SCIENTIFIC COMMITTEE

Minutes of the 8th meeting of the Working Group on Carvone

20 May 2014, Amsterdam

(Agreed on 26 May 2014)

Participants

- Working group Experts:

  Paul Brantom, Qasim Chaudhry, Karl-Heinz Engel, Jean-Charles Leblanc, Bernadette Ossendorp (Chair)

- EFSA:

  SCER Unit : Bernard Bottex, Jean Lou Dorne

1. Welcome and apologies

The Chair welcomed the participants. The purpose of the meeting was to finalise the draft opinion before it goes to the Scientific Committee for electronic review and possible adoption at the next Plenary meeting (8-9 July 2014).

2. Adoption of agenda

The agenda was adopted as tabled.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[2], EFSA screened the Annual Declaration of interest and the Specific Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

[1] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[2] http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf

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4. Adoption of the minutes of the 7th working group meeting held on 10 – 11 March 2014

The participants adopted the draft minutes of the 7th working group meeting held on 10 and 11 March 2014 via conference call. The minutes will be published on the EFSA website.

5. Scientific topic for discussion

5.1 Draft opinion on carvone (EFSA-Q-2013-00290)

The participants considered the comments made by the Scientific Committee during the 3-4 April 2014 SC Plenary meeting to update the draft opinion.

5.2 Next steps and actions

- All contributions to be sent to the Secretariat **by 6 June 2014 at the latest**
- 6 June – 20 June 2014: review of the draft opinion by the Scientific Committee. Comments to be provided to the Secretariat by email
- 20 – 27 June 2014: the working group addresses possible comments made by the Scientific Committee to update the opinion
- 1 July 2014: the draft opinion is sent to the Scientific Committee for possible adoption at the 68th SC Plenary meeting (8-9 July 2014)

6. Next meeting

A conference call will be programmed during the week of 23 – 27 June 2014 to address possible comments raised by the Scientific Committee.

SCIENTIFIC COMMITTEE

Minutes of the 7th meeting of the Working Group on Carvone

Tele-conference, 10-11 March 2014

(Agreed on 20 May 2014)

Participants

- Working Group Experts:

  Paul Brantom, Qasim Chaudhry, Karl-Heinz Engel[1], Jean-Charles Leblanc[2], Bernadette Ossendorp (Chair)

- EFSA:

  SCER Unit (Bernard Bottex, Jean Lou Dorne)

1. Welcome and apologies

The Chair welcomed the participants. The purpose of the conference call was to consider the comments made by the Scientific Committee during its last Plenary meeting to review the draft opinion.

2. Adoption of agenda

The agenda was adopted as tabled.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[3] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[4], EFSA screened the Annual Declaration of interest and the Specific Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

[1] Participated in day 1 only
[2] Participated in day 2 only
[3] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[4] http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf

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4. Adoption of the minutes of the 6th working group meeting held on 22 January 2014

The participants adopted the draft minutes of the 6th working group meeting held on 22 January 2014 via conference call. The minutes will be published on the EFSA website.

5. Scientific topic for discussion

5.1 Draft opinion on carvone (EFSA-Q-2013-00290)

The participants considered the comments *made by the Scientific* Committee during the 18-19 February 2014 SC Plenary meeting to update the draft opinion.

The draft opinion will be presented again for discussion and possible adoption at the 3-4 April 2014 Plenary meeting of the Scientific Committee. The draft opinion will be sent to the Scientific Committee for prior reading by end of 26 March 2014.

In view of the above timeframe, all identified actions and resulting contributions will be provided to the Secretariat by 18 March 2014.

6. Next meeting

No additional meeting planned. Depending on the feedback received from the Scientific Committee during the April Plenary meeting, a conference call may have to be organised to address pending issues.

SCIENTIFIC COMMITTEE

Minutes of the 6th meeting of the Working Group on Carvone

Tele-conference, 22 January 2014

(Agreed on 11 March 2014)

Participants

- Working Group Experts:

  Paul Brantom, Karl-Heinz Engel, Bernadette Ossendorp (Chair)
- EFSA:

  SCER Unit (Bernard Bottex, Jean Lou Dorne)

  DATA Unit (Saghir Bashir)

1. Welcome and apologies

The Chair welcomed the participants. The purpose of the conference call was to update Paul on the outcome of the draft opinion discussion with the Scientific Committee, as well as to review with the participants the actions agreed during the last meeting of the working group. Apologies were received from Qasim Chaudhry and Jean-Charles Leblanc.

2. Adoption of agenda

The agenda was adopted as tabled.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[2], EFSA screened the Annual Declaration of interest and the Specific Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

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4. Agreement of the minutes of the 5th working group meeting

The participants adopted the draft minutes of the 5th working group meeting held on 7-8 January 2014 in Parma. The minutes will be published on the EFSA website.

5. Scientific topic for discussion

5.1 Draft opinion on carvone (EFSA-Q-2013-00290)

The participants considered the comments made by the Scientific Committee during the 17 December 2013 SC Plenary meeting to update the draft opinion and reviewed the status of the action points agreed during the last working group meeting.

- 1.1 – previous evaluations of carvone: summarise the EMA CVMP assessment of carvone
- 1.1 – previous evaluations of carvone: rewrite the section on the pesticide EU assessment, clarifying responsibilities and when EFSA entered in the process.
- 2.2 – Legislation on flavourings: section to be updated according to the latest developments
- 3- analysis: update the section on analytical methods will be updated

- 5- Exposure: it will be clarified that all calculations are based on estimations assuming concentrations of carvone in various compartments, and not on measured values
- 5.9 – personal care products: the focus will be on carvone-containing personal care products leading to a possible oral intake, i.e. mouthwash and toothpaste
- 5.10 – estimated exposure to d- and l-carvone from veterinary use will be inserted
- 5.11 – the aggregated exposure: section will be updated based on the latest data received from EFFA and EHIA.

- 6.2.6. – new section will be added to explain which endpoint(s) was/were considered as critical and therefore worth for further BMD analysis

Saghir Bashir reported back on the analysis of the data he started. The statistical significance of the liver and kidney relative weight increase observed at the highest doses (compared to the control groups) was confirmed.

- 6.2.7 – dose response modelling. The section will be redrafted in line with the approach described in the SC guidance on BMD.

- Appendices: only the summary data will be annexed to the opinion. The raw data are presented for the information of the Scientific Committee.

6. Next steps and actions

Members of the working group to perform the above-identified actions by 7 February 2014 at the latest so that the updated opinion can be circulated to the Scientific Committee on 10 February 2014 for discussion.

7. Next meeting

A conference call will be organised on 10 March (from 14.00 to 16.00) and 11 March (from 10.00 to 12.00) to review the possible comments made by the Scientific Committee.

The opinion will then be submitted for possible adoption at the 3-4 April 2014 SC Plenary meeting.

SCIENTIFIC COMMITTEE

Minutes of the 5th meeting of the Working Group on Carvone

Held on 7-8 January 2014, Parma

(Agreed on 22 January 2014)

Participants

- **Working Group Experts:**
  - Qasim Chaudhry, Karl-Heinz Engel, Jean-Charles Leblanc, Bernadette Ossendorp (Chair)
- **EFSA:**
  - SCER Unit (Bernard Bottex, Jean Lou Dorne)

1. Welcome and apologies

The Chair welcomed the participants and explained that the purpose of the meeting was to review the comments made by the Scientific Committee during the 17 December 2013 plenary meeting to update the draft opinion.

Apologies were received from Paul Brantom.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[2], EFSA screened the Annual Declaration of interest and the Specific Declaration of interest) filled in by the experts invited for the present meeting. No conflicts of

[1] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[2] http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf

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

4. Agreement of the minutes of the 4th Working Group meeting held on 21-22 November 2013, Parma

The participants adopted the draft minutes of the 4th working group meeting. The minutes will be published on the EFSA website.

5. Scientific topic for discussion

5.1 Draft opinion on carvone (EFSA-Q-2013-00290)

The participants considered the comments made by the Scientific Committee during the 17 December 2013 SC Plenary meeting to update the draft opinion. A number of follow-up actions were identified during the meeting.

Members of the working group will update their sections, based on the actions identified during the meeting as soon as possible, and if possible before the conference call planned on 22 January 2014.

6. Next meetings

A conference call will be organised on 22 January 2014 from 10:00 to 12:00, to be prolonged if needed from 14:00 to 16:00 (Parma time) for a final check of the opinion.

The draft opinion will then be submitted for discussion to the Scientific Committee at the 18-19 February 2014 Plenary meeting.

A conference call will be organised on 10 March (from 14.00 to 16.00) and 11 March (from 10.00 to 12.00) to review the possible comments made by the Scientific Committee.

The opinion will then be submitted for possible adoption at the 3-4 April 2014 SC Plenary meeting.

SCIENTIFIC COMMITTEE

Minutes of the 4th meeting of the Working Group on Carvone
Held on 21-22 November 2013, Parma
(Agreed on 7 January 2014)

Participants

- **Working Group Experts:**
  - Paul Brantom, Qasim Chaudhry, Karl-Heinz Engel, Jean-Charles Leblanc, Bernadette Ossendorp (Chair)

- **EFSA:**
  - SCER Unit: Bernard Bottex, Jean Lou Dorne
  - DATA Unit : Davide Arcella

1. Welcome and apologies for absence

The Chair welcomed the participants, and explained that the purpose of the meeting was to finalise the first draft of the opinion that will be presented to the Scientific Committee during the Plenary meeting of 17 December 2013.

2. Adoption of agenda

The agenda was adopted without changes.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[2], EFSA screened the Annual Declaration of interest and the Specific

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Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

4. Agreement of the minutes of the 3rd Working Group meeting held on 17-18 October 2013, Parma.

5. Scientific topic for discussion

5.1 Draft opinion on carvone (EFSA-Q-2013-00290)

The participants considered the comments made by the Scientific Committee following the presentation of the opinion's contents by the Chair of the working group during the 13-14 November 2013 SC Plenary meeting:

- the data considered for the assessment will be described in the draft opinion (both the DAR and the NTP data)
- effects on testes and aspermia will be further described and considered in the opinion
- kidney effect: detailed explanation will be provided on why the male effect is not relevant for humans. Still it was noted that something is happening with females that should be discussed in the opinion
- reporting of the BMD analysis: all the tested models and their goodness-of-fit should be presented. The BMD analysis will be reported in line with what is described in the SC guidance on BMD
- exposure: the assessment will consider current use of d- and l-carvone, but also the future expected use of d-carvone as an anti-sprouting agent for food and starch potatoes. The allowed post-harvest use of spearmint oil in organic farming will also be considered for the exposure assessment. The impact on exposure of possible processing factors (e.g. peeling) will be discussed in the opinion.

6. Next steps and actions

The draft sections of the opinion will be provided to the Secretariat by 6 December 2013. The Secretariat will then merge all the contributions and circulate the resulting draft opinion for a final check of the working group by 10 December 2013

7. Next meetings

The following meeting dates were confirmed:

- The working group will meet on 7 and 8 January 2014 in Parma. The meeting will start at 14:00 on the 7th and finish at 16:00 on the 8th.
- A conference call will be organised on 22 January 2014 from 10:00 to 12:00, to be prolonged if needed from 14:00 to 16:00 (Parma time) for a final check of the opinion.

The draft opinion will be submitted for the consideration of the Scientific Committee at the 17 December 2013 Plenary meeting.

SCIENTIFIC COMMITTEE

Minutes of the 3rd meeting of the Working Group on Carvone

Held on 17-18 October 2013, Parma

Agreed on 22 November 2013

Participants

- **WG Experts:**
  - Paul Brantom[1], Karl-Heinz Engel, Jean-Charles Leblanc, Bernadette Ossendorp (Chair)
- **Hearing Experts:**
  - Wout Slob[2], Gerrit Wolterink[2]
- **EFSA:**
  - SCER Unit (Bernard Bottex, Jean Lou Dorne)
  - DCM Unit (Davide Arcella)

1. Welcome and apologies

The Chair welcomed the participants, including the hearing experts Dr. Gerrit Wolterink who was invited to provide clarifications on the toxicological assessment he did on carvone in 2000, and Dr. Wout Slob as an expert on Benchmark Dose modelling. Apologies were received from Qasim Chaudhry.

Working procedures for the working group were clarified. In view of the small size of the group, it was agreed to copy all members of the working group when circulating emails.

2. Adoption of agenda

The agenda was adopted as tabled.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[3] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[4], EFSA screened the Annual Declaration of interest and the Specific

[1] Via conference call
[2] Via conference call for agenda point N°5a
[3] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[4] http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf

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Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

4. Adoption of the minutes of the 2nd working group meeting

The participants reviewed the draft minutes of the 2nd working group meeting held on 27-28 August 2013 in Parma. Additional comments should be provided in writing to the Secretariat by Thursday 24 October at the latest. The minutes will then be considered as adopted and will be published on the EFSA website.

5. Scientific topics for discussion

5.1 Draft opinion on carvone (EFSA-Q-2013-00290)

The draft introduction was discussed.

Nomenclature

The following table will be inserted in the opinion:

EC Number	CAS Number	CIP convention	Fischer nomenclature	Dexter/laevus
218-827-2	2244-16-8	(*S*)-(+)-carvone	L(+)-carvone	d-carvone
229-352-5	6485-40-1	(*R*)-(-)-carvone	D(-)-carvone	l-carvone

It will then be explained that the d-/l-carvone nomenclature will be used throughout the opinion.

a. Toxicology

The participants reviewed the data available, the possible endpoints to be used for the assessment, and discussed the outcome of the dose-response modelling for the various selected endpoints.

b. Exposure:

Limonene

Some of the data collected show that limonene can be metabolised into carvone, i.e. has the potential to contribute to the pool of carvone exposure. The working group looked at further information on this route of exposure.

Pesticide use of carvone

The working group decided to consider the current use of carvone as a pesticide, i.e. authorised as an anti-sprouting substance for seed potatoes. It was noted that carvone is not authorised on ware and starch potatoes.

The working group was informed that caraway oil is authorised for organic farming; Further data on the uses and use levels will be collected.

Carvone as flavouring

Data collected show that carvone is used in almost all food categories. The working group agreed to use the APET model rather than the TAMDI for the exposure calculation.

Following recommendation made during the last working group meeting, the European Flavour Association and the International Organization of the Flavour Industry were contacted and asked for possible updated data on use levels of carvone as flavouring.

Natural occurrence of carvone

A table with occurrence data in various food commodities retrieved from the TNO database was presented.

Exposure to carvone from health care products

The SCCS default formulas for calculating exposure from cosmetic use were considered. Remark was made that the use of the formula is not that straight forward if not having any bioavailability data for dermal exposure.

The source of the method used in the DAR report to assess exposure to carvone from health care products will be checked.

Exposure to carvone from food supplements (alternative medications)

A small paragraph will be inserted in the opinion flagging at this possible source of exposure.

Exposure to carvone via animals fed with carvone-treated potatoes

Reference will be made in the opinion to the previous FEEDAP assessment of FRESTA® F for weaned piglets where no residues could be detected in the meat.

Exposure through breast milk

One study on the differential transfer of dietary flavour compounds into human breast milk showed the presence of a few µg/L of carvone in breast milk after women have ingested 100 mg of d-carvone.

Integrated exposure:

Since occurence data are not available for all sources of exposure, it will not be possible to run the exposure assessment using one single model.

Assessment of l-Carvone

The working group discussed how the opinion should cover the assessment of l-carvone; most of the toxicity data relate to d-carvone, while most of the exposure data relate to “carvone”, not specifying the isomer considered.

The metabolism of carvone appears to be stereoselective; as such it is not possible just to extrapolate the ADI of d-carvone to l-carvone.

6. Next meeting dates

The following meeting dates were confirmed:

- The next meeting of the working group will take place on 21 and 22 November 2013 in Parma, starting at 9.00 on 21 November, and end on 22 November at 13.00.
- The working group will then meet on 7 and 8 January 2014 in Parma. The meeting will start at 14:00 on the 7th and finish at 16:00 on the 8th.
- A conference call will be organised on 22 January 2014 from 10:00 to 12:00, to be prolonged if needed from 14:00 to 16:00 (Parma time) for a final check of the opinion.

The draft opinion will be proposed for possible adoption at the 18-19 February 2014 Plenary

SCIENTIFIC COMMITTEE

Minutes of the 2nd meeting of the Working Group on Carvone

Held on 27-28 August 2013, Parma

Agreed on 17 October 2013

Participants

- **Working Group Experts:**
  - Paul Brantom, Qasim Chaudhry, Karl-Heinz Engel, Bernadette Ossendorp (Chair)
- **Hearing Expert:**
  - Gerrit Wolterink[1]
- **EFSA:**
  - SCER Unit (Bernard Bottex, Jean Lou Dorne)

1. Welcome and apologies

The Chair welcomed the participants, including Dr. Gerrit Wolterink who was invited as a hearing expert to present the toxicological assessment he did on carvone in 2000. Apologies were received from Jean-Charles Leblanc.

2. Adoption of agenda

The agenda was adopted as tabled.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[2] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[3], EFSA screened the Annual Declaration of interest and the Specific Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

[1] Via conference call for agenda point N°4
[2] http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf
[3] http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf

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4. Adoption of the minutes of the 1st working group meeting

The participants reviewed the draft minutes of the 1st working group meeting held on 14 June 2013 via conference call. The minutes were adopted after several modifications. The minutes will be published on the EFSA website.

5. Scientific topics for discussion

5.1 Review of the data collected on carvone

a. Toxicology:

Toxicokinetics (TK):

The working group discussed the possibility to derive chemical-specific adjustment factors, instead of using the standard default value for the uncertainty factor. It should be however further clarified whether the data relate to a single enantiomer or a racemic mixture.

Pharmacodynamics

It was noted that the LD50 for L-carvone is 1.5 to 2 times lower than for D-carvone. It was reported that the two studies from which the LD50 were derived are based on human data.

Metabolism:

Several papers need to be integrated to understand the metabolism of carvone, which is stereo-selective; most of the data relate to D-carvone and it should be explored if the metabolism with L-carvone can also be identified. The working group will focus on what is happening for the rat.

Toxicity:

The first draft assessment report on carvone was created in 2000 and identified a 90-day study on rat as the critical one to derive the NOAEL (30 mg/kg bw). Although the effects observed on kidney turned out to be not relevant in humans, the other observed effects on liver and thymus weight were considered as relevant. No histopathological modification in the liver could be observed. The Secretariat will perform BMD calculations for the relevant effects.

It was noted that in the JECFA assessment of carvone based also on a 90-day study in rats performed by NTP, no similar effects could be observed while testing with higher doses. This NTP study was never published and the link for this study on the NTP website leads to the report of a study made on mice. The Secretariat will contact NTP and check whether the report of the rat study still exists.

Allergenicity

Two studies on allergenicity associated to L-carvone are reported in the REACH-CLH report. The Secretariat will retrieve these studies.

b. Exposure:

Pesticide use of carvone

An active substance can be put on a positive list but still cannot be used for food applications until an MRL has been set. Carvone therefore is currently used for potatoes used as seeds but cannot be used on potatoes intended to be used as food. The intake assessment made in the draft assessment report shows a theoretical MRL of 10 mg/kg but this value is based on rough exposure estimates (all potatoes were treated with carvone and are consumed uncooked and unpeeled)

The working group recommended for the exposure assessment to consider:

- One scenario where only potatoes used as seeds are treated with carvone
- One scenario where potatoes used both for seeds and food applications are treated but processing effects on the residues levels should be taken into account

Carvone as flavouring

The working group discussed a table with use levels of carvone provided by the European Fragrance Industry. These data refer to "carvone" in general and therefore do not allow looking at D-and L- carvone separately. These data were used to calculate to intake assessment: one from a production perspective, using the MSDI approach, the other one from a use level consideration, using the mTAMDI approach. It was noted that the resulting MSDI and mTAMDI values match. The CEF Panel, in its latest guidance document recommends using the APET approach. The APET value is calculated by summing the highest potential dietary exposure within each of the two groups ("Beverages" and "Solid foods"). Here again, the dietary exposure value calculated with this method matches with the two previous ones.

Natural occurrence of carvone

The working group discussed a table with occurrence data in various food commodities retrieved from the TNO database. It seems from these data that the contribution of the natural occurrence to the global exposure to carvone can be considered negligible.

An analysis of the various fields containing carvone, e.g. bread containing caraway seeds will be performed, so that the group gets an idea of the actual concentration of carvone food.

Exposure to carvone from health care products

Exposure to L-carvone will mostly occur from toothpaste use. SCCS will be contacted for the default values they use to calculate exposure. The contribution to the global exposure to carvone is expected to be negligible also in this case.

Exposure to carvone via animals fed with carvone-treated potatoes

Reference will be made in the opinion to a previous FEEDAP assessment where no residues could be detected in the piglet meat. This route of exposure can therefore also be considered as negligible.

Integrated exposure:

It was suggested for the various sources of exposure to use as a first step the models used by the relevant Panels. As a second step, probabilistic modelling (e.g. MCRA model) will be used to compare the data.

5.2 Structure of the opinion

The template for CONTAM opinions will be used. Responsibilities for the various sections were allocated among the members of the working group:

6. Next meeting dates

The following meeting dates were confirmed:

- 17 October (from 9.00) - 18 October 2013 (until 13.00), Parma
- 21 November (from 14.00) - 22 November 2013 (until 13.00), Parma

Tentative if the opinion is not adopted on 17 December 2013:

18 December 2013, from 10.00 to 12h00, eventually to be prolonged from 14.00 to 16.00, conference call.

This timeframe foresees a discussion of the draft opinion during the 14-15 November 2013 Plenary meeting and a possible adoption at the 17 December 2013 Plenary.

SCIENTIFIC COMMITTEE

Minutes of the 1st meeting of the Working Group on Carvone

Conference call, 14 June 2013

Agreed on 27 August 2013

Participants

- **WG Experts:**
  - Paul Brantom, Qasim Chaudhry, Karl-Heinz Engel, Jean-Charles Leblanc, Bernadette Ossendorp (Chair)
- **EFSA:**
  - SCER Unit (Bernard Bottex, Jean Lou Dorne)

1. Welcome and apologies for absence

The Chair welcomed the participants and invited them to introduce briefly their background and expertise. The objective of the meeting was to discuss the terms of reference and the information gathered by the Secretariat on carvone, and to agree on next steps and allocations of tasks to draft the opinion.

2. Adoption of agenda

The agenda was adopted with one minor modification: points 4 and 5 were inverted so that participants are provided with an overview of the background information collected so far before discussing the terms of reference of the mandate.

3. Declarations of interest

In accordance with EFSA's Policy on Independence and Scientific Decision-Making Processes[1] and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests[2], EFSA screened the Annual Declaration of interest and the Specific Declaration of interest) 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 Oral Declaration of interest at the beginning of this meeting.

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4. Terms of reference

As described in the mandate signed by the Executive Director of EFSA, the Scientific Committee is requested to:

- Derive a single ADI for carvone to be used at European level, regardless of the food sector area, and considering all previous evaluations;
- Estimate the overall exposure of European consumers to the carvone resulting from its use as pesticide, food or feed additive, as well as its natural occurrence;
- Quantify the contribution of each source of exposure to the overall exposure of carvone.

5. Scientific topics for discussion

5.1 Background information collected on carvone

Participants were provided by the Secretariat with an overview of the data collected on carvone so far. Working group members provided additional information / clarifications during the presentation.

Identification:

Two enantiomers of carvone:

- (D)-carvone present in *Carum carvi* and *Anethum graveolens*
- (L)-carvone present in *Mentha spicata*

Metabolism:

The metabolism of carvone is stereoselective and species dependent. In humans, carvone is partially excreted as such, or oxidised by CYP2C9/CYP2C19. Pharmacokinetic data in humans are available, showing a big variability among humans, and would allow to derive chemical safety adjustment factors.

It was noted that the global half-life of carvone in blood is 2.5h. The compound therefore does not bioaccumulate and is excreted rapidly in the urine.

Toxicity:

ADI of 0-1 mg/kg bw/d for (D)-carvone was set up by JECFA based on a 90-day study in rats.

Another ADI of 0.025 mg/kg bw/d is proposed in the draft assessment report (DAR) on carvone, based on a different 90 day study in rat;

In both cases, the data on which the other group based its evaluation was not available for the assessment considered.

Once all the original toxicological studies have been collected, the working group will decide on the critical one on which to base the benchmark dose calculation. The working group will have to consider whether it is possible to derive an ADI for (D)-carvone and an ADI for (L)-carvone. It was noted that in most of the studies, a mixture of (D/L)-carvone was used. Should the data not allow to derive enantiomer-specific ADIs, the most conservative ADI will be used for carvone as a whole.

Sources of exposure:

European consumers are exposed to carvone through various sources:

- Carvone (D/L-carvone with a ratio 4:1) is used (particularly in organic farming) as sprout inhibitor / growth regulator
- Exposure to residues of the above-mentioned pesticide could result from the consumption of animals or animal products that were fed with treated potatoes. An EFSA evaluation of FRESTA® F (carvone, limonene and citral) for weaned piglets did not reveal any residue in the blood or in the meat for the maximum recommended dosage and tenfold the maximum dosage.
- Carvone (both (D) and (L)-carvone) is used as a flavouring compound. It was also underlined that limonene is oxidised into carvone and may therefore contribute to the flavouring exposure.
- Natural sources: reference was made by the working group on various data sources: the TNO list (plant composition database), the table on occurrence data in natural sources (FEEDAP opinion), SC working group on botanicals.
- Personal care products

6. Next meeting dates

The following meeting dates were confirmed:

- 27 August (from 14.00) - 28 August 2013 (until 13.00), Parma
- 17 October (from 14.00) - 18 October 2013 (until 13.00), Parma
- 21 November (from 14.00) - 22 November 2013 (until 13.00), Parma

Tentative if the opinion is not adopted on 17 December 2013:

- 18 December 2013, from 10.00 to 12h00, eventually to be prolonged from 14.00 to 16.00, conference call.

This timeframe foresees a discussion of the draft opinion during the 14-15 November 2013 Plenary meeting and a possible adoption at the 17 December 2013 Plenary.