

Parma, 16th July 2012

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes

**21st Meeting of the Working Group on the
toxicological relevance of pesticide metabolites for dietary risk
assessment**

(Agreed on 16th July 2012)

Date:	19th – 20th June 2012
Time:	14:00 – 18.00 and 9:00 – 13:00 CET
Place:	Meeting Room M05, EFSA, Via Carlo Magno 1a, 43126 Parma

Participants:

WG Experts	Bernadette Ossendorp (Chair), Claudia Bolognesi, Anita Strömberg, Markus Mueller, Christiane Vleminckx, Maria Tasheva, Kiriaki Machera, Rebecca Scrivens (via audioweb)
EFSA:	Manuela Tiramani (on 19 th), Miriam Jacobs, Hans Steinkellner (on 20 th)

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Alan Boobis.

2. Adoption of agenda

The agenda was adopted as proposed

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion/ amendments based on comments received from Panel members, final review and editorial checking

Comments received from Panel members (i.e. Annette Petersen and Ton van der Linden) and other WG members received prior to this meeting were discussed and if deemed appropriate considered for revising the draft.

A lot of editorial changes were made to the opinion based on comments received (these are not listed in this notes)

It was agreed that the updated version of the opinion will be distributed to the Panel members as a room document for the Plenary meeting next day where adoption is envisaged.

5. Any other business

Hans Steinkellner

Parma, 22nd June 2012

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes

20th Meeting (Webconference) of the Working Group on the toxicological relevance of pesticide metabolites and isomer conversion for dietary risk assessment

(Agreed on 22nd June 2012)

Date:	4 th June 2012
Time:	14.00 – 17.00 CET
Place:	Webconference

Participants:

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Anita Strömberg, Markus Mueller, Christiane Vleminckx

EFSA: Manuela Tiramani, Laszlo Bura, Hans Steinkellner

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Rebecca Scrivens.

2. Adoption of agenda

It was agreed to first discuss uncertainties, then the changes proposed to the isomer chapter and then the remaining part of the opinion.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Uncertainties in the presented approaches

It was agreed to keep the Uncertainty chapter separate for the moment and to be inserted in the opinion only at a later stage. Intense discussions took place on the extent of uncertainties associated with the different parts/steps of the assessment.

5. Discussion about outstanding issues and text to be amended/inserted throughout the draft opinion including appendices

Discussion about chapter 9 Isomers

Further amendments were agreed and several additional references inserted.

Discussion about remaining chapters

A series of editorial changes were discussed and agreed and the assessment schemes were rearranged

6. Timeline and allocation of tasks for finalisation of opinion (submission to Panel colleagues for final review, distribution to the Panel, editorial checking, etc.)

The WG members will check completeness and correctness of references for their parts in time for the next meeting. The draft opinion will be sent to Panel members for review.

7. Next meeting

19 (a.m.) – 20 (p.m.) June 2012, EFSA, Parma

8. Any other business

Hans Steinkellner

Parma, 5th June 2012

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes

**19th Meeting (Webconference) of the Working Group on the toxicological relevance of pesticide metabolites and isomer conversion for dietary risk assessment
(Agreed on 5th June 2012)**

Date:	11 th May 2012
Time:	10.00 – 13.00 CET (9.00 – 12.00 UK time)
Place:	Webconference

Participants:

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Anita Strömberg, Rebecca Scrivens, Markus Mueller, Christiane Vleminckx

EFSA: Manuela Tiramani, Laszlo Bura, Hans Steinkellner

1. Welcome and apologies

The chair welcomed the participants. No apologies were received.

2. Adoption of agenda

The agenda was agreed without changes.




3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Uncertainties in the presented approaches

The experts discussed all relevant issues in regard to the uncertainties involved with the assessments of toxicological properties and exposure assessment. The uncertainty chapter was amended accordingly.

5. Discussion about outstanding issues and text to be amended/inserted throughout the draft opinion in particular

-  Isomer chapter
-  Toxicity Testing
-  Recommendations

Discussed was mainly the chapter on isomers where further text was integrated. The draft text on recommendations was discussed and several amendments agreed.

6. Timeline and allocation of tasks for finalisation of opinion (glossary, references, abbreviations)

The experts in charge with drafting the individual chapters agreed to provide input for glossary and add references for their chapters.

7. Next meeting

A further web conference was scheduled for the beginning of June.

8. Any other business

Hans Steinkellner

Parma, 10th May 2012

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes

**18th Meeting of the Working Group on the
toxicological relevance of pesticide metabolites and isomer
conversion for dietary risk assessment**

(Agreed 9th May 2012)

Date:	17 th (p.m.) – 18 th (a.m.) April 2012
Time:	14.00 – 18.00 and 9.00 – 13.00 CET
Place:	Meeting Room M 05 (ground floor) EFSA, Via Carlo Magno 1/a, Parma

Participants:

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Anita Strömberg, Kyriaki Machera, Markus Mueller (17 April only), Yolanda Pico, Rebecca Scrivens, Maria Tasheva, Christiane Vleminckx

EFSA: Laszlo Bura (17 April only), Hans Steinkellner, István Sebestyén, Deyana Shtereva

1. Welcome and apologies

Bernadette welcomed the participants. Apologies have been received from Alan Boobis, Susanne Hougaard Bennekou and Karen Hirsch-Ernst.

2. Adoption of agenda

It was agreed to change the order of the agenda and to start with isomer issues.

3. Declarations of interest

4. Finalisation of isomer chapters (addressing the ToR) and allocation of tasks

It was noted that still a series of amendments agreed at the February meeting needed to be made. The experts then discussed the entire chapter and agreed to a series of further amendments.

5. Discussion of comments received from the PPR Panel and WG members

Editorial changes in different chapters as requested by the Panel members were discussed and done if deemed appropriate.

6. Discussion of new text (abstract, summary)

The summary was agreed to be expanded on the dietary exposure strategy developed by the Panel. Additional text was added.

7. Finalisation of chapters

Agreed that all chapter to which comments have been made need to be finalised by the next meeting in particular chapters 11.2.2. Toxicity testing and 12. Recommendations

8. Checking of spelling, references, abbreviations and glossary (allocation of tasks)

Only legislation to be inserted as footnotes, the rest in form of references.

9. Next meetings

- 19th (a.m.) - 20th (p.m.) June 2012, EFSA, Parma
- The WG agreed that an additional meeting in form of a tele/webconference should be held as soon as possible.

10. Any other business

Istvan Sebestyen/Hans Steinkellner

Parma, 13 April 2012

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes

**17th Meeting of the Working Group on the
toxicological relevance of pesticide metabolites for dietary risk
assessment**

(Agreed in a written procedure on 30 March 2012)

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Date:	6th (p.m.) – 7th (a.m.) March 2012
Time:	14.00 – 18.00 and 9.00 – 13.00 CET
Place:	Meeting Room M 04 (ground floor) EFSA, Via Carlo Magno 1/a, Parma

Participants:

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Alan Boobis, Anita Strömberg, Yolanda Pico, Rebecca Scrivens, Maria Tasheva, Christiane Vleminckx, Karen Hirsch-Ernst, Susanne Hougaard Bennekou, Markus Mueller, Kyriaki Machera

EFSA: Manuela Tiramani, Laszlo Bura (7 March only), Hans Steinkellner (8 March only), István Sebestyén

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Alan Boobis.

2. Adoption of agenda

The agenda was adopted, but the order of the agenda items was modified. First the draft opinion and its annexes were discussed chapter by chapter accepting or deleting the comments, then the isomer issues were discussed.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion of the updated version of the draft scientific opinion

It was agreed that rapporteurs will draft the abstract and summary and to keep the original title of the opinion without referring to isomer issues. New text on Chapter 2.3. Comparison of residue definitions was also agreed. All toxicology chapters in particular on TTC and QSAR have been reviewed and the comments were discussed by the WG. It was agreed to include text on the conceptual framework on QSAR. For Chapter 9. Relevance of isomers tasks to be carried out were allocated to different experts. A consolidated chapter should be ready for the next meeting.

Also a consolidated text for Chapter 10.5. Critical issues on isomers will be ready for the next meeting. A description of the acute assessment scheme should be inserted in the text of the opinion. For Chapter 11.3. it was agreed that endocrine active substances should also be considered in the testing strategy chapter. The WG agreed to address in Chapter 12. Recommendations the the need for guidance to use the conversion factors. The appendices were also reviewed and several amendments were made.

5. Next meetings

17-18 April 2012 in Parma,

19-20 June 2012 in Parma – planned adoption

6. Any other business

Hans Steinkellner

Parma, 23rd February 2012

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Secretary Notes

**16th Meeting of the Working Group on the
toxicological relevance of pesticide metabolites and isomer
conversion for dietary risk assessment**

(Agreed on 23rd February 2012)

Date:	2nd (p.m.) – 3rd (a.m.) February 2012
Time:	14.00 – 18.00 and 9.00 – 13.00 CET
Place:	Meeting Room M 03 (ground floor) EFSA, Via Carlo Magno 1/a, Parma

Participants:

WG Experts

Bernadette Ossendorp (Chair), Anita Strömberg, Rebecca Scrivens, Maria Tasheva, Christiane Vleminckx, Claudia Bolognesi, Markus Mueller

EFSA:

Istvan Sebestyen, Hans Steinkellner, Edgars Felkers, Lazlo Bura
(only on the second day)

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Alan Boobis and Yolanda Pico.





2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of interest





In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion of the updated version of the draft scientific opinion chapter by chapter

-  **Review of all chapters/appendices where updates have been made or new text was introduced**
-  **Discussion on subchapters and text still missing – e.g. uncertainties for the toxicity assessment and recommendations, acute assessment scheme and testing strategies**
-  **Agreement on tasks still to be carried out and distribution to WG members**
-  **Timeline for finalisation of tasks ensuring meeting the deadline for adoption of the opinion**

A series of changes have been proposed. Amendments to the draft opinion were made were necessary.

5. Discussion on isomer conversion

-  **Discussion of the proposed strategy for addressing assessment of isomer conversion in the opinion**
-  **Discussion on further tasks to be carried out for addressing isomer conversion**
-  **Distribution of tasks to WG members**
-  **Timeline for finalisation of tasks ensuring meeting the deadline for adoption**

A first draft of the chapter providing an outline of the issues to be addressed was discussed.

A more consolidated version of the chapter will be provided for the next WG meeting on basis of these discussions.

6. Overall timeline and work plan to finalise the opinion

A revised consolidated opinion will be distributed to the WG by 23rd February

7. Next meetings

6th (pm) – 7th (am) March 2012, WG Meeting, Parma
17th (pm) – 18th (am) April 2012, WG Meeting Parma
19th (pm) – 20th (am) June 2012, WG Meeting Parma

8. Any other business

Istvan Sebestyen/Hans Steinkellner

PPR UNIT

Parma, 13th December 2011

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Draft Secretary Notes

15th Meeting of the

Working Group on the Toxicological relevance of pesticide metabolites for dietary risk assessment

(Agreed on 13th December 2011)

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Date:	24-25 November 2011
Time:	14:00–18:00, 09:00-13:00
Place:	EFSA DUS D 00/002 Largo N. Palli 5/A Parma/Italy

Participants:

WG Experts Bernadette Ossendorp (Chair), Alan Boobis, Anita Strömberg, Yolanda Pico, Rebecca Scrivens, Maria Tasheva, Christiane Vleminckx

EFSA: Manuela Tiramani, Hans Steinkellner, Edgars Felkers

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Ms Claudia Bolognesi.

2. Adoption of agenda

It was agreed to discuss the comments of other Panel members (draft opinion has been distributed to the Panel before the meeting) and also to go through the entire opinion and identifying issues for discussion.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion of the updated and consolidated version of the Draft Scientific Opinion chapter by chapter and in context with relevant/corresponding appendices

4.1. Comments from Panel experts

The Chair introduced comments submitted by different Panel members which were then discussed by the WG. Only minor changes were suggested by the Panel members. The WG agreed to these changes.

4.2. Discussion of new version of Annex A

The WG agreed to the revised text.

4.3. TTC approach for acute exposure

EFSA introduced their approach for acute exposure thresholds. The work carried out was endorsed by the WG.

4.4. Inclusion of the framework for assessing the usefulness of a QSAR model (QSAR project on developmental and neurotoxicity)

It was agreed to insert the general assessment scheme from the final report.

4.5. Discussion of the inclusion of the isomer issues in the opinion, stereoisomer discussion paper prepared by Markus

A discussion on the issue was postponed to the next meeting.

4.6. Discussion about the chronic and acute decision trees

The WG discussed the updated decision trees. Several amendments were proposed and agreed.

4.7. Discussion of issues chapter by chapter

The WG discussed unresolved issues and made amendments were appropriate.

5. Timeline, work plan to finalize the opinion

A revised draft will be prepared in time for the next meeting.

5. Miscellaneous

6. Next meetings

2nd (pm) – 3rd (am) February 2012

23rd February 2012, 10.30 – 13.00, Teleconference of WG Subgroup (tentative)

6th (pm) – 7th (am) March 2012, WG Meeting, Parma

17th (pm) – 18th (am) April 2012, WG Meeting Parma

19th (pm) – 20th (am) June 2012, WG Meeting Parma

Istvan Sebestyen/Hans Steinkellner

Parma, 2nd November 2011

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

**Minutes of the (14th) Meeting
of the Working Group (Subgroup) on the Toxicological relevance of pesticide
metabolites for dietary risk assessment**

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

(Agreed on 31st October 2011)

Date:	11 October 2011
Time:	10:00–18:00
Place:	Regus Schiphol Airport Meeting Centre Schiphol Airport, Amsterdam The Netherlands

Participants:

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Anita Strömberg, Yolanda Pico, Markus Müller, Rebecca Scrivens

EFSA: István Sebestyén, Hans Steinkellner,

1. Welcome and apologies

The chair welcomed the participants. No apologies were received.

2. Adoption of agenda

The Chair suggested adding an agenda point in which the experts give advice on the main issues still to be addressed in the opinion.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Issues still to be addressed

The different experts gave their view about remaining issues not yet addressed and issues so far insufficiently addressed in the opinion.

5. Discussion of the consolidated version of the Draft Scientific Opinion chapter by chapter and in context with relevant/corresponding appendices

The experts discussed the different chapters. Several changes to the draft text were agreed.

Extension of the mandate including also assessment of isomers

One expert agreed to take the lead in drafting relevant text on isomers and to provide a first draft document for the next meeting.

6. Miscellaneous

7. Next meetings

10th of November 2011, 10.30 -12.00, Teleconference of WG Subgroup, Discussion of draft paper on isomers

24th (pm) – 25th (am) November 2011, WG Meeting, Parma

26th (pm) – 27th (am) January 2012, WG Meeting, Parma

23rd February 2011, 10.30 – 13.00, Teleconference of WG Subgroup (tentative)

6th (pm) – 7th (am) March 2012, WG Meeting, Parma

17th (pm) – 18th (am) April 2012, WG Meeting Parma

19th (pm) – 20th (am) June 2012, WG Meeting Parma

Istvan Sebestyen/Hans Steinkellner

Parma, 17 August 2011

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

**Minutes of the of the 13th Meeting of the
Working Group on the Toxicological relevance of pesticide metabolites for
dietary risk assessment**

(Agreed by written procedure on 27 July 2011)

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Date:	28-29 June 2011
Time:	14:00–18:00, 09:00-13:00
Place:	EFSA DUS D 00/003 Largo N. Palli 5/A Parma/Italy

Participants

WG Experts Claudia Bolognesi (Chair), Anita Strömberg, Maria Tasheva,
 Christiane Vleminckx, Yolanda Pico, Markus Muller

EFSA: István Sebestyén, Hans Steinkellner, Manuela Tiramani, Edgars
 Felkers

1. Welcome and apologies

Apologies were received from Alan Boobis, Bernadette Ossendorp and Rebecca Scrivens.

2. Adoption of the agenda

The agenda was adopted without changes.

3. Declaration of interests

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion of the updated and consolidated version of the Draft Scientific Opinion chapter by chapter and in context with relevant/corresponding appendices

Issues to be considered in particular (not exhaustive):

- **TTC approach for acute exposure**
- **Discussion of the results of the Pestisar II project and its interpretation in the report**
- **Inclusion of the framework for assessing the usefulness of a QSAR model**
- **Discussion about the proposed testing strategy**
- **Work programme and timeline for finalisation of the opinion**

The WG agreed that the intermediate results obtained in regard to application of acute TTC thresholds are promising and that this approach was worth investigating. The final outcome of the analyses will be presented at the next meeting.

1.Introduction

Some text has been removed, editorial changes have been inserted.

Annex B. Residue definition in combination with analytical methods for residue monitoring

Annex B to be revised to increase its clarity. Analyses of several substances to be deleted.

Annex C. Examples from EFSA and JMPR on concluded residue definitions

Annex C to be revised and shortened in order to increase its clarity. Several substances to be removed.

Chapter 2.3. Comparison of residue definitions within and between EFSA and JMPR

Chapter to be shortened and revised reflecting the changes in Annex C.

Annex D. Examples of metabolite to parent ratio for 10 compounds

Annex D to be revised improving its readability.

Annex E. Metabolite estimations – Case studies

Changes done to Annex E have been endorsed by the WG

3. Rationale for the outsourced project

Rationale will be added for the fourth project (QSAR for development and neurotoxicity).

4. Impact of metabolic processes on the toxicological properties of pesticide residues

Text in this chapter will be further amended to improve its clarity.

4.3. Approach currently applied by EFSA in peer review of pesticides

Further editorial revisions have been made.

7. Applicability of analysis in the evaluation of developmental and neurotoxicity effects of metabolites and degradates of pesticides: outcomes of outsourced activity

An introduction will be added.

8. Potential exposure to metabolites and degradation products

8.1. Introduction

Text to be amended reflecting changes done in Appendices D and E.

8.3. Models used for calculating the acute and chronic dietary exposure

Text on EFSA model to be added.

9.2 Application of the TTC approach: acute and chronic exposure

Text on TTC values to be expanded.

9.5.1. Testing strategy

Section to be expanded.

5. Miscellaneous

6. Next meeting

Thursday 24th (pm) – Friday 25th (am) November 2011 (Parma)

Istvan Sebestyen/Hans Steinkellner

PESTICIDES UNIT

Parma, 31 May 2011

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 12th Meeting of the Working Group on the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment

(Agreed by the WG in written procedure on 18 May 2011)

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Participants

WG Experts	Claudia Bolognesi (co-chair), Alan Boobis (on 29 April), Markus Müller, Yolanda Pico, Rebecca Scrivens (participated on 28 April by phone), Anita Strömberg (co-chair), Maria Tasheva, Christiane Vleminckx
EFSA:	Miriam Jacobs, István Sebestyén, Hans Steinkellner, Manuela Tiramani

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Bernadette Ossendorp.

2. Adoption of agenda

The agenda was adopted with modifications. It was agreed to go through the opinion chapter by chapter.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Draft opinion on the evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment

The new version of the draft opinion was circulated before the meeting. Several clarifications and editorial changes have been suggested during the meeting, not all of these are reflected in the Minutes.

As a general comment it was pointed out that the glossary should be extended as well as the list with abbreviations. Elements taken over from the reports of the outsourced activities should be clearly distinguished from the scientific consideration of the WG.

It was agreed to merge chapter 2.2 and chapter 7.2.1 (to be put under Chapter 7). The definition of conversion factors given in 7.2.1 should be used solely in the new merged chapter.

In regard to the paragraph on common moiety methods the relevant text should be rephrased in order to clarify the issue.

The text of Chapter 5. Threshold of Toxicological Concern (TTC) should be harmonized with the opinion of the Scientific Committee on the TTC.

It was agreed to explore the possible use for an acute TTC in a separate subchapter. Therefore public literature and application of time adjusted TTC elsewhere should be checked. Furthermore the ratios between ARfD and ADI should be explored in order to obtain a possible TTC conversion factor for short term exposures.

The inclusion of the decision trees in the opinion has been discussed again. The WG was of the opinion that the decision trees should be inserted.

In the Critical Issues chapter text on acute TTC was changed reflecting the discussions at the meeting. Explanation of the need for acute exposure calculation should also be inserted. It was agreed to add text on when the metabolite is covered by tests with the parent compound and the description of the testing strategy when exposure to metabolites is above respective TTC levels should be inserted as a subchapter.

Discussion of Appendices

It was suggested to shorten the Appendix A or to delete it. It will be discussed on the next meeting.

The examples in the table of Appendix B should be reconsidered and replaced with more recent examples (substances in Annex I).

Tables in Appendix E should be rearranged (ie. add key to the tables upfront or add legend to every table) and colour coding should be replaced.

5. Miscellaneous

The members discussed again the inclusion of the assessment of pesticide isomers in the present opinion given the fact also that the opinion cannot be adopted before the Scientific Committee finishes its work on TTC (i.e. autumn 2011).

6. Next meetings

28th p.m. – 29th a.m. June, Parma

PPR UNIT

Parma, 25th April 2011

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

**Minutes of the 11th meeting of the Working Group
on Toxicological Relevance of Pesticide Metabolites for Dietary Risk assessment
Parma, 17-18 March 2011**

Agreed by the WG on 18th April 2011

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Participants

WG Experts	Claudia Bolognesi (chair), Rebecca Scrivens, Anita Strömberg(co-chair), Maria Tasheva, Christiane Vleminckx, Yolanda Pico, Markus Muller
Hearing experts	Ian Dewhurst, Albert Bergmann
EFSA:	István Sebestyén, Hans Steinkellner, Manuela Tiramani, Miriam Jacobs (on 17 March)

1. Welcome and apologies

The Chair (Claudia) welcomed the participants. Apologies were received from Andrew Worth, Alan Boobis and Bernadette Ossendorp.

2. Adoption of agenda

The agenda was adopted with modifications. The order of items was changed. It was agreed to discuss the draft opinion chapter by chapter.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion of the updated and consolidated version of the Draft Scientific Opinion (distributed to the PPR Panel on 7th March) chapter by chapter and in context with relevant/corresponding appendices

The consolidated version of the opinion was circulated before the meeting.

The starting point for the draft opinion were the final reports from the outsourced projects where applicability of the TTC concept, the impact of metabolism on toxicity and the applicability of QSARs were explored. It was agreed that elements taken over from the reports to be clearly distinguished from the scientific considerations of the WG.

The group agreed that more detailed text to be given on the scarcity of toxicological studies with metabolites and the fact that those available are usually acute toxicity studies.

The working assumption that there are no non-neurotoxic substances yielding neurotoxic metabolites should be explained in more details.

It was agreed that the framework presented in the JRC QSAR report regarding the evaluation of usefulness of the models should be included.

A subchapter on the use of QSAR models for determination of equivalency should be included in the next version of the draft opinion.

Additional text on models for calculating the acute and chronic dietary exposure to address the comments made on UK and EU approaches versus WHO should be inserted.

The group agreed that a section providing the considerations of the WG regarding the acute exposure will be elaborated in the next version.

TTC approaches used by the other institutions/regulatory bodies should be summarised in the relevant chapter.

It was agreed to insert detailed text on “weight of evidence” approach for assessment proposed by the WG in the next version of the draft opinion.

A new chapter was inserted during the meeting based on the text on the approach to metabolite residue estimation provided by the rapporteur.

Several clarifications and editorial changes were made in the text of the draft opinion during the discussion.

Appendices

Since the Annexes C (examples of metabolite to parent ratio for 10 compounds) and D (metabolite estimations case studies) were new and had not been considered previously by the whole WG, the approaches that had been taken were discussed

5. Miscellaneous

The WG discussed the possible extension of the current mandate to include also approaches for the evaluation of isomer mixtures.

6. Next meetings

28/29 April 2011 pm/am in Parma

28/29 June 2011 pm/am in Parma

PPR UNIT

Parma, 24th February 2011

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 10th meeting of the Working Group on Toxicological relevance of pesticide metabolites for dietary risk assessment

Parma, 20-21 January 2011

Agreed by the WG on 18th February 2011

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Participants

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Rebecca Scrivens (participated on 22 January by phone), Anita Strömberg, Maria Tasheva, Christiane Vleminckx, Yolanda Pico, Andy Hart (only for agenda point 4.d)

EFSA: István Sebestyén, Hans Steinkellner, Miriam Jacobs (on 21 January), Manuela Tiramani, Jean-Pierre Cugier (on 21 January)

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Alan Boobis, Otto Meyer, Angelo Moretto, Markus Müller, Rebecca Scrivens (on 21 January).

2. Adoption of agenda

The agenda was adopted with modifications. Included were agenda points on a discussion of the outcome of the teleconference on exposure issues that took place before the meeting, on the use of the results from the Multicase studies and the presentation from Andy Hart on an approach to assess uncertainties.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Draft opinion on the evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment

The new version of the draft opinion was circulated before the meeting. Several editorial changes have been suggested during the discussion, but not all of these are reflected in the Minutes.

a. Outcome of the teleconference

The WG overviewed the outcomes of the teleconference. It was agreed that approach to exposure calculation is crucial for further steps in the overall assessment, so all possible options have to be discussed in the opinion. In the case studies the most conservative and the least conservative option will be used to demonstrate the differences in the approaches. The observation in residue trials showed different parent/metabolite ratios depending on the length of PHI. It should be discussed in the opinion and the data on residue trials and summaries should be attached as an annex

b. Use of the results of commercial QSAR software

The results obtained in this exercise will not be included in the opinion.

c. Discussion of testing strategy based on the draft decision tree of the last meeting

It was agreed to follow the approach of the Genotoxicity WG of the SC that a reduced in vitro data package (*i.e. Ames test plus in vitro micronucleus test*) is considered as sufficient for assessment and that the 3rd in vitro test currently carried out (*i.e. an in vitro gene mutation assay*) could be omitted

d. Discussion of the new draft version of the opinion (new and revised chapters, new contributions)

Additional text to be inserted regarding neurotoxic metabolites that there is no pesticide examples of neurotoxic metabolites arising from non-neurotoxic parent compounds, but the possibility that this might occur cannot be excluded. It is important to note that these metabolites are not included in the TTC approach unless the already characterised toxicophore was formed during metabolism.

In Chapter 7 further explanation of the proposal of two in vitro tests for first tier genotoxicity evaluation (instead of three) should be provided as agreed during the teleconference

e. Discussion of new Chapter 7 Potential exposure of metabolites and degradation products in the human diet

It was discussed that considering the practice that chronic exposure assessment for parent compound is always made and acute assessment is performed when an ARfD is allocated, also for the metabolites a chronic exposure estimate will always be needed and acute exposure estimation should be made when acute effect of the metabolite is expected based on QSAR evaluation or weight of evidence assessment (on-going SLA with the JRC).

Conclusions based on information on parent/metabolite ratios at different PHIs should be added to this chapter.

f. Discussion of new Chapter 9 Uncertainties

It was agreed to draft a chapter, based on the approach that the PPR Panel took in previous opinions and in line with the Opinion of the SC on how to present uncertainty in dietary exposure assessments.

g. Finalization of the case studies

It was agreed that in the case studies the most and least conservative approach for extrapolation of parent/metabolite ratio will be used in order to work out the differences between the approaches. The first estimation will be performed by extrapolating the highest metabolite ratio from one crop to all crops (i.e. apple to all crops) and the second estimation will be performed without extrapolation applying of the ratio to the crop in which the metabolite was found.

h. Identification and discussion of other issues requesting further elaboration

Insert text that possible combined action of structurally similar metabolites and parent compounds have been considered by the PPR Panel. No further work than that is necessary

i. Discussion of work program to finalize the opinion, timelines

The WG discussed that the adoption of the opinion was planned at the June plenary meeting. Possible extension of the deadline (and consequently adoption) had to be considered should the evaluation of isomers and introduction of an additional chapter on isomers be agreed.

j. Presentation of a weight of evidence evaluation example

A “weight of evidence” evaluation example for the treatment and expression of uncertainties in risk assessment was presented to the WG members. The group agreed that presentation of this approach would be more useful in the guidance document and it is not feasible to have this approach in the opinion.

5. Miscellaneous

The WG experts agreed that the draft decision tree should be integrated in the opinion (maybe in form of an Annex).

EFSA note: EFSA proposes discussing integration of the draft decision tree in the guidance at the next meeting.

6. Next meetings

17/18 March 2011 pm/am in Parma

28/29 April 2011 pm/am in Parma

28/29 June 2011 pm/am in Parma

PPR UNIT

Parma, 04 February 2011

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

**Minutes of the 9th meeting (teleconference) of the Working Group on
Toxicological relevance of pesticide metabolites for dietary risk assessment**

Agreed by written procedure on 25 January 2011

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Date:	14 January 2011
Time:	14:00–16:00 CET
Place:	Teleconference

Participants

WG Experts Bernadette Ossendorp (Chair), Rebecca Scrivens, Yolanda Pico,
Anita Stromberg, Andy Hart

EFSA: István Sebestyén, Hans Steinkellner, Jean-Pierre Cugier

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Luc Mohimont.

2. Adoption of agenda

Adopted without comments.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion about the handling of the conversion factor

It was agreed to make the estimations of exposure on an individual metabolite basis and that the residue trial data were preferred to those from metabolism studies since they reflect actual application methods and rates and therefore give more realistic values

It was noted that case studies should be further scrutinised. The group agreed that the outcome from case studies was needed to see if the suggested approaches worked. In the opinion the different approaches should be described and that resulting recommendations should be given only in the guidance.

5. Discussion about the calculation method of the metabolite levels in the case study, how we can use the results of the case study in the opinion

Agreed that the different options for performing the exposure estimations should be presented in the opinion and also that it was important that they fit into the overall evaluation scheme.

6. Miscellaneous

PPR UNIT

Parma, 21st December 2010

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

**Minutes of the 8th meeting of the Working Group
on Toxicological relevance of pesticide metabolites for dietary risk
assessment**

25-26 November 2010

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Participants

WG Experts Bernadette Ossendorp (Chair), Claudia Bolognesi, Markus Müller, Rebecca Scrivens (only on 26 November), Anita Strömberg, Maria Tasheva, Claudia Bolognesi, Christiane Vleminckx, Angelo Moretto, Yolanda Pico, Alan Boobis

EFSA: István Sebestyén, Hans Steinkellner, Manuela Tiramani

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Otto Meyer.

2. Adoption of agenda

After adding agenda point "Service Level Agreement (SLA) with JRC" the agenda was adopted.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Service Level Agreement (SLA) with JRC (new agenda point)

A new project was started aimed at identifying QSAR models for identifying neurotoxic and developmental effects in order to insert them as assessment tool in an overall decision tree for pesticide metabolites.

The reason for this project is the need to handle short term exposures in the TTC scheme. Although the various TTC thresholds are based on chronic toxicological studies and therefore cover acute effects, the ratios between short-term and chronic dietary exposures

are often greater than the ratios between the acute and chronic toxicological reference values. As setting of an ARfD for a pesticide is in a very high proportion triggered by specific developmental and, to a lesser extent, neurotoxic effects, it was decided to investigate the potential of QSAR tools to predict these effects.

5. Draft opinion on the evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment

a) Discussion of the new draft version of the opinion (new and revised chapters)

4.1.1 Criteria for evaluating toxicological profiles of metabolites

It was agreed to add text on intermediates and on bound/conjugated residues and factors for evaluation of toxicological profile.

4.3.1 Considerations of the new OECD guidelines on toxicokinetics -OECD TG 417-

It was agreed to reduce the text to the minimum necessary.

4.3.2 Conclusion on proposal of when toxicity of metabolite can be considered covered by the parent

It was agreed that further recommendations to improve reporting format for ADME studies should be given.

7. Critical Issues

Further text and clarification on genotoxicity alert will be inserted. Further text on neurotoxicity should also be added explaining the general principles applied for this endpoint.

b) Case studies (harmonisation of exposure calculations, what do we want to benefit from the case study, where will be the results of the case study discussed and evaluated in the opinion, extension of the case study with compounds that have full data package for both the parent and metabolites)

It was agreed that case studies should be discussed in the main text of the opinion.

c) Discussion of the generic issues identified during the previous meetings (the definition of genotoxicity to be applied for the TTC, optimization of assessment strategy of genotoxicity, assessment of metabolites based on the toxicological profile of the parents, animal/non animal testing strategy when the metabolite is not covered by the studies with parent compound, acute exposure in TTC scheme, uncertainties in exposure predictions, uncertainties of application of non-testing methods)

d) Discussion of the approach of the WG to evaluate the toxicological relevance of metabolites and the decision tree suggested in the AGES report

It was agreed that a decision tree should be integrated in the guidance document.

e) Identification and discussion of other issues requesting further elaboration,

Chronic and acute exposure considerations for metabolites will be considered in the opinion. A chapter on calculation of metabolite levels and on the outsourced projects will be integrated in the opinion. An additional chapter on uncertainties in the risk assessment of metabolites will be added.

a) Discussion of work program to finalize the opinion.

It was agreed that a first draft opinion should be presented at the Plenary meeting in March and that a stakeholder workshop should be organised to discuss the risk management options that might be contained in the draft guidance.

8. Miscellaneous

9. Next meetings

Second week of January 2011 (date to be determined) - Teleconference -exposure part

20/21 January 2011 pm/am in Parma

17/18 March 2011 pm/am in Parma

28/29 April 2011 pm/am in Parma

28/29 June 2011 pm/am in Parma

PPR UNIT

Parma, 03 November 2010

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 7th meeting of the Working Group on Toxicological relevance of pesticide metabolites for dietary risk assessment

Amsterdam, 12 October 2010

EFSA / PPR Unit

Agreed by written procedure on 03 November 2010.

Participants

WG Experts	Bernadette Ossendorp (Chair), Claudia Bolognesi, Markus Müller, , Rebecca Scrivens, Anita Strömberg, Maria Tasheva,
Hearing Experts	Andrew Worth
EFSA:	István Sebestyén, Hans Steinkellner

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Alan Boobis, Angelo Moretto, Yolanda Pico, Christiane Vleminckx

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Draft opinion on the evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment

- a) New draft version of the opinion (introduction, exposure part, toxicology part, annexes 1 and 2)

The revised version of the opinion was circulated before the meeting. Text about the new OECD Guideline on Toxicokinetics (OECD TG 417) still has to be integrated. The group also agreed that guidance on when a metabolite is covered by testing the parent compound should be given. The group agreed that adding a section on the recommendations on reporting the results of the ADME studies would be useful.

Text on PBPK modelling will be added as well. It was noted that this issue of the use of livestock studies should be reflected also in the opinion. An updated version of Annex I was presented.

- b) Situation regarding the case studies (toxtree analysis, toxicological data on metabolites, harmonisation of exposure calculations, what do we want to benefit from the case study)

It should be agreed during the November meeting, how the results of the case studies will be interpreted.

- c) Discussion of the generic issues identified during the previous meeting

The group agreed that addressing the neurotoxicity issues is very important. The new project on further investigation of the applicability of QSAR analysis for the evaluation of developmental and neurotoxicity effects for the assessment of toxicological relevance of pesticide metabolites was presented.

- d) Discussion of the approach of the WG to evaluate the toxicological relevance of metabolites and the decision tree suggested in the Ages report

Due to time constraints this discussion was postponed to the next meeting.

- e) Identification and discussion of other issues requesting further elaboration, involvement of experts not attending the meetings of the core WG

Uncertainties in the assessment will be addressed in a separate chapter which should contain the lessons learnt and the issues need further research in the future.

5. Miscellaneous

- a) Feedback from OECD Washington meeting

An overview on the Guidance documents on crop field trials and livestock feeding are currently being produced by OECD was given.

6. Next meetings

25 - 26 November 2010, Parma
20 - 21 January, 2011, Parma
17 - 18 March, 2011, Parma
28 - 29 April, 2011, Parma
28 - 29 June, 2011, Parma

PPR UNIT

Parma, 16th September 2010

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 6th meeting of the Working Group on the Toxicological relevance of pesticide metabolites for dietary risk assessment

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Parma, 1st – 2nd July, 2010

Agreed by the WG on 15 September 2010

Participants

WG Experts	Bernadette Ossendorp (Chair), Claudia Bolognesi, Alan Boobis, Angelo Moretto (on 2 nd July only), Markus Müller, Yolanda Pico, Rebecca Scrivens, Anita Strömberg, Maria Tasheva, Christiane Vleminckx
EFSA:	Luc Mohimont (PPR), Istvan Sebestyen (PPR), Hans Steinkellner (PPR), Manuela Tiramani (PRAPeR), Miriam Jacobs (AMU, on 2 nd July only)

1. Welcome and apologies

The Chair welcomed the participants. No apologies were received.

2. Adoption of agenda

The agenda was adopted.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting

4. Draft opinion on the evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

- a) New draft version of the opinion (introduction, exposure part, toxicology part, annexes 1 and 2)

Two breakout groups were formed, one for the toxicology- and one for the exposure residue/section.

Discussion in breakout groups on exposure and toxicology chapters of the opinion

Exposure group:

The exposure group examined the new version of the exposure part of the opinion prepared by the rapporteur on the basis of the contributions of the members of the WG as agreed during the previous meeting.

Toxicology group:

Text has been rearranged reflecting that different substance groups have been excluded from the TTC concept based on different considerations. Text justifying why the project focussed on genotoxicity will be added.

Text on the new ADME guideline should be integrated in the opinion and suggestions for the future regarding ADME studies should be added to the text.

The group suggested discussing in this chapter the criteria when metabolites can be considered as covered by the toxicological tests with the parent compound.

Joint discussion summarizing the points agreed in the breakout groups

It was noted that there are two types of analytical methods one for use in studies for registration and one for monitoring enforcement. Text will be restructured accordingly. The proposed approach of the WG should be elaborated as a next step. The applicability of the revised decision tree from the Ages report should be discussed during the next meeting in October.

The WG adopted the minutes of the previous meetings on 20th May 2010.

5. Next meetings

Tuesday 12 October – whole day – in Amsterdam Airport
Thursday 25 November p.m. – Friday 26th November a.m. – Parma.

Luc Mohimont / István Sebestyén / Hans Steinkellner

PPR UNIT

Parma, 26th May 2010

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 5th meeting of the Working Group on the Toxicological relevance of pesticide metabolites for dietary risk assessment

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

EFSA PPR Unit

Agreed by the WG on 01/July 2010

Participants

WG Experts	Bernadette Ossendorp (Chair), Claudia Bolognesi, Alan Boobis, Angelo Moretto, Markus Müller, Yolanda Pico, Rebecca Scrivens (by phone), Anita Strömberg, Maria Tasheva, Christiane Vleminckx
Hearing Experts	---
Observers (eg.EC)	---
EFSA:	Miriam Jacobs (AMU), Manuela Tiramani (PRAPeR), Luc Mohimont (PPR), Istvan Sebestyen (PPR), Hans Steinkellner (PPR)

1. Welcome and apologies

The Chair welcomed the participants. No apologies were received.

2. Adoption of agenda

The agenda was adopted with changing the order of items 4 and 5.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting

4. Discussion about the text of the opinion

The experts discussed extensively the new version of the introduction circulated before the meeting. Several changes and clarification of the text were proposed and agreed upon. The main discussion points were the definition of pesticide residues, the relationship between EU and OECD and the collaboration with the OECD WG on Pesticides. A new paragraph was

inserted on CODEX Alimentarius/JMPR framework. The differences between JMPR and EU residue definitions were discussed as well as the insertion of a new paragraph on the progresses in residue analytical methodology and interactions with developments for comprehensive residue definition.

The content of Annex I was taken from the OECD guidance document. It was agreed that written comments will be provided in this regard.

The experts agreed that it was useful to have examples in Annex 2 showing how JMPR and EU approaches differ not only on the final decision on the residue definition for risk assessment, but also in the underpinning scientific rationale. Altogether 10-15 examples starting from the latest EU evaluations will be sufficient. The text will be updated as agreed.

5. Discussion about the results of the sample calculations

Experts were guided through the exposure calculations. It made clear that all three TTC thresholds will very likely be exceeded. Significant differences were observed between the acute and chronic exposures. The experts discussed the possibilities of the comparison of the acute exposures directly with TTCs. It was agreed that practices already existing for other types of chemicals or appropriate reviews of compared acute and chronic toxicities will be investigated. The experts agreed that possible mitigation mechanisms and expert judgement to be used for evaluating the relevance of acute exposure estimations in the TTCs framework will also be investigated. The sequence of application of the Cramer prediction tree and the read across approach will be discussed in the opinion.

The group agreed to apply the Cramer prediction tree to the metabolites of the 7 substances used as case studies. The objective is to know if a substantial percentage of the metabolites would be categorized as belonging to Class II and therefore referred to a higher TTC. As another refinement of the calculation the availability of specific toxicological data for the metabolites evaluated in the case study will be checked. It was agreed that another possibility of refinement of the exercise would be to apply computational toxicology/chemical structure assessment to metabolites not passing the genotoxicity and neurotoxicity thresholds.

The experts agreed that considering the extension taken by this exercise, the case studies will be included as an appendix to the opinion for illustrative purpose.

6. Miscellaneous

The notes of the small group teleconference meeting of 12 May were adopted by the participant to the meeting and endorsed by the WG.

7. Next meetings

Thursday 1st July p.m. and Friday 2nd July a.m. – Parma

Tuesday 12 October – whole day – Amsterdam or Brussels Airport

Thursday 25 November p.m. – Friday 26th November a.m. – Parma

Luc Mohimont / István Sebestyén / Hans Steinkellner

PPR UNIT

Parma, 12th May 2010

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the teleconference of the Working Group on the Toxicological relevance of pesticide metabolites for dietary risk assessment

Restricted group meeting on the introduction of the opinion and exposure calculations to pesticides metabolites on 12th May 2010.

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

EFSA PPR Unit

Agreed by the WG on 20/05/2010

Participants

WG Experts	Bernadette Ossendorp (Chair), Claudia Bolognesi, Yolanda Pico, Rebecca Scrivens, Anita Strömberg
Hearing Experts	---
Observers (eg.EC)	---
EFSA:	Luc Mohimont, Istvan Sebestyen, Hans Steinkellner

1. Welcome and apologies

The Chair welcomed the participants. No apologies were received.

2. Adoption of agenda

The agenda was adopted with changing the order of items 4 and 5.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting

4. Discussion about the results of the sample calculations

The participants discussed the results of the sample calculations and agreed that the trends shown by the exercise indicate that the acute and chronic exposure to pesticide metabolites will frequently exceed all three key thresholds of the TTC scheme. This applies to both

mammalian and non-mammalian metabolites. The results of the different calculations will be collated in a separate document and circulated to the members of the WG before the next meeting. During the next meeting the WG will also discuss the results of these calculations and decide whether the exercise needs to be proceeded further e.g. by including further refinements.

5. Discussion of the new version of the introduction

The commented version of the Introduction section was circulated before the teleconference. The experts agreed that a new text will be drafted on the relationship with OECD. The paragraphs related to 'Comparison of residue definition within and between EU and JMPR' and 'inconsistencies in the definitions of pesticide residues' will be amended. Further considerations will be integrated on how the line between risk assessment and risk management is drawn differently in different contexts. A discussion issue was also the definition of pesticide residues. The opinion will make clear that there are different sources of the definition, in particular regulation 396/2005. Then it was agreed that a new text will be provided on the toxicological considerations applicable to the relevance of metabolites addressing the challenges regarding both quantitative and qualitative differences between the active substances and the metabolites.

Another issue to be considered were conversion factors and the difficulty or uncertainty when these factors are to be addressed in a monitoring context. The experts agreed that uncertainty issues related to this mandate should be addressed in the opinion. Then the participants discussed the content of the Annex 2 and agreed to transfer it into a tabular form.

6. Miscellaneous

In case of problems to reach Parma by plane a telephone conference will be organised instead.

PPR UNIT

Parma, 5th May 2010

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 4th meeting of the Working Group on the Toxicological relevance of pesticide metabolites for dietary risk assessment

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

EFSA PPR Unit

Agreed by the WG in written procedure on 30 April 2010

Participants

WG Experts	Bernadette Ossendorp, Claudia Bolognesi, Alan Boobis, Otto Meyer, Angelo Moretto, Markus Müller, Yolanda Pico, Rebecca Scrivens, Anita Stromberg, Maria Tasheva, Christiane Vleminckx
Hearing Experts	-----
Observers (eg.EC)	-----
EFSA:	Luc Mohimont, Istvan Sebestyen

1. Welcome and apologies

The Chair welcomed the participants. No apologies were received.

2. Adoption of agenda

The agenda was adopted without changes. The minutes of the previous meeting were adopted.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion about the working procedure for the opinion

The experts discussed extensively how to best organise the work for the opinion as the mandate required substantial expertise in different fields. It was agreed that some topical issues could be addressed in tele-meetings between smaller groups. Since the new draft OECD guidance on the definition of residue for monitoring and for risk assessment will be duly considered for drafting the present opinion it was agreed that OECD work and EFSA collaboration with OECD should be reflected adequately in the opinion.

Uncertainties in the use of the TTC concept and the usefulness of the different QSAR models should be addressed. The working documents circulated to the group before the meeting summarized the results of the three outsourced projects very well, but new thoughts and concepts should be elaborated and integrated to the opinion.

5. Discussion in breakout groups on exposure and toxicology

Toxicology group:

The rapporteur has circulated the drafts of the Chapters 3 and 4 of the opinion before the meeting. The text on the applicability of the TTC concept was discussed in detail and several changes were proposed and agreed upon. Discussion items were also the text on the scope of the TTC concept in the present context, description of the criteria for the exclusion of certain substances, addition of relevant references, insertion of text on JECFA and EMEA approaches, application of the TTC scheme for children and for acute effects, assessment of metabolites not identified in rats and relevance of metabolites found in livestock.

Exposure group:

Discussed were OECD and also FAO activities in regard to residue definitions of pesticides. It was agreed that text on that should be inserted in the opinion. An issue was also how to define “pesticide residue” as diverging definitions existed and applied by different bodies. The EU guidance document on the assessment of groundwater metabolites had to be considered as well as it contained TTC elements. Another issue to be considered were conversion factors that are currently used only by EFSA, the complexity of establishing residue definitions for risk assessment, single definitions for all commodities vs. different definitions for particular commodities and the impact of analytical methodologies.

6. Joint discussion summarizing the points agreed in the breakout groups

The rapporteurs gave an overview on the discussion of the break out groups and the agreements achieved. The WG then discussed a preliminary scheme of testing the acute and chronic assessments of the metabolites not included in the rat metabolism. For this task EFSA and a WG member will run calculations for metabolites of 10-20 substances from the DARs and compare the chronic and acute intakes of metabolites of selected compounds to the TTC thresholds.

It was noted that the work of the Genotoxicity WG and the TTC WG of SCAF are relevant for the Panel mandate. The WG will follow their work.

7. Miscellaneous

A teleconference will be organized on 12th May from 10: to 12:00 for the residue subgroup.

8. Next meetings

Wednesday 12 May p.m. – Teleconference

Thursday 20 May p.m.

Thursday 1 July p.m. and Friday 2 July a.m.

Tuesday 12 October – whole day

Thursday 25 November p.m. – Friday 26th November a.m.

Luc Mohimont/István Sebestyén

PPR UNIT

Parma, 5th May 2010

SCIENTIFIC PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the 3rd meeting of the Working Group on the Toxicological relevance of pesticide metabolites for dietary risk assessment

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

EFSA PPR Unit

Agreed by the WG on 03 March 2010

Participants

WG Experts	Bernadette Ossendorp (Chair), Claudia Bolognesi, Alan Boobis, Otto Meyer, Rebecca Scrivens, Maria Tasheva, Christiane Vleminckx, Anita Stromberg, Yolanda Pico, Susanne Hougaard, Karen Hirsch-Ernst, Angelo Moretto, Andrew Worth, Ian Dewhurst, Albert Bergmann
Hearing Experts	---
Observers (eg.EC)	---
EFSA:	Manuela Tiramani, Miriam Jacobs, Luc Mohimont, Istvan Sebestyen, Hans Steinkellner

1. Welcome and apologies

The Chair welcomed the participants. Apologies were received from Markus Mueller.

2. Adoption of agenda

"Discussion on the structure of the work plan for the opinion" was added as an additional agenda point.

3. Declarations of interest

In accordance with EFSA's Policy on Declarations of Interests, EFSA screened the Annual Declaration of interest (ADoI) filled in by the experts invited for the present meeting. No

conflicts of interests related to the issues discussed in this meeting have been identified during the screening process or at the beginning of this meeting.

4. Discussion about the final reports from the three outsourced projects (TTC, QSAR, Metabolism)

The chair gave a brief overview about the scope of the opinion and the three outsourced projects. After the TTC report that was delivered already earlier on, the final reports from the other two projects were available now. It was aimed at having the guidance document on the residue definition ready by end of 2012. Since the new guidance document will be highly relevant also for OECD an OECD observer will be part of the WG from the next meeting on. The contractor for the TTC project gave a presentation on the final report which was endorsed by the WG members. Then the report of the project on the impact of metabolism was presented. This presentation was followed by the presentation of the QSAR project. It was pointed out by the contractor that rather late in the stage of the on-going work the scope of the project had been changed (i.e. to focus on the assessment of genotoxicity). In addition to that had an additional data set (i.e. EU classified genotoxins) been analysed as it has been judged as more adequate for the present project. The project report was endorsed by the members of the WG. After a brief discussion it was agreed by the experts that new pesticides classes could not be covered in the opinion/guidance document as they were not part of the data sets in the present projects.

5. Discussion about the structure of the opinion

The two rapporteurs for the opinion presented a draft structure for the opinion containing the main issues to be addressed in the individual chapter. The experts discussed the draft extensively and agreed to it after further suggestions for revisions.

6. Discussion about the work plan for the opinion (new agenda point)

The first draft opinion should be discussed at the next meeting of the WG on 8th of April.

7. Miscellaneous

8. Next meetings

- 8 April whole day
 - 20 May p.m. and 21 May a.m.
 - 1 July p.m. and 2 July a.m.
 - 12 October – whole day
 - 25 November p.m. – 26th November a.m.
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PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

WG on the Toxicological relevance of pesticide metabolites for dietary risk assessment

Permanent Working Group

Mandate: Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

Meeting minutes

Meeting date:	7th September 2009
Venue:	EFSA Parma DUSB 02/001,
Time:	10.00 -18.00 h

1. Welcome of the participants, apologies, declarations of interests

The Chair welcomed the participants. The meeting was attended also by

Panel members: Claudia Bolognesi, Anita Stromberg, Maria Tasheva and Christiane Vleminckx

Hearing experts: Ian Dewhurst (CRD), Albert Bergmann (AGES), Andrew Worth (JRC)

EFSA staff: Miriam Jacobs, Luc Mohimont, Hans Steinkellner and Manuela Tiramani.

Apologies: Markus Mueller, Alan Boobis, Bernadette Ossendorp.

For this meeting no other interests than those already declared in the ADoI or in a previous SDoI and screened by EFSA in accordance with its policy on declarations of interests and implementing documents thereof was declared by the experts.

2. Adoption of the draft agenda, adoption of draft secretary notes from the previous meeting (31st March)

The draft agenda was adopted without changes. Draft secretarial notes of the previous meeting were adopted prior to the meeting by written procedure.

3. Presentation and discussion of the interim reports of the QSAR and Metabolism Project and the final report of the TTC project

3.1 TTC Project.

Ian Dewhurst gave a presentation on the final report of the project. He outlined the scope of the project and described the methods applied to achieve the different goals set for the project. The final report was already endorsed by Steering Committee.

3.2 QSAR Project.

Andrew Worth presented the scope of the project and the work done at the interim stage of the project. A lot of comments have been given and the workplan for the project has been amended accordingly. The project focussed, because of the outcome of the TTC project, on the assessment of genotoxicity now.

3.3 Project on the impact of metabolism on the toxicity of active substances.

The contractor gave a presentation on the scope of the project results achieved at the interim stage of the project on impact on metabolism. It was clear already at this stage of the project that no firm conclusions could be drawn on the toxicity of a metabolite only on bases of looking at the metabolic pathway the compound followed. The work on the development of criteria when the toxicity of a metabolite can be considered as covered by the tests carried out with the parent compound is just about being started.

3.4 Possible options regarding genotoxicity at this stage.

The experts then discussed the weaknesses of some computational models regarding genotoxicity (many false positives and false negatives). Several options how to deal with genotoxicity were raised during the discussion, like for instance testing the genotoxic properties of all compounds above the TTC threshold for genotoxicity, exploring further applicability of models/combination of models and consolidating the evaluation of genotoxic potential by expert judgment.

3.5 Other points of discussion.

The experts agreed that scientific knowledge and approaches regarding pharmaceuticals could be interesting for the current mandate and should be investigated.

4. Objectives and discussions of next steps

A rapporteur each for the toxicological and for the residue part was appointed. A first proposal for the structure of the opinion will be discussed and further developed at the next meeting of the WG Toxicology of Pesticides on 29th to 30th of October.

5. Any other business

Next meeting:

9th February 2010

Luc Mohimont / Hans Steinkellner

Parma, 19 October 2009

PANEL ON PLANT PROTECTION PRODUCTS AND THEIR RESIDUES

Minutes of the meeting of the Working Group on the toxicological relevance of pesticide metabolites

London, 31st March 2009

Scientific opinion of the PPR Panel on evaluation of the toxicological relevance of metabolites and degradates of pesticide active substances for dietary risk assessment.

(Adopted by the WG on 7th September 2009)

Participants

WG Experts: Bernadette Ossendorp (Chair), Alan Boobis, Angelo Moretto and Christiane Vleminckx.

Hearing Experts Andrew Worth, Albert Bergmann and Ian Dewhurst.

Observers (e.g. EC): -

EFSA: Luc Mohimont and Hans Steinkellner.

1. Welcome and apologies

Luc Mohimont welcomed the participants. Apologies were received from Claudia Bolognesi and Markus Mueller.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of interest

EFSA secretariat screened the ADol and SDol filled in by the scientific experts invited at this meeting in accordance with EFSA's Policy on Declarations of Interests.

In addition, some WG members wished to indicate several interests at the beginning of the meeting. Bernadette Ossendorp declared an interest from her participation in drafting the OECD guidance document. Alan Boobis has been involved in other projects on TTC at international level. Angelo Moretto is a member of the Expert Consultative Group advising the contractor in the framework of a Grant Agreement performed as support to this mandate. These interests above were not deemed to represent conflicts of Interest for the experts concerned.

Ian Dewhurst, Albert Bergmann and Andrew Worth have an interest as scientific coordinators of the activities outsourced by EFSA and connected to this mandate. In accordance with EFSA's Policy on Declarations of Interests and Implementing documents thereof, and taking into account the specific matters discussed at the meeting in question, these interests were

deemed to represent conflicts of Interest (level C). For this reason, these experts were involved as hearing experts.

No other conflicts of interest related to the issues discussed in this meeting have been identified earlier during the screening process.

4. Discussions

A chair of the WG was elected.

The objectives of the mandate and the remit of the WG were discussed. The WG will first act as an exchange platform in order to coordinate outsourced scientific activities under 2 Article 36 Grant Agreements and 1 Service Level Agreement. These activities will be ongoing in 2009 and aim at providing scientific support to the mandate. The WG will be informed about the progress of these activities and will discuss options in order to optimize their respective outcomes and complementarities. The WG will later on develop and draft a scientific opinion on the evaluation of the toxicological relevance of pesticide metabolites.

It was also agreed to involve OECD in the WG given the close relationship between the objectives of this mandate and current OECD activities and published guidance regarding the residue definition of pesticides.

5. Miscellaneous.

The next meeting of the WG is planned on 7th September 2009.
