

SCIENTIFIC COMMITTEE

Minutes of the 5th meeting of the Working Group on Botanicals/QPS

Held on 2 September 2013, Amsterdam

(Agreed on 16 October 2013)

Participants

- **Working Group Experts:**

Andrew Chesson (Chair), Birgit Dusemund, Karl-Heinz Engel, Kirsten Pilegaard, Ivonne Rietjens, Vittorio Silano.

- **EFSA:**

Bernard Bottex (SCER Unit)

1. Welcome and apologies

The Chair welcomed the participants. The objective of the meeting was to work further on the opinion and come to draft conclusions that can be presented by the Chair during the next Plenary meeting of the Scientific Committee on 16 and 17 September.

Apologies for absence were received from Qasim Chaudhry. Participants were informed about the resignation of Dr. Luc Delmulle from the working group for personal reasons.

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 Processes¹ and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests², 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>

4. Adoption of the minutes of the 4th working group meeting, 8 July 2013, via conference call

The participants reviewed the draft minutes of the 4th working group meeting held on 8 July 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

Review of the draft opinion ([EFSA-Q-2012-00642](#))

The working group discussed the applicability of the QPS approach for the various situations that can be encountered with a botanical preparation:

- a. Adequate chemical characterisation of the substance(s), no reported adverse effect.
- b. Presence of substance(s) with known structure but unknown toxicity profile
- c. Presence of substance(s) of concern (thresholded or non-thresholded)
- d. Reported adverse effects but no substance(s) of concern identified
- e. Presence of uncharacterised substances

The various following case studies were identified to test the QPS approach:

- *Rosmarinus officinalis*
- *Citrus aurantium*
- *Foeniculum vulgare*
- *Camellia sinensis*
- *Ocimum tenuiflorum*

Two additional case studies will be developed to illustrate the case of a botanical preparation with no substance of concern and no reported adverse effect, and the case of a botanical preparation for which an adverse effect has been reported but the substance responsible for it is unknown, and there is an established history of (safe) use of the botanical preparation.

6. Next steps and meeting dates

The draft content of the opinion and the decision tree will be presented during the next Plenary meeting of the Scientific Committee. Feedback received will then be taken into account to develop a more advanced version of the opinion. The objective is to have the opinion submitted for possible adoption at the November 2013 SC Plenary meeting.

The following meeting dates were confirmed:

- 16 October 2013, from 14.00 to 18.00 – Conference call.

SCIENTIFIC COMMITTEE

Minutes of the 4th meeting of the Working Group on Botanicals/QPS

Conference Call, 8 July 2013

(Agreed on 2 September 2013)

Participants

- **Working Group Experts:**

Andrew Chesson (Chair), Qasim Chaudhry, Birgit Dusemund, Karl-Heinz Engel, Kirsten Pilegaard, Ivonne Rietjens, Vittorio Silano.

- **EFSA:**

Bernard Bottex (SCER Unit), Renata Leuschner (BIOHAZ Unit).

1. Welcome and apologies

The Chair welcomed the participants. Apologies for absence were received from Luc Delmulle. The objective of the meeting was to review progress in drafting the various sections of the opinion and clarify possible encountered difficulties.

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 Processes¹ and the Decision of the Executive Director implementing this Policy regarding Declarations of Interests², 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>

4. Adoption of the minutes of the 3rd working group meeting, held on 28-29 May 2013, Parma

The participants reviewed the draft minutes of the 3rd working group meeting held on 28 and 29 May 2013 in Parma. The minutes were adopted after several modifications. The minutes will be published on the EFSA website.

5. Scientific topics for discussion

Draft opinion on a Qualified Presumption of Safety (QPS) approach for the safety assessment of botanicals and botanical preparations ([EFSA-Q-2012-00642](#))

The working group reviewed the various contributions received and prepared the first draft of the opinion. The decision tree for the QPS assessment was applied to a number of case studies (*Rosmarinus officinalis*, *Citrus aurantium*, *Foeniculum vulgare*, *Camellia sinensis* and *Ocimum tenuiflorum*) and updated according to the discussion during the meeting.

6. Next meeting dates

The following meeting dates were confirmed:

- 2 September 2013, from 9.00 to 17h30 – Amsterdam Schiphol airport.

Parma, 20 June 2013

SCIENTIFIC COMMITTEE

Minutes of the 3rd meeting of the Working Group on Botanicals/QPS

Parma, 28-29 May 2013

(Adopted by the WG on 8 July 2013)

Participants

WG Experts: Andrew Chesson (Chair), Qasim Chaudhry¹, Birgit Dusemund, Karl-Heinz Engel², Kirsten Pilegaard, Ivonne Rietjens, Vittorio Silano

EFSA: Bernard Bottex, Renata Leuschner, Sarah Maria Trattig

1. Welcome and apologies

The Chair welcomed the participants. Apologies for absence were received from Luc Delmulle. The objective of the meeting was to agree on a detailed structure of the opinion.

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 Processes³ and the Decision of the Executive Director implementing this Policy regarding Declarations of Interest⁴, EFSA screened the Annual Declarations of Interest and the Specific Declarations 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 Declarations of Interest at the beginning of this meeting.

¹ Via conference call during the 2nd day

² 2nd day only

³ <http://www.efsa.europa.eu/en/keydocs/docs/independencepolicy.pdf>

⁴ <http://www.efsa.europa.eu/en/keydocs/docs/independencerules.pdf>

4. Adoption of the minutes of the 1st working group meeting, 16 November 2012, Parma

The participants reviewed the draft minutes of the 2nd working group meeting held on 4 and 5 April 2013 in Parma. The minutes were adopted after several modifications. The minutes will be published on the EFSA website.

5. Applicability of a QPS approach to case studies

The working group discussed the applicability of the decision tree proposed during the 2nd working group meeting for the following case studies identified to test the QPS approach:

- *Rosmarinus officinalis*
- *Citrus aurantium*
- *Foeniculum vulgare*
- *Camellia sinensis*
- *Ocimum tenuiflorum*

6. Applicability of *in silico* tools in the QPS approach

The working group, following a presentation from Qasim Chaudhry on *in silico* methods, discussed the possibility and adequacy of inserting this tool in the QPS assessment decision tree. The Scientific Committee of EFSA will also be consulted for advice.

7. Next steps and actions

The examples discussed during this meeting of the working group will be updated based on the meeting discussion and integrated in the first draft of the opinion that will be reviewed during the next meeting.

8. Next meeting dates

The following meeting dates were confirmed:

- 8 July 2013 (10.00 - 12.00, optionally 14.00 - 16.00) – Teleconference
- 2 September 2013, from 9.00 to 17h30 – Amsterdam Schiphol airport.

Parma, 8 April 2013

SCIENTIFIC COMMITTEE

Minutes of the 2nd meeting of the Working Group on Botanicals/QPS

Parma, 4-5 April 2013

(Adopted by the WG on 28 May 2013)

Participants

WG Experts:	Andrew Chesson (Chair), Luc Delmulle, Birgit Dusemund, Karl-Heinz Engel, Kirsten Pilegaard, Ivonne Rietjens ¹ , Vittorio Silano
EFSA:	Bernard Bottex, Renata Leuschner, Sarah Maria Trattig

1. Welcome and apologies

The Chair welcomed the participants. Apologies for absence were received from Qasim Chaudhry.

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.

4. Adoption of the minutes of the 1st working group meeting, 16 November 2012, Parma

The participants reviewed the draft minutes of the 1st working group meeting held on 16 November 2012 in Parma. The minutes were adopted after several modifications. The minutes will be published on the EFSA website.

5. Applicability of a QPS approach to case studies

The working group reviewed five case studies for which the QPS approach was tested:

- *Rosmarinus officinalis*
- *Citrus aurantium*

¹ Via conference call

- *Foeniculum vulgare*
- *Camellia sinensis*
- *Ocimum tenuiflorum*

6. Discussion the applicability of a QPS approach for the safety assessment of botanicals to be evaluated by EFSA

The applicability and usefulness of the QPS approach was discussed; The importance of knowing the chemical composition of the extract considered was underlined, as well as the need for the QPS status to be granted to large enough taxonomic groups.

The working group also discussed the need to consider exposure aspects when defining qualifications related to the QPS status.

7. Next steps and actions

The examples discussed during this meeting of the working group will be updated based on the above discussion

8. Next meeting dates

The following meeting dates were confirmed:

- 28 May 2013 (9.00 - 18.00) - 29 May 2013 (9.00 - 13.00), Physical meeting in Parma
- 8 July 2013 (10.00 - 12.00, optionally 14.00 - 16.00) - Teleconference

SCIENTIFIC COMMITTEE

Minutes of the 1st meeting of the Working Group on Botanicals/QPS Parma, 16 November 2012

(Adopted by the WG on 4 April 2013)

Participants

WG Experts: Andrew Chesson (Chair), Qasim Chaudry¹, Birgit Dusemund, Kirsten Pilegaard, Ivonne Rietjens, Vittorio Silano¹

EFSA: Bernard Bottex, Renata Leuschner, Sarah Maria Trattig

1. Welcome and apologies

The Chair welcomed the participants and started a tour de table to introduce all participants. Apologies for absence were received from Luc Delmulle.

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. For further details on the outcome of the declaration of interests at the beginning of the meeting, please refer to the Annex I.

4. Background and discussions

The participants were presented with previous EFSA work on qualified presumption of safety (QPS) and botanicals:

- Opinion of the Scientific Committee – Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA²
- BIOHAZ - Scientific Opinion on the maintenance of the list of QPS biological agents intentionally added to food and feed³

¹ Participating via teleconference

² see <http://www.efsa.europa.eu/en/efsajournal/pub/587.htm>

³ see <http://www.efsa.europa.eu/en/efsajournal/pub/2497.htm>

- Guidance document of the SCOM - Guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements⁴
- ESCO report - Advice on the EFSA guidance document for the safety assessment of botanicals and botanical preparations intended for use as food supplements, based on real case studies⁵
- EFSA - Compendium of botanicals reported to contain naturally occurring substances of possible concern for human health when used in food and food supplements⁶

The mandate was introduced to the participants. The objective of this working group is to assess whether a Qualified Presumption of Safety approach could be applied for botanicals to be evaluated by EFSA. The QPS approach has facilitated the safety assessment of microorganisms in food and will serve as a model to develop a similar generic system for botanicals.

- **Discussion the applicability of a QPS approach for the safety assessment of botanicals to be evaluated by EFSA**
 - The safety of a large number of botanicals has been requested to be reviewed by EFSA in the following areas:
 - Food Contact Materials, Enzymes, Flavourings and Processing Aids - CEF: (~ 700)
 - Additives and Products or Substances used in Animal Feed - FEEDAP: (~ 400)
 - Food Additives and Nutrient Sources Added To Food – ANS (ongoing evaluation of Ephedra and Yohimbe botanical species)
 - The QPS approach for botanicals foresees the creation of a list, determining the suitability for a presumption of safety of botanicals. The system is of anticipatory, proactive nature rather than reactive to a specific request by an organisation or business operator.
 - The development of a QPS approach (or equivalent) for botanicals would bring an element of harmonisation among EFSA Panels for the Level A (presumption of safety) assessment described in the SC guidance⁴.
- **Discussion of the scope of the EFSA opinion**
 - Given the ubiquitous use of plants in food, feed and other preparations, the definition of the scope of the approach is of major importance when contemplating a generic system for safety assessment. The approach should apply to all plants but this document will not address plants when used as raw materials in food and feed. The opinion will consider botanicals / botanical preparations used in food or feed.
 - The QPS approach should be designed to cover human health and, when relevant, safety of target animals and the environment.

⁴ see <http://www.efsa.europa.eu/en/efsajournal/pub/1249.htm>

⁵ see <http://www.efsa.europa.eu/en/supporting/pub/280r.htm>

⁶ see <http://www.efsa.europa.eu/en/efsajournal/pub/2663.htm>

- The QPS approach aims to identify the highest taxonomical unit (family, genus, species) for which it is possible to conclude on presumption of safety. Consequently any plant belonging to the same taxonomic group would be freed from the need for further safety assessment other than satisfying any qualifications specified.
- Specific aspects concerning the final preparation, e.g. solvent used, excipients would remain independent of any QPS assessment and should comply with relevant legislation.

- **Discussion of the concept of QPS within a certain level of exposure**

- Compounds of concern have been identified for numerous botanicals and are made available in the compendium. For some compounds of concern, it is possible to identify exposure levels under which they are of no concern for human health. The QPS approach includes the option to add a qualification to allow for the QPS status of a botanical.
- It was noted that health-based guidance values set for human health do not stand for animals; therefore qualifications should allow for QPS status “within a certain level of exposure”. It is recognized that the acceptability of such an approach relies mainly on the objective of not significantly increasing exposures beyond the levels linked to the safe history of use”.
- The definition of the level of exposure rather than maximum concentrations for a compound of concern is therefore crucial for the QPS approach for botanicals, since the composition and consumption may vary from one preparation to another.
- Intake assessment should be done on the basis of the intended use and in line with EU “normal” intakes derived together with the Member States.

- **Discussion of the Quantitative Structure-Activity Relationship (QSAR) approach for botanicals**

- The QSAR approach is a complementary tool used in risk assessment aiding the prediction of harmful effects, based on the structure of a compound^{7,8}. Since data gaps are expected for potential toxicological effects for a plethora of plant derived compounds, QSAR will be applied to selected examples (case studies), pending the availability of data on the chemical composition for the respective examples.
- In some cases it may be difficult to identify the active principle responsible for an effect, limiting the applicability of the QSAR approach.

- **Next steps**

The members of the Working Group will for the next meeting try to apply the QPS approach to the following examples:

⁷ See <http://www.efsa.europa.eu/en/supporting/pub/169e.htm>

⁸ See <http://www.efsa.europa.eu/en/supporting/pub/159e.htm>

Botanical name
<i>Camellia sinensis</i>
<i>Citrus aurantium</i>
<i>Foeniculum vulgare</i>
<i>Ocimum tenuiflorum</i>
<i>Rosmarinum officinalis</i>
<i>Botanical species listed in Annex B of the EFSA Compendium (no substance of concern identified, no adverse effect reported) and used as a flavouring additive</i>

The following general principles were agreed upon when going through the different examples:

- Considering the heterogeneous composition of plants, the QPS approach may be used for a specific part of the plant.
- The outcome of this preliminary assessment of the case studies will be a statement on whether the QPS approach is applicable for the respective example or not.
- When performing the assessment, the aim is to cascade down from the highest possible taxonomic level. In case a specific level is found not to be eligible to conclude on the presumption of safety, the underlying reason and problems encountered need to be reported.

5. Next meeting dates

4 April 2013 (9.00 - 18.00) - 5 April 2013 (9.00 - 13.00), Parma

Annex I

INTERESTS AND ACTIONS RESULTING FROM DECLARATIONS DONE AT BEGINNING OF THE MEETING

With regard to this meeting, Prof. Ivonne Rietjens declared her participation in the DG RTD-funded PlantLIBRA project, workpackage 3 on risk assessment (EC project number 245199). 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, the interest above was not deemed to represent a conflict of Interest for the expert concerned.