

TABLE OF CONTENTS

| | Document | File Name |
|-----------|--|------------------------------------|
| 00 | Cover page | 00 proquinazid cover |
| 01 | All comments received on the DAR | 01 proquinazid all comments |
| 02 | Reporting table all sections | 02 proquinazid rep table rev 1-1 |
| 03 | All reports from PRAPeR Expert Meetings | 03 proquinazid all reports. |
| 04 | Evaluation table | 04 proquinazid eval table rev 2-1 |

List of all reports from PRAPeR Expert Meetings

| Date | | Section |
|---------------|--|----------------------------------|
| 21-24.04.2009 | PRAPeR expert meeting 66 | Physical and Chemical Properties |
| 20-24.04.2009 | PRAPeR expert meeting 67 | Environmental Fate and Behaviour |
| 04-08.05.2009 | PRAPeR expert meeting 68 | Ecotoxicology |
| 04-08.05.2009 | PRAPeR expert meeting 69 | Mammalian Toxicology |
| 05-08.05.2009 | PRAPeR expert meeting 70 | Residues |

REPORT OF PRAPeR EXPERT MEETING 66

PROQUINAZID

Rapporteur Member State: UK

Specific comments on the active substance in the section

1. Physical and Chemical Properties

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---------------|----------|---|
| March 2009 | UK | Proquinazid addendum Vol4 (March 2009).doc |
| March 2009 | UK | Proquinazid addendum 2 Vol3 B2-B6-B8-B9 (March 2009).doc |
| December 2007 | UK | Proquinazid addendum1 Vol3 B5 (December 2007).doc |
| 2009-03-13 | UK | Proquinazid evaluation table rev1-0 (2009-03-13) |
| March 2009 | UK | Proquinazid list of endpoints (March 2009).doc |
| March 2009 | UK | Proquinazid List of references relied on (March 2009).doc |
| 2008-10-31 | UK | Proquinazid reporting table rev1-1 (2008-10-31).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

The conclusions of the meeting were as follows:

- Data on preparations:** Proquinazid 200 g/L EC
- Classification and labelling:** not discussed
- Recommended restrictions/conditions for use:** none
- Reference list:** Not discussed

Areas of concern: no specification

Appendix 1: Discussion table: PROQUINAZID

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Proquinazid (Fu)

1. Physical and Chemical Properties

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|--|--|
| | <p>Open point: 0.1 RMS should consider using the current harmonised version of the list of end points.</p> <p>See reporting table 0(1)</p> | <p>Loep partially updated</p> | <p>Open point still open: RMS to update the LoEP according to the agreed template</p> |
| | <p>Open point: 1.1 The new specification and supporting data in the addendum to Vol 4 should be considered by a meeting of experts.</p> <p>See reporting table 1(1)</p> | <p>The new specification was discussed and the meeting could not come to a conclusion on the maximum limits of three impurities [REDACTED] given justification was not acceptable for some experts. The minimum purity was also questioned by some experts. New data requirement: Applicant to provide a revised specification or a justification concerning the maximum limits of the above mentioned impurities and the minimum purity.</p> <p>Message to tox and ecotox: consider the new specification given in Addendum 2 to Annex C (March 2009) The definitive specification is that given in Table C 1.1 (do not use specifications given elsewhere in the Addendum)</p> | <p>Open point fulfilled New data requirement: Applicant to be provide justification for the limits of certain impurities and the minimum purity or a revised specification</p> |
| | <p>New data requirement 1.5: Applicant to provide justification for the limits of certain impurities and the minimum purity or a revised specification</p> | | <p>Data requirement open</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|--------------------------------|
| | <p>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.</p> <p>See reporting table 1(4)</p> | <p>Information is now included in the Addendum to Vol 4</p> | <p>Open point fulfilled</p> |
| | <p>Data requirement 1.1: How was the identity of the impurities confirmed.</p> <p>See reporting table 1(10)</p> | <p>Information is now included in the Addendum to Vol 4 and agreed by the experts</p> | <p>Data requirement closed</p> |
| | <p>Data requirement 1.2: The boiling point and temperature of decomposition needs to be addressed.</p> <p>See reporting table 1(21)</p> | <p>Information provided and included in Vol 3 and accepted by the meeting</p> | <p>Data requirement closed</p> |
| | <p>Data requirement 1.3: Applicant to address the absence of a temperature/time curve in the Gravell 1997 study auto-flammability.</p> | <p>Revised report provided by applicant and accepted by the meeting</p> | <p>Data requirement closed</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|----------------------------|
| | See reporting table 1(29) | | |
| | <p>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.</p> <p>See reporting table 1(31)</p> | It was concluded that the determination was done at the saturation concentration | Open point fulfilled |
| | <p>Data requirement 1.4: Two year shelf-life study.</p> <p>See reporting table 1(38)</p> | Information provided and summarized in Addendum to Vol 3. The studies were accepted by the meeting. | Data requirement closed |
| | <p>Open point: 1.4 The GAP should be clarified. Given the comment from the applicant.</p> <p>See reporting table 1(43)</p> | The company provided a revised table and the list of endpoints has been updated | Open point fulfilled |
| | <p>Open point: 1.5 The method for plants should be considered by a meeting of experts. The full</p> | An addendum 1 to Annex B Dec 2007 was prepared. The validation data on GC-ECD and GC-MS were accepted by the meeting. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|---|
| | <p>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.</p> <p>See reporting table 1(45)</p> | | |
| | <p>Open point: 1.6 The analytical method for milk should be considered by a meeting of experts given the poor recoveries. The egg method should also be considered given the high RSD.</p> <p>See reporting table 1(47)</p> | <p>The analytical methods for determination of residues of proquinazid in milk and egg were discussed by the meeting. It concluded that the methods were not acceptable and it should be noted in the list of end points.</p> | <p>Open point fulfilled New open point: RMS to amend list of endpoints to give the matrices covered by the residue method</p> |
| | <p>New open point 1.7: RMS to amend list of endpoints to give the matrices covered by the residue method</p> | | <p>Open point open</p> |
| | <p>List of endpoints</p> | <p>Minimum purity is open Water solubility: „filtered seawater’ should be removed Purity should be given for the water solubility Surface tension: delete 1g/L and replace by “saturated” Table of representative uses: Name of preparation is “Talendo” and “Talius” Title of GAP table: insert name of active substance Remove USD sign in the PHI column</p> | <p>Open point: The end points should be amended in accordance with the report of PRAPeR 66.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|--|----------------------------|
| | | <p>Box of analytical methods for residues: residue definitions for soil, water and air should be given</p> <p>Animal products: the covered matrices should be stated</p> <p>Henry's law constant units are given twice</p> <p>Body fluid and tissue box: "or very toxic" should be added</p> | |
| | <p>New open point 1.8: RMS to amend the list of end points according to the discussions during the PRAPeR 66 meeting.</p> | | <p>Open point open</p> |
| | <p>Message to tox and ecotox</p> <p>Please consider the new specification given in Addendum 2 to Annex C (March 2009)</p> <p>The definitive specification is that given in Table C 1.1 (it should be mentioned that Section 1 set a new data gap to be provide justification for the limits of certain impurities and the minimum purity or a revised specification)</p> | | |

Appendix 2: Evaluation table

0. General

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|---|--|---|---|
| | Section 0 Open points: 1 Points for clarification: 0 Data requirements: 0 | | | Section 0 Open points: 1 Points for clarification: 0 Data requirements: 0 |
| | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point still open: RMS to update the LoEP according to the agreed template |

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

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|---|--|--|--|
| | Section 1 Open points: 6 Points for clarification: 0 Data requirement: 4 | | | Section 1 Open points: 2 Points for clarification: 0 Data requirement: 1 |
| | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point fulfilled New data requirement: Applicant to provide justification for the limits of certain impurities and the minimum purity or a revised specification |
| | New data requirement 1.5: Applicant to provide justification for the limits of certain impurities and the minimum purity or a revised specification | | | <u>PRAPeR 66 (21 – 24 April 2009):</u> Data requirement open |
| | Open point: 1.2 The suppliers and purity of all starting materials are missing. The rapporteur | DuPont: Report DuPont-21127: Technical grade proquinazid (DPX-KQ926): Manufacturing description and formation of impurities – | 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 | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point fulfilled |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|--|--|--|--|
| | <p>stated that the information was included in the addendum but this was not the case.</p> <p>See reporting table 1(4)</p> | <p>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.</p> | <p>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.</p> | |
| | <p>Data requirement 1.1: How was the identity of the impurities confirmed.</p> <p>See reporting table 1(10)</p> | <p>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).</p> <p>████████████████████ ████████████████████ ████████████████████ ████████████████████ ████████████████████ ████████████████████ ████████████████████ ████████████████████ ████████████████████ ████████████████████</p> <p>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</p> | <p>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.</p> | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> Data requirement closed</p> |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|---|---|--|--|
| | | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Data requirement closed |
| | Data requirement 1.3: Applicant to address the absence of a temperature/time curve in the Gravell 1997 study auto-flammability. See reporting table 1(29) | DuPont: The report has been revised to include a temperature/time curve in Appendix 1. AMR 4223-96 RV 1 | The information has now been provided by the Notifier in a revised study report. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Data requirement closed |
| | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point fulfilled |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|--|--|--|--|
| | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> 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 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 | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point fulfilled |
| | 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. | 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 | 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point fulfilled |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|---|---|---|--|
| | See reporting table 1(45) | 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. | | |
| | Open point: 1.6 The analytical method for milk should be considered by a meeting of experts given the poor recoveries. The egg method should also be considered given the high RSD. See reporting table 1(47) | DuPont: Results of animal metabolism studies indicated that no MRL is necessary for proquinazid in food of animal origin and no MRL was 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 | 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 proposed. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point fulfilled New open point: 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 | | | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point open |
| | New open point 1.8: RMS to amend the list of end points according to the discussions during the PRAPeR 66 meeting. | | | <u>PRAPeR 66 (21 – 24 April 2009):</u> Open point open |
| | Message to tox and ecotox | | | |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|--|--|---|--|
| | 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) | | | |

REPORT OF PRAPeR EXPERT MEETING 67

PROQUINAZID

Rapporteur Member State: UK

Specific comments on the active substance in the section

4. Fate and behaviour in the environment

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|------------|----------|---|
| March 2009 | UK | Proquinazid addendum 2 Vol3 B2-B6-B8-B9 (March 2009).doc |
| 2009-03-13 | UK | Proquinazid evaluation table rev1-0 (2009-03-13) |
| March 2009 | UK | Proquinazid list of endpoints (March 2009).doc |
| March 2009 | UK | Proquinazid List of references relied on (March 2009).doc |
| 2008-10-31 | UK | Proquinazid reporting table rev1-1 (2008-10-31).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| None | | |

The conclusions of the meeting were as follows:

- 4. Data on preparations:** Proquinazid 200 g/L EC
- 5. Classification and labelling:** candidate for R53
- 6. Recommended restrictions/conditions for use:** none identified
- 7. Reference list:** Not discussed

Areas of concern: none identified

Appendix 1: Discussion table: PROQUINAZID

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Proquinazid (Fu=

4. Fate and behaviour

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|---|
| | <p>Open point: 0.1 RMS should consider to use the current harmonised version of the list of end points.</p> <p>See reporting table 0(1)</p> | <p>Noted. RMS will provide an update of the LoEP template after the meeting.</p> <p>Open point open.</p> | <p>Open point open.</p> |
| | <p>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.</p> <p>See reporting table 4(2)</p> | <p>DT50 values were normalised from 10 degrees C to 20 degrees for the Namsheim soil. There was no need for it since sufficient data are available at 20 C. Namsheim soil 10 degree study could be retained in this case for the parent since that soil sample was quite different than the Namsheim 20 degrees study.</p> <p>RMS and notifier proposal is to use the Namsheim 10 degrees study corrected to 20 degrees for the parent but not for the metabolites (since for the metabolite studies the two Namsheim soils were the same).</p> <p>Discussion if a 10 degree study back-calculated to 20 C can be used to be added to the DT50 data set at 20 C. In most cases the soil is identical to a 20 C study and therefore there is no use in doing this. In general, this approach is not encouraged, as temperature correction always adds an additional error to the endpoint.</p> <p>Note to RMS to include the selected soil DT50 values in the updated LoEP. Open point closed.</p> | <p>Note to RMS to include the selected soil DT50 values in the updated LoEP. Open point closed.</p> |
| | <p>Open point: 4.2</p> | <p>This clarification was presented in Column B of the evaluation table and in the addendum of March 2009 in text and as an additional column in table B.8.25b.</p> | <p>Open point closed.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|--|---|---|
| | <p>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).</p> <p>See reporting table 4(12)</p> | <p>Open point closed.</p> | |
| | <p>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.</p> <p>See reporting table 4(13)</p> | <p>The required information is presented in Column B of the evaluation table and the addendum (March 2009).</p> <p>Data requirement fulfilled.</p> | <p>Data requirement fulfilled.</p> |
| | <p>Open point: 4.3</p> <p>MS to discuss in a meeting of experts the suitability of the use of</p> | <p>Only one field DT50 was available for metabolite IN-MM991 from a Southern France site where it was found at less than 10 %. This site provided a best case degradation value for the parent. Question is if the value is not best-case for the metabolite as well.</p> | <p>Open point closed.</p> <p>New open point: RMS to derive the DT50 field for the Evesham soil and add it to the LoEP including fitting</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|--|--|--|
| | <p>soil DT50field of 54 days in PECsoil calculations for metabolite IN-MM991.</p> <p>See reporting table 4(20)</p> | <p>RMS states that the metabolite is not formed in the other field studies. However, the metabolite was found > 10 % (13.5 %) in Evesham field study (Table B8.26 original DAR). The Evesham field study reflects well the intended use (however exaggerated application rate at 3 times the recommended dose, 3 times applied). Therefore a DT50 calculation for this soil could also have been done. A tentative DisT50 of 260 days (decline from maximum occurrence onwards, SFO, chi2 19 %) was estimated at the meeting.</p> <p>This would then clearly be a more worst-case DT50 value. As the application frequency is > 1 this may impact the initial PECsoil calculation for this metabolite (depending on method of calculation). In this case, the PECsoil for the metabolites were calculated from the parent assuming application of the total dose at once. Hence no recalculation of the initial PEC is needed for the EU assessment.</p> <p>For PECsoil TWA values the DT50 of 54 days was used. However these were not used in the risk assessment which was based on initial PECsoil and therefore no new TWA values need to be calculated.</p> <p>The maximum normalised laboratory DT50 would be <u>51</u> days for IN-MM991 (Keyport soil, see Table B8.85 in original DAR), which is lower than the currently available DT50field value.</p> <p>NB It was decided (see Directive) that for PECsoil if <u>laboratory data</u> are to be used these should be <u>normalised</u> values.</p> <p>So from the available data the highest DT50 is 54 days from the field study at the S-France site.</p> <p>Open point closed.</p> <p>New open point: 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.</p> | <p>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.</p> |
| | <p>New open point: 4.7: RMS to derive the</p> | | <p>Open point open</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|----------------------------|
| | <p>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.</p> | | |
| | <p>Open point: 4.4</p> <p>MS to discuss in a meeting of experts the appropriate DT50 values of soil metabolites of proquinazid for FOCUS GW and SW modelling.</p> <p>See reporting table 4(26)</p> | <p>IN-MM671</p> <p>It is noted that the laboratory DT50 values for the metabolite IN-MM671 as derived from the studies dosed with parent were not included in the data set. See Table B8.51 of the original DAR.</p> <p>In some cases where parent showed non-SFO kinetics, no reliable fit for the metabolite was achieved. However reliable SFO DT50 for parent and metabolite IN-MM671 were derived (Keyport and Nambenheim soils) and therefore it is not clear why these were disregarded. The experts considered that the DT50 values for Keyport and Nambenheim dosed with parent should be included in the data set for IN-MM671 after they are normalised.</p> <p>NB the same soil names were used for studies with metabolite dosed and parent dosed, but it seems sufficiently certain that the soil properties (pH and texture) are different enough to treat all values as separate values.</p> <p>Inclusion of these values shifts the geomean DT50 to a higher value (from 44 to 75 days). In view of the high Koc probably there will be no impact on groundwater calculations. Indicate with a footnote in LoEP that 75 days should be used for future PECgroundwater calculations but that the EU assessment was based on 44 days and this was considered to be acceptable in view of the high Kfoc of 2333 L/kg (lowest value).</p> | <p>Open point closed</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---------|---|----------------------------|
| | | <p>For the field studies it is noted that they are analysed prior to FOCUS DegKin and therefore the non-normalised DT50_{field} values must be (and are) considered as dissipation values.</p> <p>Note: RMS to check consistency of pathway a/b as opposed to pathway 1/ 2 when updating the LoEP.</p> <p>Open point closed</p> <p>New open point: RMS to include the DT50 values for IN-MM671 as derived from parent dosed Nambenheim and Keyport in the overall geomean DT50 and indicate with a footnote in LoEP that 75 days should be used for future PEC_{groundwater} calculations but that the EU assessment was based on 44 days and this was considered to be acceptable in view of the high K_{foc} of 2333 L/kg (lowest value).</p> <p>DT50 water/sediment for IN-MM671 will be discussed at open point 4.5.</p> <p>IN-MM986 DT50 soil for groundwater modelling. Expert of the meeting confirm that the use of the lab geomean DT50 of 15 days is appropriate</p> <p>IN-MM991 DT50 soil for groundwater modelling. See open point 4.3 For IN-MM991 the remaining values after removal of the corrected 10 C Nambenheim study are 22, 36, and 51 days. However the value of 51 days should be excluded for PEC modelling since the fit was poor. The meeting recommended to use the worst-case value of 36 days for exposure assessment (of the two valid values of 22 and 36 days). This is not expected to change the outcome of the PEC_{groundwater} and PEC_{surface water} calculations and therefore no recalculation is needed.</p> <p>Open point closed.</p> | |

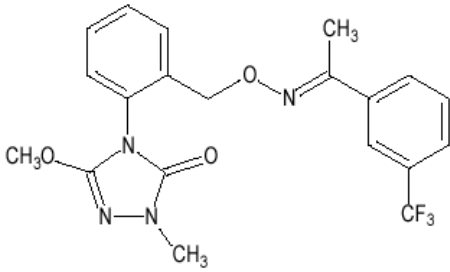
| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|--|
| | <p>Open point: 4.5</p> <p>RMS to provide in an addendum the explanation on the selection of the DT50whole system for metabolite IN-MM671 used in FOCUS SW calculation.</p> <p>See reporting table 4(30)</p> | <p>Information was provided in the addendum. It consists of a reference to the preparation of the DAR prior to FOCUS Kinetics. 300 days was chosen as default. Recalculation with the 497 days from the study (which was initially not used since the decline phase was unclear) and 1000 days did not lead to another initial PEC in STEPs 1 and 2. It did affect the TWA values but this was not critical to the aquatic risk assessment. For future calculations the default value of 1000 days is recommended in STEP 1 and 2.</p> <p>There are also STEP 3 calculations available for IN-MM671. It is not clear whether these emerge from the aquatic risk assessment. The 300 and 300 days for water and sediment should in future be replaced with 1000 and 1000 days.</p> <p>RMS to add this by a footnote to the LoEP.</p> <p>Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 4.6</p> <p>RMS to amend the list of references of studies including the studies Huber, A. 2003.</p> <p>See reporting table 4(36)</p> | <p>The study was added to the list of references relied on.</p> <p>Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Residue definition for further assessment</p> | <p>Proposal of the RMS is agreed and is as follows:</p> <p>Soil: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991</p> <p>Groundwater: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991</p> <p>Surface water: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991, IN-MM884 (aqueous photolytic metabolite)</p> <p>Sediment: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991, IN-MM884 (aqueous photolytic metabolite which might partition to sediment)</p> | <p>Open point:</p> <p>The end points should be amended in accordance with the report of PRAPeR 67.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|--|----------------------------|
| | | Air: Proquinazid | |
| | New open point 4.7: RMS to amend the list of end points according to the discussions during the PRAPeR 67 meeting. | To be updated with the discussed points above. | Open point open |

Appendix 2: Evaluation table

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> 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: 2 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 Nambenheim 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. | <u>PRAPeR 66 (21 – 24 April 2009):</u> Note to RMS to include the selected soil DT50 values in the updated LoEP. Open point closed. |
| | Open point: 4.2 RMS to provide in an | DuPont: The explanation provided by the RMS is correct. The results reported in Table B.8.24 are total | RMS: The explanation has been added to Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR. In | <u>PRAPeR 66 (21 – 24 April 2009):</u> 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 |
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| | <p>addendum clarifications on the results on material balance and concentration of proquinazid and degradates (Tables B.8.24 and B.8.25) obtained in the field dissipation study by Dean and Fisher (1999).</p> <p>See reporting table 4(12)</p> | <p>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 the approximation of the quantities below the detection limit and rounding to a single significant figure for all amounts except proquinazid.</p> | <p>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.</p> <p>The RMS considers the open point is closed.</p> | |

| 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 |
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| | <p>Data requirement 4.1:</p> <p>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.</p> <p>See reporting table 4(13)</p> | <p>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.</p> <p>IUPAC name and structure of DPX-KZ165: (E)-3-Methoxy-1-methyl-4-{2-[1-(3-trifluoro-methylphenyl)ethylideneaminoxymethyl]pheny} -1H-1,2,4-triazol-5(4H)-one</p>  | <p>RMS: The data requirement is fulfilled</p> | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> Data requirement fulfilled.</p> |
| | <p>Open point: 4.3</p> <p>MS to discuss in a meeting of experts the suitability of the use of soil DT₅₀ of 54 days in PEC_{soil} calculations for metabolite IN-MM991.</p> <p>See reporting table 4(20)</p> | <p>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 occurrence of IN-MM991 in the field will be low. The field DT₅₀ of 54 days is within the range of the DT₅₀s reported in laboratory studies and is greater than 2X the shortest lab DT₅₀. Revising the DT₅₀ used for PEC_{soil} calculations will</p> | <p>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 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</p> | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> 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 is appropriate. To delete the currently presented TWA PEC_{soil} values for IN-MM991 because these are based on a DT₅₀ value of 54 days which may be not the highest DT₅₀ value.</p> |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group |
|-----|---|--|--|--|
| | | have no effect on the conclusions of the risk assessment. | 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. | |
| | <p>New open point: 4.7:</p> <p>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.</p> | | | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> Open point open.</p> |
| | <p>Open point: 4.4</p> <p>MS to discuss in a meeting of experts the appropriate DT50 values of soil metabolites of proquinazid for FOCUS GW and SW modelling.</p> <p>See reporting table 4(26)</p> | <p>DuPont: DuPont agrees with the RMS in the approach of using lab DT₅₀ 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.</p> | <p>RMS: See reporting table 4(26) and section B.8.5.1.1 of volume 3 of the DAR for RMS comments.</p> <p>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)</p> <p>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</p> | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> Open point closed</p> |

| 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 |
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| | | | <p>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.</p> | |
| | <p>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.</p> <p>See reporting table 4(30)</p> | <p>DuPont: DuPont agrees with the RMS in that there is no impact of using DT₅₀ values of both 497 and 1000 days on initial PEC values for Steps 1 & 2.</p> | <p>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.</p> <p>The RMS considers the Open point is closed.</p> | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> Open point closed.</p> |
| | <p>Open point: 4.6 RMS to amend the list or references of studies including the studies Huber, A. 2003.</p> <p>See reporting table 4(36)</p> | <p>DuPont: DuPont agrees that the RMS will check and amend the references as necessary.</p> | <p>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 on.</p> <p>The list of references relied upon has been updated to reflect this change.</p> <p>The RMS considers the Open point is closed.</p> | <p><u>PRAPeR 66 (21 – 24 April 2009):</u> Open point closed.</p> |
| | <p>New open point 4.7:</p> | | | <p><u>PRAPeR 66 (21 – 24 April 2009):</u></p> |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group |
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| | RMS to amend the list of end points according to the discussions during the PRAPeR 67 meeting. | | | Open point open |

REPORT OF PRAPeR EXPERT MEETING 68

PROQUINAZID

Rapporteur Member State: UK

Specific comments on the active substance in the section

5. Ecotoxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|------------|----------|---|
| March 2009 | UK | Proquinazid addendum 2 Vol3 B2-B6-B8-B9 (March 2009).doc |
| 2009-03-13 | UK | Proquinazid evaluation table rev1-0 (2009-03-13) |
| March 2009 | UK | Proquinazid list of endpoints (March 2009).doc |
| March 2009 | UK | Proquinazid List of references relied on (March 2009).doc |
| 2008-10-31 | UK | Proquinazid reporting table rev1-1 (2008-10-31).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

The conclusions of the meeting were as follows:

- 4. Data on preparations:** Proquinazid 200 g/L EC
- 5. Classification and labelling:** N, R50/53
- 6. Recommended restrictions/conditions for use:** none
- 7. Reference list:** not discussed

Areas of concern: none

Appendix 1: Discussion table: PROQUINAZID

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Proquinazid (Fu)

5. Ecotoxicology

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|--|---|---|----------------------------|
| | <p>Open point: 0.1 RMS should consider to use the current harmonised version of the list of end points.</p> <p>See reporting table 0(1)</p> | <p>No action required for RMS now. Open point closed.</p> | <p>Open point closed.</p> |
| | <p>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 TER_{it} for birds and mammals should be discussed in a PRAPeR experts meeting.</p> <p>See reporting table 5(4)</p> | <p>The interval of application is 14 days. But when the default DT50 of 10 days is used, the ftwa can be calculated over 21 days according to the GD and this has been done by RMS.</p> <p>If the DT50 is in reality higher than 10 days, the risk might be underestimated. In this specific case, the TER-values will be below the trigger with ftwa over 14 days.</p> <p>However the calculations of the RMS are according to the Guidance Document. Meeting feels that the guidance should be followed and therefore agrees with the calculations by RMS. Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.2 MS to discuss in a PRAPeR expert meeting the relevant</p> | <p>Supporting information on focal species was submitted by the notifier and evaluated by RMS in the addendum. RMS considered that the information was not sufficient to change the focal species which was used in the DAR.</p> <p>The focal species should be determined at MS level.</p> | <p>Open point closed.</p> |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | <p>species proposed by the applicant to refined the long-term risk identified for the insectivorous birds in vines.</p> <p>See reporting table 5(6)</p> | <p>Meeting agrees. Open point closed.</p> | |
| | <p>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 include in an Addendum.</p> <p>See reporting table 5(11)</p> | <p>This was done. Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.4</p> <p>The TERIt for small herbivorous mammals should be update, pending of the outcome of the discussion in the open point 5(4).</p> <p>EFSA noted that if $f_{twa} = 0.64$ will be used,</p> | <p>See o.p. 5.1. Correct TERs are presented. Open point closed.</p> | <p>Open point closed.</p> |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | <p>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.</p> <p>The TER_{it} for insectivorous birds should be 217.8 in cereals.</p> <p>RMS to include the agreed long-term TERs values in an Addendum and to amend the LoEP.</p> <p>See reporting table 5(12)</p> | | |
| | <p>Open point: 5.5 RMS to include the summaries of the alga studies with the proquinazid in an Addendum.</p> | <p>This was done. The results do not have to be included in the LoE because they are >- values. Open point closed.</p> | <p>Open point closed.</p> |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | See reporting table 5(17) | | |
| | <p>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 <i>Pseudokirchneriella subcapitata</i> with a formulation acute toxicity 72h EbC50 of 1.3 mg product /l instead the <i>Daphnia magna</i>.</p> <p>See reporting table 5(18)</p> | This was done in addendum 2. Open point closed. | Open point closed. |
| | <p>Open point: 5.7 RMS should correct the wrong references in an Addendum/Corrigendum.</p> <p>See reporting table 5(19)</p> | This was done. Open point closed. | Open point closed. |
| | <p>Open point: 5.8 RMS should include the reference in an Addendum/Corrigendum</p> | This was done. Open point closed. | Open point closed. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | <p>m.</p> <p>See reporting table 5(20)</p> | | |
| | <p>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.</p> <p>See reporting table 5(23)</p> | <p>This has already been discussed at PRAPeR 63 (January 2009). Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.10 RMS should correct the wrong authors name f the reference included in Table B.9.62 in an Addendum/Corrigendum.</p> <p>See reporting table 5(24)</p> | <p>This was done. Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.11 The relevance of the significant increase in pest mites in the formulated in the</p> | <p>A significant increase of pest mites was seen in the toxic standard, which is a strange effect. RMS considers the study valid, because predatory mites and mite eggs were initially reduced both in the treatment and in the toxic standard. The increase of pest mites could have been caused by competition issues or by variation.</p> <p>Meeting agrees with RMS. Open point closed.</p> | <p>Open point closed.</p> |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | <p>German field study should be discussed by the MS.</p> <p>See reporting table 5(29)</p> | | |
| | <p>Open point: 5.12</p> <p>The chronic endpoint for earthworms exposed to the metabolite IN-MM671 should be discussed in a PRAPeR meeting.</p> <p>See reporting table 5(31)</p> | <p>See DAR Table B.9.8.1 on page 635. There seems to be a treatment related effect on body weight at the highest concentration but no statistical significance was found despite the SD. Meeting agrees that the statistics should be checked. Even if the NOEC is set at the low dose of 12.5 mg/kg soil, the TER is still acceptable.</p> <p>The statistics have been checked during the meeting and were found to be correct. Therefore the endpoint does not have to be updated. Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.13</p> <p>MS to discuss in a PRAPeR expert meeting the validity and representativeness of the post-emergence tier 1 test for non-target plants.</p> <p>See reporting table 5(34)</p> | <p>The tier 1 tests were not done according to GLP (they date from 2003). Since the a.s. is a fungicide and other data indicate low risk to terrestrial plants, RMS considers that new studies are not necessary. Preliminary trials (screening data) would be accepted for a fungicide and those do not have to be according to GLP.</p> <p>Meeting agrees. Open point closed.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.14</p> <p>MS to discuss in an expert meeting the need of further information (studies) to assess the effects</p> | <p>See open point 5.13. Open point closed.</p> | <p>Open point closed.</p> |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | of proquinazid to non-target plants. See reporting table 5(35) | | |
| | Message from section 1: 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) | Noted. Action will be taken if necessary when the specification is confirmed. | Message noted, action will be taken if necessary when the specification is confirmed |

Appendix 2: Evaluation table

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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 TERIt 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 underestimated 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 underestimated 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’. | <u>PRAPeR 68 (4 – 8 May 2009):</u> 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 | 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 | <u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed. |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group |
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| | | <p>occurrence and feeding patterns in different crops.</p> <p>Information on the Stonechat diet can be found in a recent publication by Revaz, E., <i>et al.</i> 2008 on the "Foraging ecology and reproductive biology of the Stonechat <i>Saxicola torquata</i>: 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.</p> <p>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.</p> | <p>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.</p> | |
| | <p>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 include in an Addendum.</p> | <p>DuPont: No comment – action for RMS to amend end point list</p> | <p>RMS: Corrected end points as stated in reporting table. Other changes pending outcome of PRAPeR discussion.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group |
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| | See reporting table 5(11) | | | |
| | <p>Open point: 5.4</p> <p>The TERIt for small herbivorous mammals should be update, pending of the outcome of the discussion in the open point 5(4).</p> <p>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.</p> <p>The TERIt for insectivorous birds should be 217.8 in cereals.</p> <p>RMS to include the agreed long-term TERs values in an Addendum and to amend the LoEP.</p> <p>See reporting table 5(12)</p> | <p>DuPont: We agree with the statement already provided by the RMS in the reporting table (point 5(12)):</p> | <p>RMS: No additional comment pending outcome of discussion in open point 5(4).</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the evaluation group |
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| | <p>Open point: 5.5 RMS to include the summaries of the alga studies with the proquinazid in an Addendum.</p> <p>See reporting table 5(17)</p> | <p>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.</p> <p>Proquinazid technical: DuPont-21531: EC₅₀ > 0.12 mg a.s./L (highest rate tested) AMR 4168-96, Revision No. 1: EC₅₀ 0.615 mg a.s./L (area under growth curve) Proquinazid 200 g/L EC: DuPont-21739: Cell density EC₅₀ – 1.3 mg/L Growth rate EC₅₀ – 2.5 mg/L Area under curve EC₅₀ – 1.4 mg/L DuPont-11234: Cell density EC₅₀ – 1.3 mg/L Growth rate EC₅₀ – 3.3 mg/L Area under curve EC₅₀ – 1.2 mg/L</p> <p>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.</p> | <p>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.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |
| | <p>Open point: 5.6</p> | <p>DuPont: We agree with the proposed correction and note that the aquatic</p> | <p>RMS: The corrected classification text is provided in Addendum 2, dated</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u></p> |

| 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 |
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| | <p>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 <i>Pseudokirchneriella subcapitata</i> with a formulation acute toxicity 72h EbC50 of 1.3 mg product /l instead the <i>Daphnia magna</i>.</p> <p>See reporting table 5(18)</p> | <p>toxicity classification is not changed.</p> | <p>March 2009, to Annex B (Volume 3) of the DAR.</p> | <p>Open point closed.</p> |
| | <p>Open point: 5.7 RMS should correct the wrong references in an Addendum/Corrigendum.</p> <p>See reporting table 5(19)</p> | <p>DuPont: No comment, requirement for RMS to correct references</p> | <p>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.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |
| | <p>Open point: 5.8 RMS should include the reference in an Addendum/Corrigendum.</p> <p>See reporting table 5(20)</p> | <p>DuPont: No comment, requirement for RMS to include reference</p> | <p>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.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |
| | <p>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</p> | <p>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</p> | <p>RMS: No additional comment.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |

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| | list of endpoints. See reporting table 5(23) | at lower steps. | | |
| | 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. | <u>PRAPeR 68 (4 – 8 May 2009):</u> 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 studies. In the German field study the pest mite numbers were already 1.4-times higher in the proquinazid 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 <i>Typhlodromus pyri</i> was the dominant predatory mite species (> 99%), which | RMS: No additional comment. | <u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed. |

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| | | <p>is known not to depend on the availability of pest mites as food source (pollen is a sufficient food source for this species).</p> <p>The overall field evidence therefore indicates that proquinazid treatment is not likely to result in significant adverse effects on predatory mites.</p> | | |
| | <p>Open point: 5.12</p> <p>The chronic endpoint for earthworms exposed to the metabolite IN-MM671 should be discussed in a PRAPeR meeting.</p> <p>See reporting table 5(31)</p> | <p>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 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.</p> | <p>RMS: No additional comment.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |
| | <p>Open point: 5.13</p> <p>MS to discuss in a PRAPeR expert meeting the validity and representativeness of the post-emergence tier 1 test for non-target plants.</p> | <p>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.</p> | <p>RMS: No additional comment.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |

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| | See reporting table 5(34) | | | |
| | <p>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.</p> <p>See reporting table 5(35)</p> | <p>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.</p> <p>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 latest, around one month before harvest.</p> <p>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.</p> <p>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.</p> | <p>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.</p> | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Open point closed.</p> |

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| | | <p>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 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.</p> <p>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</p> | | |

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| | | <p>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.</p> <p>No phytotoxicity as a result of the application of Proquinazid 200 g/L EC was recorded in any of the above 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.</p> | | |
| | <p>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</p> | | | <p><u>PRAPeR 68 (4 – 8 May 2009):</u> Message noted, action will be taken if necessary when the specification is confirmed</p> |

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| | minimum purity or a revised specification) | | | |

Report of PRAPeR Expert MEETING 69

PROQUINAZID

Rapporteur Member State: UK

Specific comments on the active substance in the section

2. Mammalian Toxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|------------|----------|---|
| March 2009 | UK | Proquinazid addendum 2 Vol3 B2-B6-B8-B9 (March 2009).doc |
| 2009-03-13 | UK | Proquinazid evaluation table rev1-0 (2009-03-13) |
| March 2009 | UK | Proquinazid list of endpoints (March 2009).doc |
| March 2009 | UK | Proquinazid List of references relied on (March 2009).doc |
| 2008-10-31 | UK | Proquinazid reporting table rev1-1 (2008-10-31).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** Proquinazid 200 g/l EC
5. **Classification and labelling:** R40
6. **Recommended restrictions/conditions for use:** none
7. **Reference List:** not discussed

Areas of concern: none

Appendix 1: Discussion table: PROQUINAZID

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Proquinazid (Fu)

2. Mammalian toxicology

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|--|---|---|
| | <p>Open point: 0.1 RMS should consider to use the current harmonised version of the list of end points.</p> <p>See reporting table 0(1)</p> | <p>Noted</p> | <p>Open point open: RMS to update the LoEP according to the agreed template</p> |
| | <p>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.</p> <p>See reporting table 2(2)</p> | <p>The RMS submitted an Addendum to the DAR.</p> <p>There were ocular findings in both the 90 day and 1 year dog studies presented. No clear conclusion as to whether these findings were a systemic or a local effect could be made by the RMS.</p> <p>In the 1 year study there was a slight increase in incidence of ocular discharge at 15 mg/kg bw/d in females and on this basis the RMS proposes a NOAEL of <15 mg/kg bw/d for females (based on advice from the UK ACP). A NOAEL of 15 mg/kg bw/d for males is proposed based on reduced body weight gain. Experts discussed whether this was compound or treatment related. Based on the data from both the 90 day and 1 year dog studies (results at the highest doses and the increase in trend with increased dosing) it is considered to be compound related.</p> <p>In the 90 day study ocular findings were found in females at all dose levels on day 1.</p> <p>Experts agreed that for 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.</p> | <p>Open point fulfilled.</p> <p>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.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | | Open point fulfilled. | |
| | <p>Open point: 2.2 MSs to discuss the ARfD value.</p> <p>See reporting table 2(8)</p> | <p>The RMS ARfD proposal is 0.2 mg/kg bw based on applying a 100 safety factor on the dog 90 d study (based on minimal acute effect on ocular discharge at 19 mg/kg bw/d, the 19 mg/kg bw/d is a LOAEL). DE proposes an ARfD of 0.3 mg/kg bw based on the developmental toxicity study in rats. At 60 mg/kg bw/d there was a loss in bodyweight and reduced feed consumption in feed (NOAEL = 30 mg/kg bw d).</p> <p>As the findings in the 90 day dog study were considered to be adverse (although the mechanism is unclear) the majority of experts agreed to be conservative and use the 90 day dog study in setting the ARfD. As the effect observed in the 90 day dog study at 19 mg/kg bw/d was minimal and in 1 animal it was agreed to use the standard 100-fold safety factor.</p> <p>ARfD agreed = 0.2 mg/kg bw</p> <p>Open point fulfilled.</p> | <p>Open point fulfilled.</p> <p>ARfD = 0.2 mg/kg bw</p> |
| | <p>Open point: 2.3 MSs to discuss dermal absorption of proquinazid representative formulation.</p> <p>See reporting table 2(9)</p> | <p>The dermal absorption of proquinazid (using the lead product) was investigated using an in vivo rat study and in vitro human and rat skin studies. It was noted that the dilution used was not as dilute as the proposed in-spray dilutions (1.3 g/l versus 0.05-0.5 g/l).</p> <p>Based on the in vivo data the RMS proposes 5% for the concentrate and 18% for the dilution based on the amount absorbed after 6 hour exposure and the amount excreted over the next 24h. These values were adjusted for relative absorption through rat and human skin to give 2% for the concentrate and 12% for the dilution.</p> <p>The proposal from DE was 3% for the concentrate and 15% for the dilution and DE did not agree with the correction values applied by the RMS due to bioavailability of the active.</p> <p>The proposal from the RMS was accepted by experts.</p> | <p>Open point fulfilled</p> <p>Dermal absorption: 2% for the concentrate 12% for the dilution</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|---|
| | | Open point fulfilled. | |
| | <p>Open point: 2.4 MSs to agree on the input parameters and models to calculate operator, worker and bystander exposure.</p> <p>See reporting table 2(11)</p> | <p>The use of EUROPOEM to refine the exposure assessment via broadcast air assisted sprayers using UK POEM is now considered to be acceptable (there is ongoing work within EFSA to use EUROPOEM as a method of refinement).</p> <p>It is noted that using the German model safe use can be demonstrated.</p> <p>Open point closed.</p> | Open point closed. |
| | <p>Message from section 1: Please consider the new specification given in Addendum 2 to Annex C (March 2009)</p> <p>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)</p> | <p>The RMS outlined impurities in the new specification presented in the Addendum to the DAR.</p> <p>The impurity [REDACTED] s increased from [REDACTED] (it is noted that PhysChem have proposed to decrease this) and there are two new impurities to the proposed specification [REDACTED]. All other impurities are present at <1% apart from [REDACTED]</p> <p>[REDACTED] tested in an old batch up to [REDACTED] and is present in rat metabolism. No concerns were identified by experts.</p> <p>[REDACTED] structurally very similar to proquinazid [REDACTED] and is expected to have a similar metabolism and toxicological profiles both quantitatively and qualitatively. No concerns were identified by experts.</p> <p>[REDACTED] not of concern as the levels are lower in the new proposed specification than in batch KQ926-45 where it has been fully tested. No concerns were identified by experts.</p> <p>See Addendum to Annex C (Table C.1.8) for full details.</p> <p>Experts questioned why the rat multigeneration study conducted on material from the old production process was not evaluated by the RMS as it appears that the results</p> | <p>Message noted and discussed by experts.</p> <p>See Addendum to Annex C (Table C.1.8) for full details.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---------|---|----------------------------|
| | | <p>showed greater toxicity than the study conducted on material from the current production process.</p> <p>The notifier stated that the rat multigeneration study was repeated as it was started prior to the updated guidelines being finalised, there were problems with the sperm methods and it was conducted on material from the old production process. This issue was highlighted an issue by experts in the meeting and it was discussed whether the RMS should evaluate the study conducted on material form the old production process. However, as the study was performed on material from the old production process with higher levels if impurities it was not considered necessary for the risk assessment of the material from the current production process by experts/EFSA.</p> | |

Appendix 2: Evaluation table

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
|-----|--|--|---|---|
| | 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. | <u>Toxicological relevance of ocular discharge in dogs</u> 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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| | | | <p>dosing. However systemic exposure of the eye to the test substance/metabolites may have contributed to the ocular irritation seen at other times.”</p> <p>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.</p> <p><u>NOAELs in 1-year dog study</u></p> <p>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).</p> <p>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 who were concerned about the ocular discharge in females at 15 mg/kg bw/d.</p> | |

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| | | | <p>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).</p> <p><u>To conclude:</u> 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).</p> | |
| | <p>Open point: 2.2 MSs to discuss the ARfD value.</p> <p>See reporting table 2(8)</p> | <p>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 NEST1 is <<100% indicating that proquinazid when used according to the proposed GAP does not represent an acute dietary risk to sensitive population groups.</p> | <p>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, 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</p> | <p><u>PRAPeR 69 (4 – 8 May 2009):</u></p> <p>Open point fulfilled.</p> <p>ARfD = 0.2 mg/kg bw</p> |

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|-----|--|--|---|---|
| | | | <p>reproduced at page 20 of Addendum 2, dated March 2009, to Annex B (Volume 3) of the DAR.)</p> <p>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).</p> <p>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.</p> | |
| | <p>Open point: 2.3 MSs to discuss dermal absorption of proquinazid representative formulation.</p> <p>See reporting table 2(9)</p> | <p>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).</p> | <p>Dermal absorption of proquinazid from Proquinazid 200 g/L EC (lead product) was investigated <i>in vitro</i> using rat and human skin and <i>in vivo</i> in the rat.</p> <p>Tests were conducted with the undiluted formulation and with a 1.3 g/L aqueous dilution. The tested dilution was however not as dilute as the proposed in-use spray dilutions (0.05-0.5g/l).</p> | <p><u>PRAPeR 69 (4 – 8 May 2009):</u></p> <p>Open point fulfilled</p> <p>Dermal absorption: 2% for the concentrate 12% for the dilution</p> |

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| | | | <p>RMS proposed dermal absorption values of 2% (concentrate) and 12% (dilution). These proposals were calculated from values determined in the <i>in vivo</i> rat study, with adjustment for relative absorption through rat and human skin <i>in vitro</i>.</p> <p>In the <i>in vivo</i> study with a 6 h exposure there considerable delayed absorption. The RMS therefore considered the <u>percentage of dose absorbed by rats <i>in vivo</i> relevant to operator risk assessment</u> 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).</p> <p>The <u>rat: human adjustment factor</u> was based on the difference in the <u>percentage absorption</u> calculated <i>in vitro</i> for rat and human skin (and took account of radiolabel in tape strips of the stratum corneum).</p> <p>DE considered (see reporting table) that worst-case assumptions based on the outcome of <i>in vivo</i> and <i>in vitro</i> studies should be used. At least, these assumptions should cover the <u>absorbable</u> dose in the <i>in vitro</i> study with human skin. Therefore 3% (concentrate) and 15% (dilution)</p> | |

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| | | | <p>were suggested (ie the amount in receptor fluid plus tape stripped human skin at the end of the 6h exposure).</p> <p>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.</p> <p>RMS does not support the DE proposal because the data clearly show that for rat skin the <u>absorbable</u> dose of proquinazid was much greater when determined <i>in vitro</i> than when determined <i>in vivo</i>. Hence it would seem likely that the <u>absorbable</u> dose of proquinazid through human skin <i>in vitro</i> would <u>over estimate</u> absorption through human skin <i>in vivo</i>.</p> <p><u>To conclude, RMS still considers dermal absorption values of 2% (concentrate) and 12% to be appropriate for use in the risk assessment of Proquinazid 200 g/L EC.</u></p> <p>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.</p> | |

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| | <p>Open point: 2.4 MSs to agree on the input parameters and models to calculate operator, worker and bystander exposure.</p> <p>See reporting table 2(11)</p> | <p>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.</p> | <p>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.</p> <p>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.</p> | <p><u>PRAPeR 69 (4 – 8 May 2009):</u></p> <p>Open point closed.</p> |
| | <p>Message from section 1 to 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</p> | | | <p><u>PRAPeR 69 (4 – 8 May 2009):</u></p> <p>Answer from section 2 to section 1: Message noted and discussed by experts.</p> <p>See Addendum to Annex C (Table C.1.8) for full details.</p> |

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| | certain impurities and the minimum purity or a revised specification) | | | |

REPORT OF PRAPeR EXPERT MEETING 70

PROQUINAZID

Rapporteur Member State: UK

Specific comments on the active substance in the section

3. Residues

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|------------|----------|---|
| 2009-03-13 | UK | Proquinazid evaluation table rev1-0 (2009-03-13) |
| March 2009 | UK | Proquinazid list of endpoints (March 2009).doc |
| March 2009 | UK | Proquinazid List of references relied on (March 2009).doc |
| 2008-10-31 | UK | Proquinazid reporting table rev1-1 (2008-10-31).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|------|----------|-----------|
| none | | |

The conclusions of the meeting were as follows:

- Data on preparations:** Proquinazid 200 g/L EC
- Classification and labelling:** none
- Recommended restrictions/conditions for use:** none
- Reference List:** not discussed

Areas of concern: none

Appendix 1: Discussion table: PROQUINAZID

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Proquinazid (Fu)

3. Residues

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|---|---|
| | <p>Open point: 0.1 RMS should consider to use the current harmonised version of the list of end points.</p> <p>See reporting table 0(1)</p> | <p>An updated version of the list of end points (March 2009) was submitted for the meeting.</p> | <p>Open point fulfilled.</p> |
| | <p>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.</p> <p>See reporting table 3(4)</p> | <p>Significant fraction of TRR was found in grape berries. The notifier postulated that it was lignin. Similar extraction was carried out in the wheat study, postulated lignin fraction in straw approx. 13.6%.</p> <p>Postulated lignin fraction was not further investigated in the grape study. Notifier has carried out study on apple with detailed investigation of the lignin fraction, and has compared the results with the grape study. RMS has already received the apple study. Experts discussed if it can be expected to get clear information concerning the identification of the lignin fraction from the apple study. It remained unclear whether the apple study provided more information since the study was not available to the experts.</p> <p>It was discussed if literature for the method for investigation of the lignin fraction (Bjorkman procedure) is available.</p> <p>RMS should evaluate the apple study or at least the relevant part on the extraction and identification of lignin in the apple study and correlate the findings with the grape study.</p> | <p>Open point fulfilled.</p> <p>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).</p> |
| | <p>New open point 3.6 identified during PRAPeR 70 meeting: RMS to evaluate the apple metabolism</p> | | <p>Open point open</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|-----|---|--|---|
| | study or to compare the investigation of the lignin fraction in the grape study with the procedure described in literature (Bjorkman). | | |
| | <p>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.</p> <p>See reporting table 3(7)</p> | <p>According to RMS, additional information of the notifier clarified the diet was on DM basis. Therefore, recalculating the dietary burden comparing the intake in goat metabolism study to the highest calculated intake, the N rate in the goat metabolism study has changed from 200 to 175.</p> <p>Results for livestock dietary intake in the DAR not conclusive. The input values are not mentioned.</p> <p>Input values to be used were discussed: straw 0.84 mg/kg grain 0.04 mg/kg</p> | Data requirement fulfilled. |
| | <p>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.</p> <p>See reporting table 3(8)</p> | <p>According to RMS, additional information of the notifier clarified the diet was on DM basis. Therefore, recalculating the dietary burden comparing the intake in hen metabolism study to the highest calculated intake the N rate in the hen metabolism study has changed from 400 to 330.</p> <p>This has no impact on the evaluation as a hen study is not triggered by the dietary intake from the representative use (see OP 3.2 below).</p> | Data requirement fulfilled. |
| | <p>Open point: 3.2 It should be considered by a meeting of experts if there is a need for any further</p> | <p>In goat study TRR in fat is low. However, in poultry high TRR was found in fat. Hen study was too short (5 days) to reach plateau. Hen study was grossly overdosed (330 N). Therefore, extrapolation to estimated intake is problematic.</p> <p>Meeting discussed how the issue should be addressed.</p> <p>According to guideline, study normally should be carried out until the plateau reached,</p> | <p>Open point fulfilled.</p> <p>On the basis of the notified uses the study is not triggered.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | <p>data on residues in poultry given that the compound is fat soluble and may accumulate.</p> <p>See reporting table 3(9)</p> | <p>usually 14 days if surrogate for feeding study. If needed only for identification of metabolites, 3 days are sufficient.</p> <p>According to intake from notified uses, the study was not triggered.</p> <p>Residues in fat in poultry are parent (log pow 5.5). Metabolite IN-MW977 probably more polar than parent but possibly also fat soluble (log pow around 3 modelled with ChemSketch and PrologD-Pallas). Metabolite not observed in fat of poultry, however, in goat fat the metabolite was found in equal amounts to parent.</p> <p>On the basis of the notified uses a hen metabolism study is not triggered.</p> <p>On the basis of the available data no residues >0.01 mg/kg are expected in hen tissues. However, doubts exist concerning the plateau which was not reached in the eggs. The experts agreed that if a metabolism study is necessary for future uses, the study should be carefully reassessed.</p> | <p>If a hen metabolism study is necessary for future uses, the study should be carefully reassessed.</p> |
| | <p>Open point: 3.3</p> <p>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.</p> <p>See reporting table 3(11)</p> | <p>Trigger for ruminant metabolism study is exceeded. 175 N study was carried out in goats. Residue definition should be proposed as study is available and triggered.</p> <p>Meeting discussed possible residue definition. Residue definition should include metabolite IN-MU210 as major residue in all goat matrices.</p> <p>With regard to monitoring no method of analysis for metabolite IN-MU210 is available. According to RMS, monitoring method for parent is available in animal matrices. However, parent is only found in goat fat in sufficient amounts. Goat metabolism data indicate the metabolite IN-MU210 would be sufficient for ruminants, but in terms of poultry residues, parent should be included in the residue definition for animal matrices.</p> <p>In cereals one major metabolite IN-MW977 was found (1/3 parent, 2/3 metabolite in cereal straw). It was also found in the ruminant fat (24% TRR), but ruminant study was only carried out with parent. Higher levels of the metabolite IN-MW977 in ruminant matrices could be expected when cereal commodities are used in animal feeding. IN-MW977 was not found in hen matrices (see discussion in open point 3.2 above).</p> <p>Therefore, it was agreed that the following residue definition in animal matrices should be proposed for risk assessment: Sum of proquinazid and metabolites IN-MU210 and IN-</p> | <p>Open point fulfilled.</p> <p>Residue definitions for animal matrices have been proposed:</p> <p>For risk assessment: sum of proquinazid and metabolites IN-MU210 and IN-MW977 expressed as proquinazid</p> <p>For monitoring: sum of proquinazid and metabolites IN-MU210 expressed as proquinazid</p> <p>Message 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</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | | <p>MW977 expressed as proquinazid.</p> <p>For monitoring, either two different residue definitions for ruminant and poultry, or a common residue definition including parent and metabolite should be proposed. Eventually it was agreed that the following residue definition in animal for monitoring matrices should be proposed: Sum of proquinazid and metabolite IN-MU210, expressed as proquinazid.</p> <p>For the time being, on the basis of the notified uses, a ruminant feeding study is not triggered. On the basis of the available data no residues >0.01 mg/kg of parent or any metabolite in the residue definition for RA are expected in animal tissues.</p> <p>The experts took into account the 175N rate in the goat study and the fact that IN-W977 is only found in fat in higher amounts that will not exceed 0.01 mg/kg even if fed to animals in amounts observed in cereal straw.</p> <p>On the basis of the proposed residue definition for monitoring risk managers may consider to set MRLs for food of animal origin on the LOQ of the analytical method for monitoring (probably still to be developed for metabolite IN-MU210).</p> <p>Message 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.</p> | <p>monitoring (sum of proquinazid and metabolites IN-MU210 expressed as proquinazid) will be set.</p> |
| | <p>Open point: 3.4 The GAP should be clarified. Given the comment from the applicant.</p> <p>See reporting table</p> | <p>The GAP was clarified by the applicant. The changes are not relevant for residue assessment.</p> | <p>Open point fulfilled. Changed GAP has no impact on residue assessment.</p> |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | 3(13) | | |
| | <p>Open point: 3.5 If the tox reference values are changed a revised risk assessment will be required.</p> <p>See reporting table 3(19)</p> | <p>If the toxicology section were to change the reference values, risk assessment will be changed.</p> <p>Post meeting note: The meeting on toxicology has confirmed the reference values proposed by the RMS in the DAR (ADI 0.01 mg/kg bw/day (2 yr rat study, SF 100); ARfD 0.2 mg/kg bw (90 day dog study, SF 100))</p> | <p>Open point fulfilled. No change in tox reference values.</p> |
| | <p>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.</p> | <p>According to reporting table 3(14) a need for further action for the RMS was identified by the experts. The validation data for the pre-registration method used in grape residue trials to be reported by RMS in an addendum, preferably in the format presented for cereals method (table B.7.26 DAR).</p> | <p>Open point open</p> |
| | <p>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.</p> | <p>Parent and in particular metabolite IN-MM671 are extremely stable in soil (DT90 >1yr). Rotational crop metabolism study: Study does not include results for plant back interval of 365 days. Metabolite IN-MM671 is more critical than parent. It is present in the soil of up to 65% of the applied radioactivity after 120 days and therefore sufficiently covered by the 120 day plant back interval. Study was carried at 3N based on the application rate for wheat. Because of the very long DT90, we need maximum concentration of parent and metabolite in the soil considering potential accumulation to calculate the actual N rate.</p> | <p>Open point open</p> |
| | <p>New open point 3.9: LoEP to be updated in accordance with the decisions of the meeting.</p> | <p>In the light of the decisions taken by the meeting, the list of endpoints has to be updated accordingly.</p> | <p>Open point open</p> |

Appendix 2: Evaluation table

3. Residues

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
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| | Section 3 Open points: 5 Points for clarification: 0 Data requirement: 2 | | | Section 3 Open points: 4 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 (<i>as above</i>) giving base soluble residues which formed a precipitate (21-42% TRR) upon acidification. Incorporation of ¹⁴ C- | 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 | 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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| | | proquinazid unextractable residues into apple lignin was confirmed by isolation of lignin fractions using dioxane/water (Bjorkman procedure) and dioxane/acid. Approximately 33% TRR was released and characterized as lignin using literature procedures. | available. | |
| | 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). | | | <u>PRAPeR 70 (4 – 8 May 2009):</u> Open point open |
| | 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. See reporting table 3(7) | DuPont: The goat was dosed at 91.5 mg/kg diet. The daily dose (118.5 mg) was administered <i>via</i> capsule and the feed, consisting of a commercial lab diet and alfalfa cubes and hay, was provided <i>ad libitum</i> . The moisture content of the feed was not determined and dietary intake 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 | It appears from the additional information provided by the Notifier that the dose rate was on a diet <i>dry matter</i> 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 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 | <u>PRAPeR 70 (4 – 8 May 2009):</u> Data requirement fulfilled. |

| No. | <u>Column A</u> Conclusions of the EFSA Evaluation Meeting | <u>Column B</u> Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | <u>Column C</u> Rapporteur Member State comments on main data submitter / applicant comments | <u>Column D</u> Recommendations PRAPeR Expert Meeting / Conclusions of the Evaluation Meeting |
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| | | <p>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.</p> <p>Adjustments for feed dry matter content would not impact the overall study outcome and should not necessitate study reconsideration.</p> | <p>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.</p> <p>RMS believes that the data requirement is addressed.</p> | |
| | <p>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.</p> <p>See reporting table 3(8)</p> | <p>DuPont: Hens were dosed at 15.6 mg/kg diet. The daily dose (1.95 mg) was administered <i>via</i> capsule and the feed, consisting of a commercial lab diet, was provided <i>ad libitum</i>. The moisture content of the feed was not determined and dietary intake calculations were not corrected for dry 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</p> | <p>It appears from the additional information provided by the Notifier that the dose rate was on a diet <i>dry matter</i> 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 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</p> | <p><u>PRAPeR 70 (4 – 8 May 2009):</u> Data requirement fulfilled.</p> |

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|-----|--|--|---|--|
| | | <p>(~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.</p> <p>Adjustments for feed dry matter content would not impact the overall study outcome and should not necessitate study reconsideration.</p> | <p>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.</p> <p>RMS believes that the data requirement is addressed.</p> | |
| | <p>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.</p> <p>See reporting table 3(9)</p> | <p>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 needing to conduct a poultry metabolism study. In addition, the poultry study was conducted at an exaggerated rate (400N) and detectable residues are unlikely in poultry</p> | <p>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.</p> | <p><u>PRAPeR 70 (4 – 8 May 2009):</u> Open point fulfilled.</p> <p>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.</p> |

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|-----|--|---|---|---|
| | | commodities. | | |
| | <p>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.</p> <p>See reporting table 3(11)</p> | <p>DuPont: Minimal transfer of ¹⁴C-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.</p> | <p>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.</p> | <p><u>PRAPeR 70 (4 – 8 May 2009):</u> Open point fulfilled. Residue definitions have been proposed:</p> <p>For risk assessment: sum of proquinazid and metabolites IN-MU210 and IN-MW977 expressed as proquinazid</p> <p>For monitoring: sum of proquinazid and metabolites IN-MU210 expressed as proquinazid</p> |
| | <p>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.</p> | | | |
| | <p>Open point: 3.4 The GAP should be clarified. Given the comment from the</p> | <p>DuPont: In the DAR the minimum application rate for Italy and Germany is cited as 40 g a.s./ha and the</p> | <p>The Notifier has provided a revised GAP table for clarification. The revisions relate to the use on grapes</p> | <p><u>PRAPeR 70 (4 – 8 May 2009):</u> Open point fulfilled. Changed GAP has no impact on residue</p> |

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|-----|---|--|---|---|
| | <p>applicant.</p> <p>See reporting table 3(13)</p> | <p>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.</p> <p>A revised GAP table is provided</p> | <p>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.</p> <p>The RMS considered this point addressed.</p> | <p>assessment</p> |
| | <p>Open point: 3.5 If the tox reference values are changed a revised risk assessment will be required.</p> <p>See reporting table 3(19)</p> | <p>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.</p> | <p>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 experts have concluded. The LOEP will be revised</p> | <p><u>PRAPeR 70 (4 – 8 May 2009):</u> Open point fulfilled. No change in tox reference values</p> |

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|-----|---|--|---|--|
| | | | 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. | | | <u>PRAPeR 70 (4 – 8 May 2009):</u> Open point open |
| | 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. | | | <u>PRAPeR 70 (4 – 8 May 2009):</u> Open point open |
| | New open point 3.9: LoEP to be updated in accordance with the decisions of the meeting. | | | <u>PRAPeR 70 (4 – 8 May 2009):</u> Open point open |