuPont and the RMS both demonstrate that potential exposure for the supported uses is below the AOEL in all scenarios using the German model thus demonstrating safety for operators when using proquinazid according to the proposed GAP. DuPont agrees with the proposed refinements to the UK POEM modelling that have been proposed by the RMS in the DAR and considers that acceptable exposure of operators, bystanders and workers has been demonstrated for proquinazid.	RMS: Data from the EUROPOEM database was used to estimate/refine the exposure estimates for application of proquinazid to grapevines only for the UK POEM estimates. These data were used to provide a more realistic estimate of exposure for this use. Justification for this approach is given in the DAR, Vol 3, Section B. 6. 14. 1. 2, Estimation of Operator Exposure – UK POEM. Levels of systemic exposure for the supported uses are below the AOEL in all scenarios using the German model. On this basis, acceptable exposure of operators, bystanders and workers have been demonstrated for proquinazid.	PRAPeR 69 (4 – 8 May 2009): Open point closed.
	Message from section 1 to			PRAPeR 69 (4 – 8 May 2009):

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	section 2: Please consider the new specification given in Addendum 2 to Annex C (March 2009) The definitive specification is that given in Table C 1.1 (it should be mentioned that Section 1 set a new data requirement to be provide justification for the limits of certain impurities and the minimum purity or a revised specification)			Answer from section 2 to section 1: Message noted and discussed by experts. See Addendum to Annex C (Table C.1.8) for full details.

3. Residues

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	Section 3 Open points: ***5*** Points for clarification: ***0*** Data requirement: ***2***			Section 3 Open points: ***1*** Points for clarification: ***0*** Data requirement: ***0***
	Open point: 3.1 In the grape metabolism study the lignin fraction was only postulated and this should be considered by a meeting of experts. See reporting table 3(4)	**DuPont:** Unextractable grape fruit residues (~32-36%TRR) were subjected to mild (sequential enzyme, mild base and mild acid) and strong (refluxing acid and base) digestion. Mild conditions released ~4% of the unextractable radioactivity. Most of the unextractable radioactivity (~23%TRR from Day 14 sample) was released under stronger alkaline conditions. The precipitate which formed upon acidification was characterized as lignin. Results on unextractable residues in the grape study were correlated with similar results from a proquinazid apple metabolism study (DuPont-4313). Unextractable residues in the apple study were submitted to similar tests (*as above*) giving base soluble residues which formed a precipitate (21-42% TRR) upon acidification. Incorporation of ^{14}C-proquinazid unextractable residues into apple lignin was confirmed by isolation of lignin fractions using dioxane/water	From the study report for the grape metabolism study it can be seen that the Notifier has made reasonable attempts to extract additional radioactivity from the un-extractable residues using acid and base hydrolysis. The Notifier has addressed the concern that the precipitate formed on acidification of the basic extract was only postulated to be lignin by reference to an apple metabolism study. In this study additional work was conducted using published methodology to identify if the un-extracted radioactivity was bound to lignin and concludes that the radioactivity was confirmed as lignin. This apple metabolism study was not originally submitted to the RMS however has since been made available.	PRAPeR 70 (4 – 8 May 2009): Open point fulfilled. New open point (see below): RMS to evaluate the apple metabolism study or to compare the investigation of the lignin fraction in the grape study with the procedure described in literature (Bjorkman).

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		(Bjorkman procedure) and dioxane/acid. Approximately 33% TRR was released and characterized as lignin using literature procedures.		
	New open point 3.6 identified during PRAPeR 70 meeting: RMS to evaluate the apple metabolism study or to compare the investigation of the lignin fraction in the grape study with the procedure described in literature (Bjorkman).			PRAPeR 70 (4 – 8 May 2009): Open point open RMS (27 May 2009) To be completed and submitted to EFSA by end June 2009. RMS (27 July 2009) Evaluation and conclusion provided in Addendum 3 to Annex B (Volume 3) of the DAR, dated July 2009 Written procedure Open point fulfilled Björkman procedure to investigate lignin fraction in apples reported and compared with grape study Note: any other information in apple metabolism study not peer reviewed
	Data requirement 3.1: In the goat metabolism study it should be clarified what the intake was on a feed dry matter basis. Once this is clarified the study should be reconsidered.	**DuPont:** The goat was dosed at 91.5 mg/kg diet. The daily dose (118.5 mg) was administered *via* capsule and the feed, consisting of a commercial lab diet and alfalfa cubes and hay, was provided *ad libitum*. The moisture content of the feed was not determined and dietary intake	It appears from the additional information provided by the Notifier that the dose rate was on a diet *dry matter* basis. This will affect the level of exaggeration at which the studies were conducted, however not by a significant amount. Using the dietary burden calculated in the DAR (Table	PRAPeR 70 (4 – 8 May 2009): Data requirement fulfilled.

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	See reporting table 3(7)	calculations were not corrected for dry matter content (90% for the Rumilab® feed and 89% for alfalfa meal and hay), consistent with typical experimental practices and regulatory guidance in effect at the time of study conduct (1996). The study was conducted at an exaggerated rate (~200 times the anticipated daily dietary burden to cattle) allowing for exposure to and metabolism of both proquinazid and its primary metabolites. Most of the administered dose (*ca.* 63%) was excreted. Radioactivity associated with all edible tissues, milk, and blood accounted for <1% of the dose indicating that there is no potential for bioaccumulation of proquinazid or its metabolites. Adjustments for feed dry matter content would not impact the overall study outcome and should not necessitate study reconsideration.	B.7.39) the worst case dietary burden is for beef cattle and = 0.5174 mg/kg diet (dry matter). The metabolism study was conducted at a rate of 91.5 mg/kg diet which equates to ca 175 N. In the DAR the exaggeration was stated to be *ca* 200N. Although there is a difference in the level of exaggeration the overall conclusions reached in the DAR about the study remain the same and therefore no reconsideration is needed. RMS believes that the data requirement is addressed.	
	Data requirement 3.2: In the hen metabolism study it should be clarified what the intake was on a feed dry matter basis. Once this is clarified the study should be reconsidered.	**DuPont:** Hens were dosed at 15.6 mg/kg diet. The daily dose (1.95 mg) was administered *via* capsule and the feed, consisting of a commercial lab diet, was provided *ad libitum*. The moisture content of the feed was not determined and ddietary intake calculations were not corrected for dry	It appears from the additional information provided by the Notifier that the dose rate was on a diet *dry matter* basis. This will affect the level of exaggeration at which the studies were conducted, however not by a significant amount. Using the dietary burden calculated in the DAR (Table	PRAPeR 70 (4 – 8 May 2009): Data requirement fulfilled.

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	See reporting table 3(8)	matter content, consistent with typical experimental practices and regulatory guidance in effect at the time of study conduct (1996). The study was conducted at an exaggerated rate (~400 N times the anticipated daily dietary burden to hens) allowing for exposure to and metabolism of both proquinazid and its primary metabolites. Most of the administered dose (*ca.* 88%) was excreted. Radioactivity associated with all edible tissues, eggs, and blood accounted for ≤1% of the dose indicating no potential for bioaccumulation of proquinazid or its metabolites. Adjustments for feed dry matter content would not impact the overall study outcome and should not necessitate study reconsideration.	B.7.39) the dietary burden for poultry = 0.0468mg/kg diet (dry matter). The metabolism study was conducted at a rate of 15.6 mg/kg diet which equates to ca 330 N. In the DAR the exaggeration was stated to be *ca* 400N. Although there is a difference in the level of exaggeration the overall conclusions reached in the DAR about the study remain the same and therefore no reconsideration is needed. RMS believes that the data requirement is addressed.	
	Open point: 3.2 It should be considered by a meeting of experts if there is a need for any further data on residues in poultry given that the compound is fat soluble and may accumulate. See reporting table 3(9)	**DuPont**: DuPont concurs with RMS' assessment that additional poultry residue data are not required. Discussions on fat soluble residues are not directly applicable to proquinazid. Residue trial data indicate levels of proquinazid and its principal cereal metabolite (IN-MW977) were generally less than the LOQ (0.02 mg/kg) in poultry feed (wheat, barley, rye, oats and triticale grain); below the EU trigger for	Estimated poultry intakes are below the relevant trigger value that leads to the requirement for a metabolism study. The metabolism study shows that significant residues in animal products are unlikely. Even if residues were likely to accumulate in the fat, it is considered unlikely that accumulation would lead to detectable residues in products of animal origin based on the exaggerated dose rate data provided.	PRAPeR 70 (4 – 8 May 2009): Open point fulfilled. On the basis of the notified uses the study is not triggered. If hen metabolism study is necessary for future uses, the study should be carefully reassessed.

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		needing to conduct a poultry metabolism study. In addition, the poultry study was conducted at an exaggerated rate (400N) and detectible residues are unlikely in poultry commodities.		
	Open point: 3.3 It should be considered by a meeting of experts if it is necessary to set a residue definition for ruminants. If it is necessary then it should be considered if the available data are sufficient for risk assessment purposes. See reporting table 3(11)	**DuPont:** Minimal transfer of ^{14}C-proquinazid equivalent residues to milk, eggs, and edible tissues was observed in livestock metabolism studies conducted at exaggerated dose levels (900-2200 times the anticipated daily dietary burden to beef and dairy cattle and about 1900 times the anticipated daily dietary burden to poultry). No significant terminal residues are anticipated in milk, eggs, or meat, and no residue definition is required.	When residues are not expected to be found in animal products based on an animal metabolism study, we do not consider it is necessary to set a residue definition for animal products (even if the mg/kg diet intake trigger is exceeded). The metabolism study gives an indication of potential for residues based on experimental observation whereas the intake value highlights a theoretical estimate of exposure. The RMS agrees with the notifier that no residue definition is required.	PRAPeR 70 (4 – 8 May 2009): Open point fulfilled. Residue definitions for animal matrices have been proposed: For risk assessment: sum of proquinazid and metabolites IN-MU210 and IN-MW977 expressed as proquinazid For monitoring: sum of proquinazid and metabolites IN-MU210 expressed as proquinazid
	Message from section 3 to section 1: An analytical method for monitoring will be necessary if MRLs in food of animal origin according to the proposed residue definition for monitoring (sum of proquinazid and metabolites IN-MU210 expressed as proquinazid) will be set.			

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	Open point: 3.4 The GAP should be clarified. Given the comment from the applicant. See reporting table 3(13)	**DuPont:** In the DAR the minimum application rate for Italy and Germany is cited as 40 g a.s./ha and the minimum application rate for Greece is cited as 25 g a.s./ha. These rates equate to the maximum rate that could be applied at the first application based on the bird and mammal risk evaluation. On the basis of the proposed use rate of a 5 g/hL dilution applied at a volume of 300 – 1500 L/ha for Greece and Italy and at 400 – 1500 L/ha for Germany the minimum rate that could be applied, based on the minimum spray volume at the first application timing is 15 g a.s./ha in Greece and Italy and 20 g a.s./ha in Germany. A revised GAP table is provided	The Notifier has provided a revised GAP table for clarification. The revisions relate to the use on grapes only and reflect the difference in application rate per ha that can arise due to the use of different water volumes. The only changes to the rates are to the minimum rate of a.s./ha therefore as the residues trials were conducted at the worst case highest dose rate/ha the revision to the GAP has no impact on the residues assessment provided in the DAR. The RMS considered this point addressed.	PRAPeR 70 (4 – 8 May 2009): Open point fulfilled. Changed GAP has no impact on residue assessment
	Open point: 3.5 If the tox reference values are changed a revised risk assessment will be required. See reporting table 3(19)	**DuPont:** The short term dietary risk assessment was conducted by the RMS on the basis of an ARfD of 0.2 mg/kg and demonstrated an acceptable margin of safety. If the ARfD were to be change to 0.3 mg/kg then there would be no adverse effect on the risk assessment.	We note that if the ARfD were to change to the higher value then the risk assessment presented in the DAR would be a worst case and agree that if the tox reference values are changed that the risk assessment will need to be revisited, however we believe it would be wise to wait until the peer reviewed tox end points are available to avoid further revisions after the toxicological meeting of	PRAPeR 70 (4 – 8 May 2009): Open point fulfilled. No change in tox reference values

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			experts have concluded. The LOEP will be revised after the meeting of experts to take into account any changes to the reference values.	
	New open point 3.7 identified during PRAPeR 70 meeting: Method validation data (method used in grape residue trials) to be reported by RMS in an addendum			PRAPeR 70 (4 – 8 May 2009): Open point open RMS (27 May 2009) To be completed and submitted to EFSA by end June 2009. RMS (27 July 2009) Reported in Addendum 3 to Annex B (Volume 3) of the DAR, dated July 2009. Written procedure Open point fulfilled
	New open point 3.8 identified during PRAPeR 70 meeting: RMS to calculate the actual N rate on the basis of the residues in soil and re-evaluate on this basis the rotational crop study.			PRAPeR 70 (4 – 8 May 2009): Open point open RMS (27 May 2009) To be completed and submitted to EFSA by end June 2009. RMS (27 July 2009) Calculation provided in Addendum 3 to Annex B (Volume 3) of the DAR, dated July 2009. Written procedure Open point still open Re-assessment of rotational crop study

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				not peer reviewed
	New open point 3.9: LoEP to be updated in accordance with the decisions of the meeting.			PRAPeR 70 (4 – 8 May 2009): Open point open RMS (27 May 2009) LOEP updated – any necessary further amendments following consideration of open points will also be conducted by end June 2009. Written procedure Open point fulfilled

4. Environmental fate and behaviour

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group
	Section 4 Open points: ***6*** Points for clarification: ***0*** Data requirement: ***1***			Section 4 Open points: ***0*** Points for clarification: ***0*** Data requirement: ***0***
	Open point: 4.1 MS to discuss in a meeting of experts the selection of laboratory soil DT50 values of proquinazid and its metabolites to be considered in the risk assessment. See reporting table 4(2)	**DuPont:** DuPont agrees with the RMS in that it is reasonable to normalise DT_{50} values from 10°C to 20°C for metabolite IN-MM671, and that the change in DT_{50} values from the RMS-calculated value of 54 days to the EFSA-calculated value of 58 days is small and would not alter the regulatory decision since all groundwater modelling concentrations are <0.001 µg/L.	**RMS:** See reporting table point 4(2). For parent proquinazid the RMS considers it appropriate to normalise the soil DT50 from 10 °C to 20 °C as though the Nambsheim soils have the same name they are distinctly different in their properties. For the metabolites the RMS agreed that the process was not appropriate as the same soil was used in the same study (i.e. the soil properties were the same). However, it was noted that the DT50 values are similar and that PECgw values for the metabolite in question are all<0.001 µg/l indicating that changing the DT50 values is unlikely to alter the risk assessment and therefore the regulatory decision. The RMS proposes that it is unnecessary to recalculate PEC values.	PRAPeR 66 (21 – 24 April 2009): Note to RMS to include the selected soil DT50 values in the updated LoEP. Open point closed. RMS (27 May 2009) LOEP updated Written procedure Open point closed
	Open point: 4.2	**DuPont:** The explanation provided by	**RMS:** The explanation has been	PRAPeR 66 (21 – 24 April 2009):

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	RMS to provide in an addendum clarifications on the results on material balance and concentration of proquinazid and degradates (Tables B.824 and B.8.25) obtained in the field dissipation study by Dean and Fisher (1999). See reporting table 4(12)	the RMS is correct. The results reported in Table B.8.24 are total radioactivity (TRR) in the soil horizons for each replicate plot reported as the concentration equivalent to proquinazid. TRR was determined by combustion of the homogenized soil sample. Table B.8.25 reports the mean concentration of proquinazid and three metabolites in the two replicate plots following extraction of the soil and analysis of the extract by HPLC. Unidentified metabolites and unextractable residues were not reported in Table B.8.25. For the 0 DAT data point presented by EFSA as an example, the appropriate comparison is between the mean TRR from Table B.8.24 (0.22+0.18/2=0.2) and the sum of residues for 0 DAT in Table B.8.25 plus unextractable residues (0.03 mg/kg), an unidentified metabolite (<0.01 mg/kg), and unresolved radioactivity reported as “Other” (0.01 mg/kg). Using the convention that results less than the detection limit may be represented by one-half the detection limit in the calculation, the sum of the components, (0.125+0.01+ 0.005+0.02+0.005+0.01+0.03 = 0.205 mg/kg) is equal to the TRR (0.2 mg/kg), a 100% recovery considering	added to Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR. In addition Table B.8.25 has been updated by the RMS by adding in results for unextracted radioactivity. This is now reported as Table B.8.25b in the addendum. The RMS considers the open point is closed.	Open point closed

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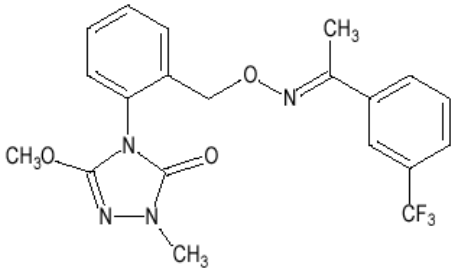
		the approximation of the quantities below the detection limit and rounding to a single significant figure for all amounts except proquinazid.		
	Data requirement 4.1: Applicant to provide information on the identity of DPX-KZ165 co-formulated with proquinazid in the field dissipation studies (Zietz et al., 2003a; Zietz et al., 2003b) and soil residue studies. See reporting table 4(13)	**DuPont:** The test substance was a commercial formulation containing proquinazid (4.6%) and DPX-KZ165 (4.7%). Development of DPX-KZ165 was halted in 1999. IUPAC name and structure of DPX-KZ165: (E)-3-Methoxy-1-methyl-4-{2-[1-(3-trifluoro-methylphenyl) ethylideneaminooxymethyl]pheny} -1H-1,2,4-triazol-5(4H)-one 	**RMS:** The data requirement is fulfilled	PRAPeR 66 (21 – 24 April 2009): Data requirement fulfilled.
	Open point: 4.3 MS to discuss in a meeting of experts the suitability of the use of soil DT50field of 54 days in PECsoil calculations for metabolite	**DuPont:** IN-MM991 was detected in significant concentrations in only one of 8 field dissipation studies and accounted for about 7% of the applied radioactivity in a laboratory study. We agree with the RMS that the	**RMS:** The RMS's previous comments made in the reporting table at 4(20) still apply and are reproduced below: RMS: comment relates to IN-MM991. This must be taken in the context of the overall low observed formation for	PRAPeR 66 (21 – 24 April 2009): Open point closed. New open point: RMS to derive the DT50 field for the Evesham soil and add it to the LoEP including fitting statistics if fitting

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	IN-MM991. See reporting table 4(20)	occurrence of IN-MM991 in the field will be low. The field DT_{50} of 54 days is within the range of the DT_{50}s reported in laboratory studies and is greater than 2X the shortest lab DT_{50}. Revising the DT_{50} used for PEC_{soil} calculations will have no effect on the conclusions of the risk assessment.	this metabolite in the field. The maximum level reached in field studies was 7.4% (based on peak concentrations of parent and metabolite)and thus we conclude that under field conditions that there will be a relatively low occurrence. In conclusion the RMS agrees with the Applicant's argumentation. There is no impact on the conclusion reached in the risk assessment.	is appropriate. To delete the currently presented TWA PECsoil values for IN-MM991 because these are based on a DT50 value of 54 days which may be not the highest DT50 value. RMS (27 May 2009) LOEP updated Written procedure Open point closed
	New open point: 4.7: RMS to derive the DT50 field for the Evesham soil and add it to the LoEP including fitting statistics if fitting is appropriate. To delete the currently presented TWA PECsoil values for IN-MM991 because these are based on a DT50 value of 54 days which may be not the highest DT50 value.			PRAPeR 66 (21 – 24 April 2009): Open point open. Written procedure Open point closed
	Open point: 4.4 MS to discuss in a meeting of experts the appropriate DT50 values of soil metabolites of proquinazid for FOCUS GW and SW modelling.	**DuPont**: DuPont agrees with the RMS in the approach of using lab DT_{50} values for the metabolite over field values, and that using metabolite degradation data from studies where the metabolites were used as the starting material was a reasonable approach.	**RMS:** See reporting table 4(26) and section B.8.5.1.1 of volume 3 of the DAR for RMS comments. The RMS's previous comments made in the reporting table at 4(26) still apply and are reproduced below (see also section B.8.5.1.1 of Volume 3 of the DAR)	PRAPeR 66 (21 – 24 April 2009): Open point closed

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	See reporting table 4(26)		RMS: an explanation for use of laboratory derived degradation DT50 values rather than use of field derived dissipation rates is made in section B.8.5.1.1 of Volume 3 of the DAR. Slow dissipation of metabolite IN-MM671 is probably linked to slow formation in the field. It was also considered that using metabolite degradation data from studies where the metabolites had been used as the starting material was a reasonable approach. This is because this approach removes some uncertainty generated due to the correlation which occurs between metabolite formation and degradation parameters calculated from studies on active substances.	
	Open point: 4.5 RMS to provide in an addendum the explanation on the selection of the DT50whole system for metabolite IN-MM671 used in FOCUS SW calculation. See reporting table 4(30)	**DuPont:** DuPont agrees with the RMS in that there is no impact of using DT_{50} values of both 497 and 1000 days on initial PEC values for Steps 1 & 2.	**RMS:** The explanation provided in the reporting table 4(30) has been added to Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR. The RMS considers the Open point is closed.	PRAPeR 66 (21 – 24 April 2009): Open point closed.
	Open point: 4.6 RMS to amend the list or references of studies	**DuPont:** DuPont agrees that the RMS will check and amend the references as necessary.	**RMS:** The RMS considers that the studies of Huber, A., 2003, DuPont 13553 and DuPont 13554 should not be included in the list of studies relied	PRAPeR 66 (21 – 24 April 2009): Open point closed.

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	including the studies Huber, A. 2003. See reporting table 4(36)		on. The list of references relied upon has been updated to reflect this change. The RMS considers the Open point is closed.	
	New open point 4.7: RMS to amend the list of end points according to the discussions during the PRAPeR 67 meeting.			PRAPeR 66 (21 – 24 April 2009): Open point open Written procedure Open point closed

5. Ecotoxicology

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	Section 5 Open points: ***14*** Points for clarification: ***0*** Data requirements: ***0***			Section 5 Open points: ***0*** Points for clarification: ***0*** Data requirements: ***0***
	Open Point: 5.1 The use of a time window of 14 days instead 21 days in the estimation of the factor time weighted average (f_{twa}) used to estimated the TERlt for birds and mammals should be discussed in a PRAPeR experts meeting. See reporting table 5(4)	**DuPont:** The current SANCO guidance (Section 3.5 of SANCO/4145/2000) states that, although residues may be under-estimated when the interval is shorter than the time window, „with a time window of 3 weeks and a DT_{50} of 10 days [as assumed in the first tier risk assessment] the inaccuracy is small and the [twa] factor of 0.53 can be used uncorrected', therefore we consider that the use of a 21day time window is justified for the long term risk assessment for proquinazid.	RMS: Our conclusion of the reporting table still stands (below): We agree that given the 14 day application interval it would be logical to use a 14 day twa when estimating foliar residues. However, the current SANCO guidance (Section 3.5 of SANCO/4145/2000) states that, although residues may be under-estimated when the interval is shorter than the time window, „with a time window of 3 weeks and a DT50 of 10 days [as assumed in the first tier risk assessment] the inaccuracy is small and the [twa] factor of 0.53 can be used uncorrected'.	PRAPeR 68 (4 – 8 May 2009): Open point closed.
	Open point: 5.2 MS to discuss in a PRAPeR expert meeting the relevant species proposed by the applicant to refined the long-term risk identified for the insectivorous birds in vines. See reporting table 5(6)	**DuPont:** The species proposed for refinement of the long term risk assessment to insectivorous birds in vines were derived from the results of an extensive literature survey conducted by RIFCON (2005) in which 105 reports published between 1963 and 2004 were evaluated for information relevant to species occurrence and feeding patterns in	RMS: The paper is summarised and considered in Addednum 2 to Volume 3 (Annex B) of the DAR dated March 2009. It is the view of the RMS that although the paper potentially shows that the diets of Yellowhammer and Stonechat are broadly similar. However we consider the information is not	PRAPeR 68 (4 – 8 May 2009): Open point closed.

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		different crops. Information on the Stonechat diet can be found in a recent publication by Revaz, E., *et al*. 2008 on the "Foraging ecology and reproductive biology of the Stonechat *Saxicola torquata*: comparison between a revitalized, intensively cultivated and a historical, traditionally cultivated agro-ecosystem"(J. Ornithology, Vol. 149, pages 301-312). The diet was found to consist of 30 – 32% Orthoptera, 27-36% Lepidoptera (primarily caterpillars) and 12 – 23% Coleoptera which is comparable with the dietary intake values used in the refined risk assessment presented for proquinazid. If the indicator species used in the risk assessment are not considered representative for certain member states than we propose this should be addressed at the Member State level when considering product reauthorisation.	conclusive and we re-iterate our previous opinion that if the indicator species used in the risk assessment are not considered to be representative for certain Member States, then this issue should be considered at product re-registration as a Member State issue.	
	Open point: 5.3 RMS to correct the acute TERs in the list of endpoints and include the following TER values: SHM in cereals 391.8, IM in cereals 10989, SHM in vine 396 values in to	**DuPont**: No comment – action for RMS to amend end point list	RMS: Corrected end points as stated in reporting table. Other changes pending outcome of PRAPeR discussion.	PRAPeR 68 (4 – 8 May 2009): Open point closed.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group
	include in an Addendum. See reporting table 5(11)			
	Open point: 5.4 The TERlt for small herbivorous mammals should be update, pending of the outcome of the discussion in the open point 5(4). EFSA noted that if f_{twa} = 0.64 will be used, then long-term TERs values were 10.35 for small herbivorous mammals (SHM) in cereals, and **3.9** for SHM in vine following 4 x 75 g a.s./ha. This means that the trigger of 5 is not met in vine with the higher application rate and a refined assessment is needed. If 4x50 g a.s./ha is applied a TER of 5.86 will be the result. The TERlt for insectivorous birds should be 217.8 in cereals. RMS to include the agreed long-term TERs values in an	**DuPont:** We agree with the statement already provided by the RMS in the reporting table (point 5(12)):	RMS: No additional comment pending outcome of discussion in open point 5(4).	PRAPeR 68 (4 – 8 May 2009): Open point closed.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group
	Addendum and to amend the LoEP. See reporting table 5(12)			
	Open point: 5.5 RMS to include the summaries of the alga studies with the proquinazid in an Addendum. See reporting table 5(17)	**DuPont:** New algae studies were conducted with technical proquinazid (DuPont-21531) and Proquinazid 200 g/L EC (DuPont-21739) to address concerns regarding the validity of the original studies raised at the National level by Germany. The results of these new studies are comparable with the results from the studies submitted with the Proquinazid dossier. Proquinazid technical: DuPont-21531: EC_{50} > 0.12 mg a.s./L (highest rate tested) AMR 4168-96, Revision No. 1: EC_{50} 0.615 mg a.s./L (area under growth curve) Proquinazid 200 g/L EC: DuPont-21739: Cell density EC_{50} – 1.3 mg/L Growth rate EC_{50} – 2.5 mg/L Area under curve EC_{50} – 1.4 mg/L DuPont-11234: Cell density EC_{50} – 1.3 mg/L Growth rate EC_{50} – 3.3 mg/L Area under curve EC_{50} – 1.2 mg/L	RMS: Summaries of the two submitted algal studies are included in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR. Both were conducted to OECD 201 and in accordance with the principles of GLP. The studies met their validity criteria and are suitable for the risk assessment.	PRAPeR 68 (4 – 8 May 2009): Open point closed.

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		Based on the maximum FOCUS Step-2 PEC value for proquinazid applied in vines of 1.98 µg a.s./L all TER values are > the Annex VI trigger of 10.		
	Open point: 5.6 Even taking into account that the classification should not change of R51, RMS should correct the text to clarify that most sensitive specie was being the green algae *Pseudokirchneriella subcapitata* with a formulation acute toxicity 72h EbC50 of 1.3 mg product /l instead the *Daphnia magna*. See reporting table 5(18)	**DuPont:** We agree with the proposed correction and note that the aquatic toxicity classification is not changed.	RMS: The corrected classification text is provided in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.	PRAPeR 68 (4 – 8 May 2009): Open point closed.
	Open point: 5.7 RMS should correct the wrong references in an Addendum/Corrigendum. See reporting table 5(19)	**DuPont**: No comment, requirement for RMS to correct references	RMS: The corrected references are provided in a revised section 9.2.55 in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.	PRAPeR 68 (4 – 8 May 2009): Open point closed.
	Open point: 5.8 RMS should include the reference in an Addendum/Corrigendum.	**DuPont**: No comment, requirement for RMS to include reference	RMS: The reference is provided in a revised first paragraph to Section 9.2.5.3 of Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.	PRAPeR 68 (4 – 8 May 2009): Open point closed.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group
	See reporting table 5(20)			
	Open Point: 5.9 MS to discuss the proposal from the EFSA to include all relevant FOCUS Step 3 and Step 4 scenarios but only for the most sensitive organism, which drives the RA, in the list of endpoints. See reporting table 5(23)	**DuPont:** The proposal from EFSA appears to be useful to show the complete risk assessment for the most sensitive species. This could be added to the current evaluation based on the maximum PEC values from all FOCUS scenarios and all test organisms failing at lower steps.	RMS: No additional comment.	PRAPeR 68 (4 – 8 May 2009): Open point closed.
	Open point: 5.10 RMS should correct the wrong authors name f the reference included in Table B.9.62 in an Addendum/Corrigendum. See reporting table 5(24)	**DuPont**: No comment, typographical error to be rectified	RMS: The typographical error is corrected in a revised section 9.4.1.1 in Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.	PRAPeR 68 (4 – 8 May 2009): Open point closed.
	Open point: 5.11 The relevance of the significant increase in pest mites in the formulated in the German field study should be discussed by the MS. See reporting table 5(29)	**DuPont:** We agree with the statement already provided by the RMS in the reporting table (point 5(29)). In addition no significant effects from proquinazid treatment occurred in the German field study on predatory spider mite numbers (mites or eggs) and there were no statistically significant effects from proquinazid on either predatory mite or pest mite numbers in the other two similar field	RMS: No additional comment.	PRAPeR 68 (4 – 8 May 2009): Open point closed.

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		studies. In the German field study the pest mite numbers were already 1.4-times higher in the proqinazid treatment compared to the control and toxic reference treatment. Much higher and significant increases in pest mite populations occurred following use of the toxic reference. In the German field study *Typhlodromus pyri* was the dominant predatory mite species (> 99%), which is known not to depend on the availability of pest mites as food source (pollen is a sufficient food source for this species). The overall field evidence therefore indicates that proquinazid treatment is not likely to result in significant adverse effects on predatory mites.		
	Open point: 5.12 The chronic endpoint for earthworms exposed to the metabolite IN-MM671 should be discussed in a PRAPeR meeting. See reporting table 5(31)	**DuPont:** We agree with the statement already provided by the RMS in the reporting table (point 5(31)). In addition although the mean adult body weight increased in all groups, yet it was extremely variable. There were no statistically significant differences in body weight between the treatments and the control. Also, there was no clear trend that might suggest a treatment related effect. In terms of reproductive performance, although	RMS: No additional comment.	PRAPeR 68 (4 – 8 May 2009): Open point closed.

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		the number of juveniles per treatment was highly variable between groups, there were no statistically significant differences between the treatments and the control. Also, there was no clear trend that might suggest a treatment related effect.		
	Open point: 5.13 MS to discuss in a PRAPeR expert meeting the validity and representativness of the post-emergence tier 1 test for non-target plants. See reporting table 5(34)	**DuPont:** Although the study was not conducted to GLP the study is considered to be scientifically valid and included treatment of six test species (3 dicotyledons and 3 monocotyledons) at the highest proposed application rate of 75 g a.s./ha.	RMS: No additional comment.	PRAPeR 68 (4 – 8 May 2009): Open point closed.
	Open point: 5.14 MS to discuss in an expert meeting the need of further information (studies) to assess the effects of proquinazid to non-target plants. See reporting table 5(35)	**DuPont:** Proquinazid 200 g/L EC can be applied twice to cereals. The first application should be made preventatively, from the 5-leaf stage (BBCH 25), before disease has become established in the crop. A second application can be made up to mid flowering (BBCH 65) in wheat and up to before first spikelet of inflorescence is visible (BBCH 49) in barley, rye, triticale and oats. On grape, 4 applications of Proquinazid 200 g/L EC can be made at a 14-day minimum interval. Proquinazid 200 g/L EC will be used from the 3-leaf growth stage till, at the	RMS: The Notifier's case is reasonable in that application is made in spring when many crops will have already emerged but it is possible that some non-target plants may still be emerging. In the absence of a pre-emergence test we suggest a label warning phrase may be appropriate.	PRAPeR 68 (4 – 8 May 2009): Open point closed.

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		latest, around one month before harvest. Based on the proposed application timings for Proquinazid 200 g/L EC in cereals and grapes it is unlikely that pre-emergence exposure of crops in neighbouring fields will occur as at the time proquinazid is used most crops will have emerged. In addition to the non-target plant study provided in the Proquinazid Dossier further information from greenhouse screening and field development trials has been included in the Biological Dossier submitted to Member States. This information is summarised here. Greenhouse studies done in 1995, to address the activity of the parent compound as a weed control agent and in general the impact on other plants including adjacent crops, showed that, Proquinazid 200 g/L EC applied at rates as high as 2 kg/ha either pre- or post-emergence has no herbicidal activity on monocotyledonous and dicotyledonous weeds. It is very safe when applied to apple, cucumber, rice and tomato seedlings grown under greenhouse conditions. While the primary objective of these tests was to		

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		evaluate disease control, phytotoxicity measurements were made in parallel. The tests were conducted between 1993 and 1998 at the DuPont Stine-Haskell Research Center (Delaware, USA) using small plants sprayed to run-off with the fungicide. Proquinazid 200 g/L EC was applied at rates up to 500 mg/L or 100 g/ha active substance. Considering the fact that greenhouse-grown crops are generally more sensitive than field grown plants, this data suggests proquinazid has a high margin of crop safety. In addition specific field trials have been conducted in Europe between 1996 and 2003 to assess the effect of Proquinazid 200 g/L EC on crops likely to be found in the neighbourhood of a vineyard. Proquinazid 200 g/L EC was applied to tomatoes (1 trial), apples (8 trials), peaches (1 trial), potato (1 trial), peas (2 trials), sugarbeet (8 trials) and scarole (1trial). Proquinazid 200 g/L EC was applied at rates ranging from 20 g a.s. /ha to 200 g a.s. /ha depending on the crop. No phytotoxicity as a result of the application of Proquinazid 200 g/L EC was recorded in any of the above		

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		mentioned crops. Considering the fact that the dose of product drifting from a vineyard would be significantly less than that applied to the vines, we conclude that the risk of damage to neighbouring crops is negligible.		
	Message from section 1 to section 5: Please consider the new specification given in Addendum 2 to Annex C (March 2009) The definitive specification is that given in Table C 1.1 (it should be mentioned that Section 1 set a new data requirement to be provide justification for the limits of certain impurities and the minimum purity or a revised specification)			PRAPeR 68 (4 – 8 May 2009): Answer from section 5 to section 1: Message noted, action will be taken if necessary when the specification is confirmed